BIOLOGICAL WARFARE DEFENSE VACCINE RESEARCH AND DEVELOPMENT PROGRAM

HEARING

BEFORE THE

SUBCOMMITTEE ON NATIONAL SECURITY, VETERANS AFFAIRS AND INTERNATIONAL RELATIONS

OF THE

COMMITTEE ON GOVERNMENT REFORM

HOUSE OF REPRESENTATIVES

ONE HUNDRED SEVENTH CONGRESS

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BIOLOGICAL WARFARE DEFENSE VACCINE RESEARCH AND DEVELOPMENT PROGRAM

TUESDAY, OCTOBER 23, 2001

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON NATIONAL SECURITY, VETERANS AFFAIRS AND INTERNATIONAL RELATIONS,
COMMITTEE ON GOVERNMENT REFORM,
Washington, DC.

The subcommittee met, pursuant to notice, at 10 a.m., in the Hubert H. Humphrey Building, Hon. Christopher Shays (chairman of the subcommittee) presiding.

Present: Representatives Shays, Sanders, Putnam, Lantos, Kucinich, Tierney, and Weldon.

Staff present: Lawrence Halloran, staff director and counsel; Robert Newman, Kristine McElroy, and Thomas Costa, professional staff members; Nicholas Palarino, senior policy advisor; Jason Chung, clerk; David Rapallo, minority counsel; and Earley Green, minority assistant clerk.

Mr. SHAYS. I'd like to call this hearing to order, and to welcome our witnesses and our guests.

On behalf of the entire subcommittee I want to thank Secretary Thompson for enabling us to hold this field hearing in the Humphrey Building this morning. Through their unhesitating willingness to help us go forward, despite continued closure of the House Office buildings, the Secretary and his extraordinary staff demonstrating once again as they have so many times since September 11th their determination to conduct the Nation's business despite enormous challenges.

We convene this hearing in an unaccustomed place to discuss an unprecedented need for vaccines to protect against the most unnatural outbreaks of disease imaginable, biological terrorism. In reaching beyond familiar places and customary ways of doing business, we heed the wise counsel of Abraham Lincoln who advised a Nation facing the terror of civil war that, "The dogmas of the quiet past are inadequate to the stormy present. The occasion is piled high with difficulty and we must rise with the occasion. As our case is new, so we must think anew and act anew. We must disenthrall ourselves and then we shall save our country."

Thinking anew requires confronting hard, new realities. There is no absolute immunity to biological attack. Nature's varied and virulent arsenal of pathogens will always outnumber and out-gun our immunological defenses. The prospect of genetically engineered organisms only compounds our peril.

Still many people are justifiably concerned. We seem medically unprepared to deter or defend against attacks using agents anthrax and smallpox, long considered likely terrorists for biological warfare weapons. Almost 2 years ago, this subcommittee found the Department of Defense [DOD], anthrax vaccine immunization program overtly dependent on the sole source manufacturer of a dated, logistically cumbersome medical technology. We recommended the mandatory, force-wide program be scaled back while a new, more easily manufactured and more easily administered vaccine was developed.

Those recommendations were not followed. Today, as the threat of anthrax infection has become a grim reality, we remain without adequate supplies of either the old or a new anthrax vaccine. Witnesses today will address what is being done in the short and long term to provide greater protection against anthrax attacks.

The current stockpile of smallpox vaccine is very limited and very old. A recent exercise entitled, "Dark Winter" modeled the extreme, but nonetheless plausible, scenarios of a multi-site smallpox attack. The exercise vividly demonstrated the critical importance of the right amount of vaccine, at the right place, at the right time to protect the public health. While hopefully still a remote possibility, the potentially catastrophic consequence of a smallpox outbreak have prompted accelerated efforts to develop new vaccines against the highly contagious viral disease.

The anthrax and smallpox vaccine development efforts, and others underway, raise important questions about the future of our national bioterrorism preparedness. How much should current regulatory standards be modified to accommodate development and production of new vaccines? How can the effectiveness of new immunizations be demonstrated when there is no naturally occurring disease to test against? It is not ethical to expose otherwise healthy people to lethal pathogens.

In the event an outbreak occurs before a biological defense is fully approved, how will those receiving the inoculation be informed they are using an investigational product? If the official risk/benefit calculation degenerates into little more than "anything is better than nothing," how will the public be protected from the flood of useless potions and magic anti-terrorism elixirs sure to appear on the Internet?

To address these questions, we are fortunate to be able to call upon the Secretary of Health and Human Services, Tommy Thompson. Representatives from the Department of Defense, the General Accounting Office and the vaccine industry will also give us the benefit of their expertise and insights.

I'd like to welcome again our witnesses, and Secretary Thompson, in a second we'll swear you and hear your testimony. But I would like to call on our members, first our senior member and the ranking member of the International Relations Committee, Mr. Lantos.

[The prepared statement of Hon. Christopher Shays follows:]

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Statement of Rep. Christopher Shays
October 23, 2001

On behalf of the entire Subcommittee, I want to thank Secretary Thompson for permitting us to hold this "field" hearing in the Humphrey Building this morning. Through their unhesitating willingness to help us go forward despite continued closure of the House office buildings, the Secretary and his extraordinary staff demonstrated once again, as they have so many times since September 11th, their determination to conduct the nation's business despite enormous new challenges.

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Thinking anew requires confronting hard new realities. There is no absolute immunity to biological attack. Nature's varied and virulent arsenal of pathogens will always outnumber and outgun our immunological defenses. The prospect of genetically engineered organisms only compounds our peril.

Still, many people are justifiably concerned we seem medically unprepared to deter or defend against attacks using agents – anthrax and smallpox – long considered likely terrorist or biological warfare weapons. Almost two years ago, this Subcommittee found the Department of Defense (DoD) Anthrax Vaccine Immunization Program overly dependent on the sole-source manufacturer of a dated, logistically cumbersome medical technology. We recommended the mandatory, force-wide program be scaled back while a new, more easily manufactured and more easily administered vaccine was developed. Those recommendations were not followed. Today, as the threat of anthrax infection has become a grim reality, we remain without adequate supplies of either the old or a new anthrax vaccine. Witnesses today will address what is being done in the short and long term to provide greater protection against anthrax attacks.

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The anthrax and smallpox vaccine development efforts, and others underway, raise important questions about the future of our national bioterrorism preparedness. How much should current regulatory standards be modified to accommodate development and production of new vaccines? How can the effectiveness of new immunizations be demonstrated when there is no naturally occurring disease to test against? It is not ethical to expose otherwise healthy people to lethal pathogens. In the event an outbreak occurs before a bio-defense vaccine is fully approved, how will those receiving the inoculation be informed they are receiving an investigational product? If the official risk/benefit calculation degenerates into little more than "Anything is better than nothing," how will the public be protected from the flood of useless potions and magic anti-terrorism elixirs sure to appear on the Internet?

To address these questions, we are fortunate to be able to call upon the Secretary of Health and Human Services, Tommy Thompson. Thank you for accepting our invitation to testify; and thank you again for providing the room so all our witnesses could testify today. Representatives from the Department of Defense, the General Accounting Office and the vaccine industry will also give us the benefit of their expertise and insights.

Welcome. We look forward to your testimony.

Mr. LANTOS. Thank you very much, Mr. Chairman.

Let me first commend you for your extraordinary leadership during the course of many years in calling our attention to critical issues facing the American people. If there is any member of people who deserves high praise, it's Christopher Shays. And I'm delighted publicly to pay tribute to you.

Mr. SHAYS. Excuse me. I'm just going to once again encourage people to turn off their phones, if that's what we're hearing right now. Thank you.

Mr. LANTOS. Mr. Chairman, this past weekend I had several of my grandchildren visiting me. I took them to the Roosevelt Memorial. The Roosevelt Memorial has a number of remarkable statements made by our great, late President. The one that has been quoted ad nauseam and ad infinitum, and accurately, is that we have nothing to fear but fear itself. But I found among the quotes at the Roosevelt Memorial another one which is singularly apropos to our hearing this morning. I would like to focus my opening remarks on that other quote.

It basically says that society should not exert itself on behalf of the few who have too much, but should do its utmost to help the many who have too little. Now, this has a very contemporary ring, because earlier this year we dealt with a major tax package. And the one issue which we have not yet approached seriously, following September 11th, is the imperative need in our society to revisit the lopsided tax package that provided enormous benefits for the wealthiest amongst us and very little for the people who are in the low or middle income brackets.

Now, we are looking at everything anew following September 11th. The cliche is that this is a whole new world. But the one thing that has received very little attention is the need to revisit the allocation of the basic resources of this society. I find that in a sense, this became quite obvious when Members of Congress were given far quicker response than employees of the U.S. Postal Service when we faced this particular crisis.

And I would like to suggest to all of us on the congressional panel here, and to all of our colleagues, that since very few of us understand the technical complexities of the issues we deal with in this entire field, our responsibility is to deal with policy issues. Mr. Secretary, yesterday the president of the American Public Health Association criticized the administration's program of $300 million and called for a minimum of a $1 billion in this field.

This is just the beginning of a whole range of gigantic demands on the public purse. Congress has shown itself more than willing to step up to the plate and to vote any amount we need to provide security for the American people. But the time has come to re-examine an initially misguided tax package which now looks nothing short of obscene. The American people will simply not stand for re-examining old ramifications of our lives following September 11th, but not touch a tax package which so unfairly and in a singularly inappropriate fashion, singles out the wealthiest amongst us for benefits.

I would very much hope that you will use your influence within the Cabinet, and you have a great deal of influence, and I can assure you, many of us will use our very limited influence at the

White House to deal with this issue. Because the full range of requirements, way beyond the issue we are discussing this morning, will have to have the support of the American people and it will not have that support unless there is a feeling of fairness in terms of sacrifice, contribution and commitment.

Thank you, Mr. Chairman.

Mr. SHAYS. I thank the gentleman. Mr. Putnam.

And let me thank the gentleman, the vice chairman, who has been very active on this committee and played a major role.

Mr. PUTNAM. Thank you, Mr. Chairman. I want to thank you for the leadership that you have shown in holding a number of hearings on terrorism and on bioterrorism. I welcome our distinguished panel, although I am curious as to what they can contribute to our discussion on tax policy and the previous legislation that the Congress has taken up and passed out with overwhelming support regarding the Nation's tax policy.

We're here to discuss the biological threats that are out there, the status of the threat that this Nation faces and how equipped we are to deal with an outbreak. And that's something that Secretary Thompson has a great deal of experience in and has certainly gained a great deal more in in the previous several weeks.

We have had a number of hearings that have pointed out some of the shortcomings of our Government's preparedness and the limited capacity to produce sufficient quantities of vaccine, and we look forward to hearing the status of that production capacity. We are in a new world, we are in a new situation where together, pulling in the same direction, moving toward the common goal, we can assure the public that we are adequately prepared, that we do have sufficient stockpiles of vaccine, that we have developed adequate protocols of prophylaxis and treatment to meet this new threat. And that's what it is, a new threat.

I think that it will require new resources. It will require reprioritization of what had been the direction that the Government and the budget policies were taking. But I do take some exception to the fact that an accusation has been laid out that the Congress has somehow been treated differently. Every American should know that they have access to the best health care system in the world, headed up by the most dedicated professionals from the CDC level right down to the local hospital.

The background that this committee has developed through a succession of hearings has established that we do have the finest public health system, and there are ways for us to continue to reinforce the effort that those hard working men and women put into this, improving surveillance techniques, improving the dissemination of information, to be on the lookout for things like anthrax and smallpox and botox and bubonic plague. Those are areas where hopefully together we can continue to take this hearing, working hand in hand with the administration, with both sides of the aisle, with both chambers, to move forward to the American people.

With that, I yield back the balance of my time.

Mr. SHAYS. I thank the gentleman.

I would call on Mr. Sanders, who has been with this committee at almost every hearing, and I thank the gentleman.

Mr. SANDERS. And I thank you, Mr. Chairman, for the leadership that you've shown in this whole area, and we welcome the Secretary to be with us today.

As the chairman indicated when he began, we are meeting in an unusual facility for us, at an unusual time and dealing with a subject that I think many of us would have hoped never to have to deal with. But I think as Americans, and as the U.S. Government, it is imperative for us now to take the hardest look that we can at the most nightmarish situations that we can imagine. I think that's what the American people want, and they want us to come up with the best solutions that we can come up with. This is not pleasant, we're not happy about it, but that's something that we have to do.

Let me tell you just very briefly some of the areas that I am concerned about. No. 1, that in fact we have to lay out what the plans may be of fiendish minds who want to destroy Americans. And it's not a pleasant intellectual scenario to get into, but we have to do that. And then we have to determine from a counter-terrorism point of view, how can we prevent the implementation of those plans.

There is in the report information that we have received from the committee indications that a 1993 report by the U.S. Congressional Office of Technology Assessment estimated that between 130,000 and 3 million deaths could follow the aerosolized release of 220 pounds of anthrax spores upwind of the Washington, DC, area. In other words, it is conceivable that somebody flying in a two-seat passenger plane can do horrendous damage to this country. How do we stop that? Very difficult. But questions that we have to got to ask.

In the event that a tragedy occurs, how do we make certain that our people are immunized? If people become sick, what procedures are in place to treat them? The truth of the matter is, and let me disagree with my friend a moment ago who talked about our system being the strongest in the world. In many ways, we are not the strongest health care system in the world. If, God forbid, a disaster struck us today in a large city, do we really believe that millions of people know where to go, in a short period of time to get the medicine that they need?

We have 44 million people who have no health insurance whatsoever. We have tens of millions of people who don't know who their physician is. We do not, in fact, have a strong public health infrastructure in this country, and I think we should use this crisis to build one. So that if, God forbid, there is a tragedy, and if we are able, and I'm sure the Secretary will talk about this, get the medicine and the drugs out to people, to make sure that those drugs are distributed in a way that people can calmly receive them, rather than develop a sense of panic about where they go and so forth.

The other issue that I want to touch upon, Mr. Secretary, and you know that this is an issue of deep concern to me, is the role of the pharmaceutical industry in this whole situation. I am concerned and have been concerned for years that the pharmaceutical industry remains, year after year, the most profitable industry in this country, and that they charge the people in the United States by far the highest prices in the world.

Now, that may be a discussion for another day. But what is appropriate today, if we are dealing with Cipro, and if we are dealing with vaccines, it is incumbent upon our Government to tell the pharmaceutical industry that they can forget about their profits, that we need that product, as much of that product as we need, as quickly as possible, and we need it at a cost that is affordable to individuals and to the U.S. Government.

You are aware, no doubt, that the Canadian Government said to Bayer, I guess, the manufacturer of Cipro, thank you, but no thank you, we will do it generic. My understanding, and you can correct me if I'm wrong, that in India, there is a generic that sells for 3 cents a pill, compared to what an American consumer, the $4 or $5 that an American consumer would pay going to a drug store here. Now, if that is true, there is something to be learned from that. My point here, sir, is that we've got to protect the American people and not pharmaceutical industry profits, and we've got to tell them to come on line and work with us.

So there are a whole lot of issues out there, this is an uncharted territory. I know that you, Mr. Secretary, are working as hard as you can, and we will work with you. And let's see if we can go forward to make sure that the American people have the protection to which they are entitled.

Mr. SHAYS. Thank you. At this time, then we'll get to you, Mr. Secretary, I will recognize the ranking member of the committee, Mr. Kucinich.

Mr. KUCINICH. Thank you very much, Mr. Chairman, for calling this hearing and I appreciate the work that you have done over the many years in calling this country's attention to the challenges that could be presented by biological warfare.

While I intend to be fully involved in the questioning, I'd like to confine my remarks to kind of like the climate that we're in. Last week, Congress left the Capitol under the threat of a biological attack, anthrax. And I think that the American people at this time are looking for stability from their Government, they're looking for certainty from their Government, and we're going to have to do the best we can to provide that.

We have to keep in mind that despite the fact that we have had buildings that have been contaminated, that this is a government of the people, not a government of buildings. And we can decontaminate buildings, we can make sure that buildings are secure. But we can never lose that commitment to government of the people and be cowered by terrorists or panicked, or turn against each other in moments of uncertainty.

The underlying and fundamental unity which created this country is a good place for us to always begin from, whether we're Democrats or Republicans, whether we're Congress or the administration. We have to appeal to that fundamental unity, the thing that holds us together as a Nation, so that there will be no challenge that will be so great that it cannot be met without splintering this Government or this country.

I have confidence that this administration and this Congress will work together to meet the challenge of dealing with biological, chemical or any other kind of terrorism. But we must be resolute in our intention to see that those principles of government of the

people are not shaken to their foundation in moments of uncertainty and even panic. We're a stronger country than that.

So with that in mind, and in that spirit, I look forward to hearing from the witnesses, and look forward to this opportunity to see what we may be able to do to better secure our Nation. Thank you very much.

Mr. SHAYS. Thank you.

You're a patient man, Mr. Secretary, and you are someone who fortunately is where you are. What we will do is just take care of this business, and we'll swear you in, we'll hear from your statement. I just need to ask unanimous consent that all members of the subcommittee be permitted to insert their prepared statements into the record and that the record remain open for 3 days for that purpose.

Without objection, so ordered. And I ask further unanimous consent that all witnesses be permitted to insert an opening statement into the record, and that the record remain open for 3 days for that purpose.

Mr. Secretary, with you is Dr. Anthony Fauci from NIH and Dr. Scott Lilibridge, Special Assistant for Bioterrorism from your office, I believe. We'll ask all three of you to stand and we'll swear you in and then we'll hear your statement. Thank you.

[Witnesses sworn.]

Mr. SHAYS. Mr. Secretary, thank you for honoring us with your presence. You have as much time as you'd like.

STATEMENT OF TOMMY G. THOMPSON, SECRETARY, DEPARTMENT OF HEALTH AND HUMAN SERVICES

Secretary THOMPSON. Thank you very much, Chairman Shays. And let me echo what other members of the committee have already said, congratulations and thank you for your leadership in this area. It's very much appreciated by me personally, and I know by the Nation, and I thank you.

I also want to thank Congressmen Kucinich and Sanders and Tom Lantos and Adam Putnam and appreciate your dedication. I appreciated all of your opening statements and I hope to respond to most of the things that have already been announced by the members. I thank you very much for being here.

Thank you for inviting me to join you today, and thank you for coming down from the Hill to the HHS building. I will try to make you feel at home.

The President and the entire administration are committed to preventing bioterrorism. Our rapid and effective reports and efforts on September 11th and the days immediately following have certainly demonstrated that commitment. Even before then, I had been working vigorously with Dr. Scott Lilibridge, who's the gentleman on my right, one of the Nation's leading experts on bioterrorism. I asked him to join my team and come up from CDC in Atlanta and have his office right next to my office on the sixth floor. Since June, he has become my special assistant for national security and bioterrorism on domestic preparedness.

On my left is Anthony Fauci, who is of course the Director of NIH of Allergy and Infectious Diseases, and I believe, the foremost

scientist in the world on vaccines. I believe he is eminently qualified to answer any and all questions dealing with that subject.

That's characteristic of the seriousness with which the President of the United States and this administration have since taking office and taking the need for preparedness. That ability to respond has been tested on September 11th and more recently with the current anthrax investigations. Let me emphasize that we have worked together with our partners across all levels of Government, from the Federal Bureau of Investigation to the U.S. Postal Service, from local hospitals to county governments, to address these more recent terrorist events.

And soon after the first case of anthrax exposure in Florida, the Department of Health and Human Services, through the CDC, alerted all public health departments in the country to be on the lookout for anthrax-like symptoms, including those associated with inhalation and cutaneous.

As you know, anthrax is not contagious. Contracting inhalation anthrax, for example, is fundamentally different from exposure to the agent. You would have to inhale 8,000 to 10,000 spores of anthrax into your lungs before actually coming down with the disease. So simply having anthrax spores in one's nose does not mean that you are infected with anthrax.

The drug Ciprofloxin, commonly known by its brand name, Cipro, is effective in the treatment of inhalation anthrax, even after infection. And Representative Sanders, I want you to know that I made that crystal clear to Bayer, that we will not accept the price that they offered, and we will be negotiating this afternoon. I hope you will be satisfied with the outcome.

We have taken and continue to take every precaution, and we have made Cipro available to the widest number of people suspected of being exposed to inhalation anthrax. But other drugs, such as Doxycycline and penicillin have been approved by FDA as treatments for anthrax, and they're generic. The FDA's approval will include instructions on what dose to use and how long to treat the inhalation form of anthrax.

The CDC has asked the local hospitals in and around the Nation's Capital pay particular attention to any suspicious respiratory or skin infections. We at the Department have been monitoring hospitals in the area, and are closely monitoring the cases of two postal workers who are infected with inhalation anthrax in the District of Columbia. We're all deeply saddened by the deaths of two local postal employees whose deaths have been linked to anthrax. Our thoughts and prayers are with their families.

And throughout the past month, the CDC and local public health departments have been working hard to trace back the source of the anthrax tainted letters that have been received in this country. They've used the best science to follow the trail of these letters, and they've used the best science to assess the risk of anthrax exposure to employees, both at the work places where the letters were received and at the postal facilities where the letters pass through.

Public health officials are relying heavily on science as they track these letters, identify those who may have been exposed and determine a course of treatment. These efforts were evident in the Flor-

ida and New York cases, where the letters were identified and those who may have been exposed were tested and treated. The CDC has done a good job of finding the letters in question and getting treatment to those at risk. The work of the CDC has likely saved many from serious illness and death.

We have good science. But it is also, ladies and gentlemen, an evolving science. Remember, we have never had cases of anthrax attacks in this manner before. It is a new challenge that we are all facing. We also need to get ahead of the science. We will be even more, gentlemen, aggressive in securing the safety of our postal workers who may have been exposed to a tainted letter. CDC, the Union and the Postal authorities are meeting this afternoon in order to find ways to better secure the safety of all employees.

Therefore, I am making it clear today to this committee and to the American public, the Centers for Disease Control, that when a case of anthrax does emerge, we will immediately move in at any and all postal facilities that might have handled that piece of mail. We will build a scientific link between the post office of the postmark and the recipient of the letter.

In other words, we'll not only immediately begin testing and treatment at the site where the letter was received, but simultaneously begin testing and treatment at all postal facilities through which that letter may have passed. And we will make medicine immediately available to those employees who may have been at risk of exposure. We have plenty of antibiotics to treat anthrax, and we're going to err on the side of caution in making sure people are protected.

I ask for the cooperation and partnership of local public health departments in this endeavor. We're also going to lend the U.S. Postal Service our scientific expertise in developing ways to protect postal workers as they sort and deliver the mail, as well as what technology might help in making mail rooms more safe. We've been assisting the Postal Service from the onset, and we're going to continue to make our resources and expertise available to them. We're having a meeting this afternoon to finalize and be able to improve those terms.

Postal workers have a tough job. It's a job that becomes even tougher in some parts of the country. But we're going to ease their burden by going to the greatest lengths to make sure that their health is protected. If we even remotely suspect that an anthrax tainted letter may have passed through a facility, we're going to get there, test the facility and make the appropriate treatment available to those who may have been exposed. We're going to act quickly and if need be, let the science catch up to our actions. If it turns out postal workers did not come in contact with anthrax spores, we can always take them off the antibiotics. Never has our Nation's public health surveillance been more important. And the dedicated public servants in the Department of Health and Human Services as well as the public health officials in all our local communities are committed to being even more thoroughly prepared to respond tomorrow than we are today.

And I know, I know some critics are charging that our public health system is not prepared to respond to a major bioterrorism attack. And I know that some State and local labs are feeling over-

whelmed right now as they respond to people's natural fears about what might be waiting in their mail. And I understand that our local first responders are also feeling overburdened. But the response from State and local authorities to each and every threat is continuing and will continue. And we should be proud of how well everybody has responded to events that have broken our hearts even as they have steeled our resolve.

But we must continue our efforts to be better prepared for future events. So in an effort to ensure the Department is fully prepared and better coordinated, I recently announced the creation of a bioterrorism advisory committee in my office. And Dr. D.A. Henderson, who certainly is renowned for his role in eradicating smallpox, heads that committee. Dr. Henderson and his staff will provide seasoned advice to the Department on all bioterrorism activities including efforts to improve State and local preparedness.

And just this last week, President Bush requested an additional $1.5 billion to strengthen our ability to prevent and respond to a bioterrorism attack. Of the total funds requested, two-thirds are being designated for the production of vaccines and antibiotics. In addition, the President has requested $300 million for improving State and local readiness, which specifically includes $122 million for training communities in distribution of the medicines during an emergency, Representative Sanders. We must accelerate the production of vaccines and antibiotics. And we must invest in essential programs to ensure the speedy and orderly distribution of antibiotics and other supplies in the event of a major bioterrorism event.

The President's request includes $643 million to expand the national pharmaceutical stockpile and $509 million to speed the purchase of 300 million doses of smallpox. And with these resources, HHS will expand its program capabilities to respond to an all hazardous event.

As you all know, there are currently eight Push Packs, each consisting of 50 tons of medical supplies, available as part of the stockpile. Each one includes no less than 84 separate types of supplies, things like antibiotics, needles and IVs, a tablet counting machine and oxygen masks. And each Push Pack provides a full course of antibiotics and other medical supplies, and is able to be shipped to an area within 12 hours to help State and local response efforts. We were able to deliver one Push Pack into New York City on September 11th within 7 hours.

These Push Packs have enough drugs to treat 2 million individuals for inhalation anthrax following exposure. I have directed that the stockpile development should be increased for inhalation anthrax so that 12 million persons can be treated. The CDC will reach that level of response within the next 12 months.

I also want to point out the President signed an Executive order yesterday urging us to go ahead quickly on this program. With the additional resources, we will also add 4 more Push Packages to a total of 600 tons of medical supplies from the current 8, and have them strategically located across the country, making more emergency supplies available and augmenting our existing supplies.

The President and my Department are also committed to the development and the approval of new vaccines and therapies. The

CDC, the Food and Drug Administration and the National Institutes of Health, all agencies within HHS, are collaborating with the Defense Department and other agencies to support and encourage research to address the scientific issues related to bioterrorism. The capability to detect and counter bioterrorism depends to a significant degree on the state of relevant medical science. Our continuing research agenda, in collaboration with CDC, FDA, NIH and DOD is critical to our overall preparedness.

So let me outline several other areas that our budget requests. The President is calling for $88 million to expand our capacity to respond to bioterrorism incidents, including $20 million for the CDC's rapid response and advanced technology and specialty labs, which provide quick identification of the suspected agents and the technical assistance to State labs. Also included in this amount as $20 million to support additional expert epidemiology teams that can be sent to States and cities to help them respond quickly to infectious disease outbreaks and other public health risks.

And let me reiterate my conviction, personally, that every State should have at least one federally funded epidemiologist who has graduated from the Epidemic Intelligence Service training program, like Scott Lilibridge has. Every State health department, I believe, should have one.

The President is also asking for $50 million to strengthen the metropolitan medical response system, to increase the number of large cities that are able to fully develop their MMRS units. It is imperative that we work closely with cities to ensure that their MMRS units have the proper equipment and training, increasing that from 97 to 122.

We're also providing $50 million to assist hospitals and emergency departments in preparing for and responding to incidents requiring mass immunizations and treatment. And we're providing $10 million to augment State and local preparedness by providing training to State health departments on bioterrorism as well as emergency response.

The President is also requesting $40 million to support early detection surveillance to identify potential bioterrorism agents which includes Web-based disease notification to the health community nationwide. This amount will provide for the expansion of our Health Alert Network, more commonly referred to as HAN, which helps early detection of disease to 75 percent of the Nation's 3,000 counties. I wish and hope to have all counties connected in the coming years.

We're providing $15 million to support the increased capacity in no less than 78 laboratories in 45 States. This funding will enhance our ability to identify and detect all critical biological agents, and we're implementing a new hospital preparedness effort to ensure that our health facilities have the equipment and training they need to respond to mass casualty incidents.

Finally, as to food safety, the President is also requesting $61 million to enhance the frequency and the quality of imported food inspections, and to modernize the import data system to enable us to detect tainted food. This funding will also provide for 410 new FDA inspectors to help ensure that our food is better protected.

The administration has sent to Congress legislation to strength our ability to protect the Nation's food supply. This measure will require prior notice of imported food shipments, enhancing our ability to inspect food, allowing for detention of food suspected of being tainted, and providing flexibility for the FDA to approve drugs and other treatments for dealing with illness resulting from biological attacks.

Mr. Chairman, let me conclude by noting that despite the events of recent days, every American must and should continue to live their lives, working, spending time with family, having a meal out or shopping at the local mall. And they should be able to do that with confidence.

American citizens can be sure that their government agencies, local, State and Federal, are ready to respond to biological warfare and bioterrorism quickly and effectively throughout the country. None of us enjoys contemplating bioterrorism. But as responsible public servants, doing so is a matter of fulfilling the public's trust in us. And under the leadership of President Bush, we're taking all the steps necessary to keep america safe in an era when biological and chemical attacks are as possible as they are unthinkable.

I want to thank you, Mr. Chairman, for letting me speak about this matter of critical importance. And now I'm glad to answer your questions.

[The prepared statement of Secretary Thompson follows:]

Testimony
Before the Committee on Government Reform
Subcommittee on National Security, Veterans Affairs and International Relations
United States House of Representatives

Civilian Preparedness for Biological Warfare and Terrorism: HHS Readiness and Role in Vaccine Research and Development

Statement of
Tommy G. Thompson
Secretary,
Department of Health and Human Services

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Mr. Chairman and Members of the Subcommittee, thank you for inviting me here today. The Department of Health and Human Services (HHS) welcomes your interest in our efforts to respond to terrorist events, including uses of biological weapons against the civilian population. To that end, I am happy to discuss HHS's readiness to protect the American people from acts of biological terrorism and our role in vaccine research and development.

HHS READINESS TO RESPOND TO MASS CASUALTY EVENTS

Although the Department of Defense (DOD) has developed defenses for biological warfare, there are additional concerns that need to be addressed to provide an adequate civilian defense from a bioterrorist attack. The potential list of microbial pathogens that threaten civilian populations is larger than that of classical biological warfare threats. HHS's identification of the major bioterrorism threat agents – a list developed in collaboration with experts in medicine and public health, law enforcement, and national security – is included as an Appendix to this testimony. Moreover, the populations to be protected are different from those generally involved in combat situations because the civilian community includes people of all ages and health status.

As you know, local and state governments bear much of the initial burden and responsibility for providing an effective response by medical and public health professionals to a terrorist attack on the civilian population. If the disease outbreak reaches any significant magnitude, however, local resources will be overwhelmed, and the federal government will be required to provide protective and responsive measures for the affected populations. HHS is working on a number of fronts to assist our partners at the state and local level, including local

hospitals and medical practitioners, to deal with the effects of biological, chemical, and other terrorist acts.

Metropolitan Medical Response System

Since Fiscal Year 1995, for example, HHS through its Office of Emergency Preparedness (OEP) has been developing local Metropolitan Medical Response Systems (MMRS). Through contractual relationships, the MMRS uses existing emergency response systems -- emergency management, medical and mental health providers, public health departments, law enforcement, fire departments, EMS and the National Guard -- to provide an integrated, unified response to a mass casualty event. As of September 30, 2001, OEP has contracted with 97 municipalities to develop MMRSs. During FY 2002, we intend to invest $20 million in 25 additional cities (for a total of 122) for bioterrorism-related planning through the MMRS and to help them improve their medical response capabilities. MMRS contracts require the development of local capability for:

- Early recognition - to be able to alert local, state, and federal public health officials of potential problems;
- Mass patient care -- including the establishment of auxiliary, temporary treatment facilities or procedures for the movement of overflow patients to other geographic areas for care;
- Local medical staff trained to recognize disease symptoms so that they can initiate proper treatment;

- In the case of a bioterrorist event, mass immunization or prophylactic drug treatment for groups known to be exposed, groups that may have been exposed, and populations not already exposed but at risk for exposure from secondary transmission and/or a contaminated environment;
- Acceptance and distribution of material from the National Pharmaceutical Stockpile;
- Mass fatality management to provide respectful and safe disposition of the deceased, including animals; and
- Infection control, including assessment of the extent of contamination to the environment and identification of risk management steps to assure safe re-entry of the potentially contaminated areas.

National Disaster Medical System (NDMS)

As HHS's action agent for responding to requests for assistance and resources, OEP also manages the National Disaster Medical System (NDMS), which was established in partnership with DOD, the Department of Veterans Affairs (VA), the Federal Emergency Management Agency (FEMA), and the Public Health Service Commissioned Corps Readiness Force. The NDMS can be called into action, depending upon the severity of the event, to assist in providing needed services to ensure the continued health and well being of disaster victims..

The National Disaster Medical System is a group of more than 7,000 volunteer health and support professionals who can be deployed anywhere in the country to assist communities in which local response systems are overwhelmed or incapacitated. Organized into 44 Disaster

Medical Assistance Teams, these volunteers would provide on-site medical triage, patient care and transportation to medical facilities. Four National Medical Response Teams (NMRTs), which travel with their own caches of pharmaceuticals, have capabilities to detect illness-causing agents, decontaminate victims, provide medical care and remove victims from the scene. Three of the four NMRTs can be mobilized and deployed anywhere in the nation; the fourth is permanently stationed in the Washington, D.C. area. The NDMS also includes Disaster Mortuary Operations Response Teams that handle the disposition of the remains of victims of major disasters, as well as provide for victim identification and assistance to their families.

NDMS response teams can arrive in an area to supplement local responders within 12 hours of a request. The system capability includes providing in-hospital care for up to 100,000 victims. Other activities that OEP has undertaken to help states and local communities develop their preparedness for mass casualties include but are not limited to:

- Development of competency standards for physicians, nurses and paramedics that focus on the emergency care and definitive treatment of mass casualties from nuclear, biological or chemical incidents;
- Guidelines for hospital mass casualty procedures that focus on in-hospital decontamination and medical practices for mass contaminated patients who arrive in hospital emergency rooms; and
- Mass casualty treatment protocol reviews/updates that will provide clinical guidelines for the treatment of patients exposed to a biological or chemical weapon of mass destruction.

Pharmaceutical Stockpiles

The Department of Veterans Affairs is one of the largest purchasers of pharmaceuticals and medical supplies in the world. Capitalizing on this buying power, HHS and VA have entered into an agreement under which the VA manages and stores specialized pharmaceutical caches for OEP's National Medical Response Teams. The VA has purchased many of the items in the pharmaceutical stockpile. The VA is also responsible for maintaining the inventory, ensuring its security, and rotating the stock to ensure that the caches are ready for deployment with the specialized National Medical Response Teams.

HHS has also developed the National Pharmaceutical Stockpile Program (NPS) into a major national security asset. The purpose of the NPS is to be able to rapidly respond to a domestic biological or chemical terrorist event with antibiotics, antidotes, vaccines and medical materiel to help save lives and prevent further spread of disease resulting from the terrorist threat agent. Operated by HHS's Centers for Disease Control and Prevention (CDC), the NPS Program would provide an initial, broad-based response within 12 hours of the federal authorization to deploy, followed by a prompt and more targeted response as dictated by the specific nature of the biological or chemical agent that is used.

One of the NPS "12-hour Push Packages" was brought to operational status on September 11th. CDC delivered a 12-hour Push Package of pharmaceuticals and medical supplies by ground, vendor managed inventory by air, and a technical advisory team in New York City, all within 7 hours of my order to deploy. Three out of the four non-military aircraft in United States

airspace on the night of September 11th were carrying National Pharmaceutical Stockpile assets and personnel to New York City.

The Stockpile Program was developed as a supplementary response asset mainly to address biological and chemical terrorism. But following the events of September 11th, the program is now being expanded for response to an all-hazards event. The Stockpile presently is able to provide a full course of anthrax post-exposure prophylaxis to more than 2 million persons. I have directed that the Stockpile development should be accelerated to provide anthrax prophylaxis to 12 million persons, and CDC will reach that level of response within the next 12 months. We will also add four more push packs to the eight already located across the country, making more emergency supplies available and augmenting our existing supplies of 400 tons by another 200 tons.

But we must accelerate the production of vaccines and antibiotics and invest in essential programs to ensure the speedy and orderly distribution of antibiotics and other supplies in the event of a biological event. That is why the President has called for an additional $1.5 billion in federal funding for those areas most critical to our ability to respond to bioterrorist threats. His proposal includes include $643 million to expand the National Pharmaceutical Stockpile and $509 million to speed the development and purchase of smallpox vaccine.

HHS ROLE IN VACCINE RESEARCH AND DEVELOPMENT

With the support of Congress, the President has implemented a government-wide emergency response package to help deal with the tragic events of September 11th. This

complements efforts already underway to prepare our nation against such heinous attacks, including threats of bioterrorism. For example, CDC, the Food and Drug Administration (FDA), and the National Institutes of Health (NIH), all within HHS, are collaborating with the DOD and other agencies to support and encourage research to address scientific issues related to bioterrorism. The capability to detect and counter bioterrorism depends to a substantial degree on the state of relevant medical science. In some cases, new vaccines, antitoxins, or innovative drug treatments need to be developed, manufactured (or produced), and/or stocked. Moreover, we need to learn more about the pathogenesis and epidemiology of the infectious diseases that do not affect the U.S. population currently. We have only limited knowledge about how artificial methods of dispersion may affect the infection rate, virulence, or impact of these biological agents. HHS's continuing, collaborative, research agenda at CDC, FDA, NIH, and with DOD, is critical to overall preparedness.

Let me briefly outline the vital role that HHS agencies, particularly the FDA and NIH, play in our Nation's research and development agenda for vaccines.

Food and Drug Administration

Even before the events of September 11, HHS's Food and Drug Administration actively cooperated with DOD in the operation of DOD's vaccine development program and the maintenance of their stockpile program. Any vaccine development, whether by DOD or private industry, must be in accordance with FDA requirements that ensure the safety, effectiveness and manufacturing quality of the finished product. FDA provides assistance to DOD and others

regarding the studies required to develop new vaccines, as well as assistance during all phases of development. FDA also works with DOD's office that screens new and unusual ideas for development of products to treat diseases and develop diagnostic tools.

Within FDA, the Center for Biologics Evaluation and Research (CBER) reviews biological products, including vaccines, products derived from human blood, and many products produced by recent advances in biotechnology. The scope of CBER's regulatory responsibility extends to both approved (licensed) products and investigational products (unlicensed products). CBER is responsible for evaluating the safety, purity, and potency of these biological products. Bio-warfare defense vaccines undergo the same CBER review process as for all other vaccines and biologic products.

FDA will work with potential sponsors of experimental therapies, such as vaccines, at all stages of the product development process in order to stimulate scientific interchange and clarify FDA regulatory requirements. From a regulatory perspective, there are four stages in vaccine development:

1. The pre-Investigational New Drug (IND) stage (before the product is used in people);
2. The IND stage (where human use occurs under well-defined study conditions);
3. The license application stage for vaccines (where FDA reviews the results of the clinical studies and the manufacturing process, facilities and equipment); and,
4. The post-licensure stage (surveillance following approval of the product for marketing).

Under statutory authority, a sponsor of a new vaccine must submit an IND prior to initiating clinical trials. FDA determines within 30 calendar days from receipt of an IND

whether it is appropriate for the IND to proceed or, if necessary, to place an IND on clinical hold, in order to protect the safety of human subjects. This is a difficult task for novel therapies with relatively unknown risks. IN emergency situations, FDA provides a more rapid review. FDA may approve immediate emergency use of an investigational product, in advance of an IND submission, in cases where FDA has ordinarily previously reviewed the product information.

In the IND, the sponsor describes the composition, source, and method of manufacture of the product and the methods used in testing its safety, purity, and potency; provides a summary of all laboratory and pre-clinical animal testing performed; and provides a description of the proposed clinical study and the names and qualifications of each clinical investigator.

The IND process generally is described as having three phases prior to product approval. However, the distinctions between these phases are not absolute. Phase 1 trials are focused on basic safety. For vaccines, Phase 1 trials also usually evaluate the immune response elicited by the vaccine. These trials are usually small - generally between 20 and 100 subjects - and they frequently are done in healthy "normal volunteers" and may last just several months. Phase 2 trials often include several hundred subjects, are often randomized, and last anywhere from several months to several years. These trials usually include individuals who are at high risk for the infectious disease of interest. Unless severe reactions or a lack of effectiveness surface during the first two phases, the sponsor may decide to perform one or more Phase 3 studies that can include from several thousand to tens of thousands people. These Phase 3 trials are intended to provide a definitive measure of effectiveness, as well as continue the evaluation of the product's safety. The size of the efficacy trial will depend upon the expected incidence of disease

that the vaccine is intended to prevent. If, at the end of Phase 3 trials, the manufacturer believes there are adequate data to show that the vaccine is safe and effective for its intended use, the manufacturer submits a license application to the Agency.

A sponsor of a vaccine under review must also provide adequate product labeling to allow health care providers to understand the vaccine's proper use, including its potential benefits and risks, to communicate with patients, and to safely deliver the vaccine to the public.

When all of the clinical, chemistry, pre-approval inspection, manufacturing, labeling and other issues have been adequately resolved, FDA will approve the application. Licensing a new vaccine is only one stage of FDA's oversight of vaccine safety. Following issuance of the license, there is continued post-marketing surveillance of the product by monitoring adverse events through the Vaccine Adverse Event Reporting System. Subsequent to the issuance to the license, FDA also monitors the manufacturer's production activities through FDA inspections to determine the manufacturer's compliance with good manufacturing practices (GMP) regulations. Because of the complex manufacturing processes for most biological products, manufacturers generally must submit samples of each licensed vaccine lot, along with manufacturing testing results, to FDA for review and permission to release the lot for distribution.

National Institutes of Health

The NIH bioterrorism research program, spearheaded by the National Institute of Allergy and Infectious Diseases, includes both short- and long-term research targeted at the design, development, evaluation and approval of diagnostics, therapies and vaccines needed to control

infections caused by microbes with potential for use as biological weapons. Specifically, this research includes the development of:

- Rapid, accurate diagnostics for natural and bioengineered microbes;
- Effective antimicrobial medicines to treat those infected;
- Protective vaccines for those at risk of exposure;
- Basic research to provide the essential underpinnings for other research areas; and
- Genome sequence research on potential bioterrorism agents. (The results of this, coupled with other biochemical and microbiological information, are expected to facilitate the development of diagnostics, therapies and vaccines.)

The National Institute of Allergy and Infectious Diseases efforts have primarily focused on the bioterrorist threats posed by anthrax and smallpox, and many of these efforts are carried out in collaboration with other Federal agencies.

NIAID formed a Working Group on Anthrax Vaccines (WGAV) in 1998 to develop and test a new vaccine that could be used in response to a bioterrorist event. Such a vaccine must be capable of generating protective immunity against inhalation spores within a relatively short period of time after 1-2 immunizing doses. Through an Inter-Agency Agreement, NIAID is collaborating with the Department of Defense's U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) on a research plan to develop a new vaccine based on the use of recombinant protective antigen vaccine (rPA) to protect all ages of the American public, including military personnel. In preparation for Phase 1 clinical trials of rPA vaccines, NIH is working with CDC, FDA and DoD to refine standard serological tests to assess the effectiveness

of anthrax vaccines. These tests would enable comparison of new rPA vaccines to the currently licensed anthrax (or AVA) vaccine. If the new vaccine is capable of generating a rapid immune response, it may provide a quick transition to protective immunity to those individuals undergoing treatment with antibiotics due to an anthrax exposure.

The NIAID also has expanded the national research capacity substantially over the past few years on those bioterrorist threat agents of greatest concern. First, NIAID has solicited from the scientific community research proposals on anthrax and other bacterial pathogens, in an effort to further encourage research that may lead to better means of diagnosis, prevention, and treatment.

Second, NIAID recently awarded administrative supplements to several active research grants to further studies on how anthrax causes disease, which could expedite the development and implementation of novel, more effective therapeutic intervention strategies. NIAID also anticipates funding several new research proposals on the molecular mechanisms involved in the germination of anthrax spores *in vivo*; such work may provide the basis for a novel and very promising post-attack strategy, one that would be more acceptable than the widespread use of antimicrobial drugs which are not specific for anthrax and, when given to large groups of exposed individuals, may promote the development of antibiotic resistant strains of other bacteria.

Through an Inter-Agency Agreement with the Office of Naval Research, NIAID has provided funding to help complete work on sequencing the DNA of the chromosome of anthrax; additional funds were also provided by the Department of Energy for this purpose. The

information derived from this genome-sequencing project should be of great value in developing rapid diagnostic tests, as well as new vaccines and antibiotics therapies against mutant strains of anthrax.

NIAID research on smallpox focuses on extending existing vaccine stocks to increase the number of available doses, developing new vaccines and treatments, as well as diagnostic tools to detect the disease quickly. Although a worldwide immunization program eradicated smallpox disease decades ago, small quantities of smallpox virus still exists under guarded conditions at CDC and in Russia, but several rogue nations may have samples. NIAID, in collaboration with DOD, CDC, and the Department of Energy, funds increased research to:

- Develop and evaluate at least three antiviral drugs with preclinical activity against smallpox and vaccinia viruses and acceptable clinical safety;
- Extend the usefulness of the currently available, older vaccine by doing human studies to see if we can "stretch" available stocks by diluting it;
- Help develop a safe, sterile smallpox vaccine grown in cell cultures using modern technology;
- Explore development of a vaccine that can be used in all segments of the civilian population (i.e., the immune-suppressed, pregnant mothers, etc.); and
- Increase our knowledge of the genome of smallpox and related viruses.

Currently, NIAID is preparing to launch a Phase 2 clinical trial to further evaluate the effectiveness of different strengths of vaccine in order to possibly expand the use of the limited

smallpox vaccine supply; CDC and FDA have cooperated to ensure that the NIH study is carried out as expeditiously as possible.

In addition, NIAID and DOD's Defense Advanced Research Projects Agency (DARPA) have funded a collaborative effort involving those two agencies along with four academic centers, the CDC, USAMRIID, and the American Type Culture Collection that will focus on designing and implementing an "Orthopoxvirus Genomics and Bioinformatics Resource Center." This Center will conduct sequence and functional comparisons of genes to provide insights for the selection of targets for the design of antiviral and vaccine strategies. The Center will design and maintain relational databases to store, display, annotate and query genome sequences, structural information, phenotypic data and bibliographic information. Part of the effort will include development of and maintenance of a "Poxvirus Bioinformatics Resource Center" website to facilitate the availability of this data for other researchers.

Conclusion

Mr. Chairman, let me again emphasize that the Administration is taking aggressive steps to make sure that our country is well protected from bioterrorism. Moreover, the government – at all levels – is responding to bioterrorist threats, and responding well. We should be vigilant and cautious, but should not let terrorists frighten us unduly. Do not let them scare you into not living your life. That would help our enemies achieve what they are trying to do – terrorize American citizens.

Contemplating bioterrorism is unpleasant, but it is imperative. Under the leadership of President Bush, we are taking all the steps necessary to keep America safe in an era when biological and chemical attacks are as possible as they are unthinkable.

Thank you, Mr. Chairman, for letting me speak about this matter of critical importance. I will be happy to answer any questions which you or members of the Subcommittee may have.

APPENDIX
CRITICAL BIOLOGICAL AGENTS

The U.S. Public Health system and primary healthcare providers must be prepared to address varied biological agents, including pathogens that are rarely seen in the United States. The critical agents are listed below in priority order:

Category A

High priority agents include organisms that pose a risk to national security because they can be easily disseminated or transmitted person-to-person; cause high mortality, with potential for major public health impact; might cause public panic and social disruption; and require special action for public health preparedness.

Category A Agents:

- variola major (smallpox)
- *Bacillus anthracis* (anthrax)
- *Yersinia pestis* (plague);
- *Clostridium botulinum* toxin (botulism)
- *Francisella tularensis* (tularaemia);
- filoviruses,
  - Ebola hemorrhagic fever; and
  - Marburg hemorrhagic fever; and
- arenaviruses,
  - Lassa (Lassa fever)
  - Junin (Argentine hemorrhagic fever) and related viruses

Category B

Second highest priority agents include those that are moderate easy to disseminate; cause moderate morbidity and low mortality; and require specific enhancements of CDC's diagnostic capacity and enhanced disease surveillance.

Category B Agents

- *Coxiella burnetti* (Q fever)
- *Brucella* species (brucellosis);
- *Burkholderia mallei* (glanders)
- alphaviruses,
  - Venezuelan encephalomyelitis,
  - eastern and western equine encephalomyelitis;
- ricin toxin from *Ricinus communis* (castor beans);
- epsilon toxin of *Clostridium perfringens*; and
- *Staphylococcus* enterotoxin B

A subset of List B agents includes pathogens that are food or waterborne. These pathogens include but are not limited to:

- *Salmonella* species,
- *Shigella dysenteriae,*
- *Escherichia coli* O157:H7
- *Vibrio cholerae*, and
- *Cryptosporidium parvum.*

Category C

Third highest priority agents include emerging pathogens that could be engineered for mass dissemination in the future because of availability; ease of production and dissemination; and potential for high morbidity and mortality and major health impact.

Category C Agents

- Nipah virus,
- hantaviruses,
- tickborne hemorrhagic fever viruses
- tickborne encephalitis viruses,
- yellow fever, and
- multidrug-resistant tuberculosis.

Mr. SHAYS. Thank you, Mr. Secretary, for your thorough statement.

I again want to thank you for allowing us to use your facility and also thank you again for your presence here before the committee. It's the intention of the chairman to have 5 minute questions for each Member and then we'll do a second round where we'll go 10 minutes if any Member wants to.

I just want to set up the stage for my question. We've had three commissions that have come before our committee, the Gilmore Commission, the Bremey Commission, the Hart-Rudman Commission, and all of them have basically said to this committee and in their reports that we haven't had a proper assessment of the terrorist threat, that we don't have a strategy to deal with it, and we aren't organized effectively to implement a strategy. That's what they said last year, and obviously things have changed. You have a President who has put Tom Ridge in charge of reorganizing to maximize our effort.

We recognize that the best thing that could happen is that we would detect and prevent an attack, whether it was catastrophic or sand in the gears, which is really what we have right now. We have in that process a crisis, if an attack is underway and how does the Government deal with it, and then we have, if an event occurs, we have the criminal justice system trying to discover where this attack happened, who's responsible and so on, and who do we hold accountable. I would parenthetically say, though, I view all this not as a criminal action, I view it as an act of war. I think we are at war.

And then we come to what we call the crisis management, where FEMA comes into play and so on. I put you pretty much in that category of the crisis has occurred.

Secretary THOMPSON. Right.

Mr. SHAYS. And this hearing is to look at the role vaccines play in civilian preparedness. You're free to speak on anything, and obviously, the Members are free to ask anything they want. I know you'll respond as you choose.

But one of the things we want to know is, what are the near and long term roles of vaccines in preparedness against biological warfare and terrorism, how adaptable is the current regulatory process to the development and approval of biowarfare defense vaccines? That's kind of the thrust of the hearing.

So with that as the thrust, I'm interested to know, do you plan or are you recommending that we vaccinate the entire U.S. population for, say, a smallpox outbreak?

Secretary THOMPSON. No, we do not. If I could just set my response a little bit longer than just that very quick response, if I might, Mr. Chairman. I want everybody to know that right now, as soon as a consequence happens, we would immediately put in order and put on notice our 7,000 individuals that belong to our 90 DMAT teams throughout the United States.

As soon as a crisis happens, they contact the State health department, who contacts CDC. We would send immediately some epidemiologists from Atlanta to that locale. And they would work in cooperation with the local hospital, the local emergency workers and the State health department to develop a plan.

They would then call us with that plan. In the Humphrey building we've got a huge room downstairs set aside in which we have people like Scott Lilibridge and other professionals around. That's on the sixth floor and I hope you'll go down and look at it before you leave today, members of the committee. Then they would send out whatever they need as far as extra personnel, as well as medical supplies.

In regard to your specific question on vaccination, we have, as you know, 15.4 million dosages of smallpox vaccine right now. And Dr. Tony Fauci is doing research right now to determine if we could dilute that down five to one or ten to one. Ten to one you would only have an effective rate of about 70 percent. Five to one we think it's going to be around 90 percent. And that would be very effective, 90 to 95 percent. We would then have 77 million dosages.

That has been analyzed by Tony Fauci and the people out at NIH and they say it's very potent and very effective. We have enough diluent and needles to handle the 15.4 million dosage of smallpox.

We are in the process, we sent out what is called a request for information, I met with the pharmaceutical companies, several of them last week, and seven companies now have indicated they would like to get involved in issuing some sort of a bid to produce smallpox vaccine.

Mr. SHAYS. Could I just ask you in this regard, after you've done your experimentation with animals, you have to go through one phase where you do a handful of, a protocol on humans, for initial safety and to see how well it immunizes. Then you go to phase two, which could take 2 years to much longer, with several hundred patients, to determine the safety and efficacy. Then you go to phase three, where you're dealing with even more. It's hard for me to know how we can reach a timetable.

Secretary THOMPSON. That's why Dr. Fauci is here, because we have already worked that out, Mr. Chairman.

Mr. SHAYS. Let me just say, after you answer, and then I'll go to Mr. Kucinich.

Dr. FAUCI. Mr. Chairman, what we're talking about is trying to expand the availability and dosage of an already approved vaccine. So it's a different story from having to go to a new vaccine, we're talking about the dilution studies on the existing smallpox vaccine.

Mr. SHAYS. Is this the vaccine that is——

Dr. FAUCI. In the stockpile—yes, absolutely. This is the highly effective vaccine that we used to vaccinate routinely until 1972, and in 1972 it was discontinued. We have 15.4 million doses in the U.S. Government reserve. That is already an approved vaccine.

The studies that were done preliminarily on 60 individuals compared a broad range of dilutions. We took the undiluted, which we know works, decades of history tell us it works, there's safety, obviously there are some issues we could discuss about the risk-benefit of that, because they are uncommon but nonetheless potentially serious toxicities with that.

Mr. SHAYS. Let me just interrupt you a second, there, and say that though this is an older vaccine which is truly not as pure, it's there and it is approved.

Dr. FAUCI. Right.

Mr. SHAYS. But aren't we ultimately looking to produce a new vaccine?

Dr. FAUCI. We are. There are——

Mr. SHAYS. That's really what I was asking.

Dr. FAUCI. Exactly. We have an immediate plan to answer the question, what happens if something happens a month, a week, 3 months from now, what happens if something happens 6 months to a year? And the Department under the Secretary's leadership has tasked us to put together a plan which addresses the immediate, the intermediate and the long range. The question you asked about the initial doses of the diluted one, that's the immediate plan. So you have 15.4 million doses.

We did a preliminary study last spring where we compared the undiluted with 1 to 10 with 1 to 100. We found out that the 1 to 100 dilution didn't work very well, it did not induce a very significant take. Let me explain, because I know that the question you asked is very relevant.

This is something that's being tested for safety and take rate. And by take rate, we mean to get that characteristic skin reaction which traditionally and historically has been highly correlated with protection against smallpox infection. We'll never be able to do a challenge study because it would be unethical and unthinkable to challenge someone with smallpox.

So we're asking, what is the safety in the diluted component, and what is the take rate. On that preliminary study, we found that it was about 70 percent take rate. Since that we felt was not adequate enough, we redesigned a larger study, which is a 650-patient study. The screening has started, the vaccinations will start within a few weeks. In that study, we compare 1 to 10 with 1 to 5 with undiluted.

Since we know in the previous study that we got 70 percent take rate on the one——

Mr. SHAYS. Is this with animals that we're doing this?

Dr. FAUCI. No, this is humans, sir. And this is not a phase one study. This is called a phase four study, because it's done with an already approved product.

Mr. SHAYS. Let me just say this to you, I'm a little uneasy given that I'm the chairman here, going over my 5 minutes. But I do want this issue, so I'll allow the other members to have the same amount of time.

I just want to separate the old method that's in storage, you haven't yet addressed the new one. I don't even want you to yet, because that's a longer issue and we'll take it up later.

Dr. FAUCI. Right.

Mr. SHAYS. But since you started with the existing stock, if you don't have smallpox, an outbreak, how are you really able to determine its efficacy? Because you can't afflict people with smallpox to see if it works.

Dr. FAUCI. Right. And let me try to explain that.

As I mentioned just a moment ago, we have a lot of historical experience that when you get a take, namely you have the characteristic reaction——

Mr. SHAYS. Define a take again.

Dr. FAUCI. A take is, if I get a vaccination and I put the drop on my shoulder, many of us who were born before 1972, if you look on your shoulder, you see a very faint little scar. It's a little prickly type scar. What happens is you put a drop on your shoulder and you take a typical, classical needle, a bifurcated needle, and you put about 15 jabs until there's a little bit of blood, in an area about 5 millimeters.

It's a primary take if you haven't been vaccinated before. If it's someone like you or I who have been vaccinated before, we would have a secondary take. My daughters would have a primary take. What that would mean is that after a period of time, you'd have the gradual evolution of what looks like a pustule, inflamed, and then a scab, and then ultimately the scab falls off.

We know that is correlated with protection. So even though we can't and should not challenge someone, we have extraordinary historical information that a take is associated with protection.

So the studies that we're doing, and let me just finish briefly what I was saying, that the ones that have just recently started, that will be finished by the beginning of the year, the end of January, the beginning of February, will determine if you compare the undiluted vaccine, which we know works, with a 1 to 5 and a 1 to 10. For example, the 1 to 5, let's say it gives us a 90 percent take. It's not a unreasonable assumption, but we have to do the experiment first, before we can give you that information.

If the one to five gives you a very good take rate, and is safe, then you have the potential for over 75 million doses available to you. That's the immediate plan. And as you mentioned, we can go later on into what the intermediate and long term plans are.

Mr. SHAYS. Let me just summarize what I believe you basically have said in the answer, that there is no intention to have a universal vaccination program.

Dr. FAUCI. Correct.

Secretary THOMPSON. That's correct.

Mr. SHAYS. That could only happen, obviously, if we had new production with a new vaccine, which, in my understanding, we're moving forward with that. And our other members may get to that question.

But in terms of existing stock, you are basically saying, the 12 million that is——

Dr. FAUCI. 15.4.

Mr. SHAYS. Well, 12 is in great shape, and then it's questionable.

Dr. FAUCI. Sure.

Mr. SHAYS. OK. But if we use the 15, that you think ultimately that you're going to see a one to five time——

Secretary THOMPSON. Five to one.

Mr. SHAYS. And this will be FDA approved?

Dr. FAUCI. It is not unreasonable to assume that the one to five, but we have to do the study.

Secretary THOMPSON. It will be FDA approved.

Mr. SHAYS. But you're saying, not that you're ordering them to, but that you won't move forward unless it's FDA approved?

Secretary THOMPSON. Right.

Dr. FAUCI. The FDA is going to be involved.

Mr. SHAYS. I just want to make sure.

Dr. FAUCI. Yes. The FDA will be involved in looking at the safety and the take rate. Were there any unusual reactions when you diluted it, was there something that was not predictable? So there certainly will be FDA involvement. This isn't something that we do and just give it.

Secretary THOMPSON. If I could just say something really quick, we have increased the purchase from Acambis from 40 million doses to 54. That's the one that has the exclusive contract. And they have indicated that they will have that delivered to us by next July.

Mr. SHAYS. But I don't want to get on the new one yet, just because it raises questions about—I'd be here another 20 minutes. I used at least 10 minutes, and Mr. Kucinich, you have 10 minutes.

Mr. KUCINICH. Thank you very much, Mr. Chairman.

Mr. Secretary, I want to explore the connection between threat assessment incidents and Government response, if I may. First of all, to just put things in perspective here, does the administration have any information that the incidents of reports of anthrax are more widespread than the incidents that we've seen reported at various media outlets and in the Capital here?

Secretary THOMPSON. Congressman, some of that stuff is classified and I don't think we should be discussing it.

Mr. KUCINICH. Well, we need to know. It would be comforting for the American people to know, is this a widespread problem or is it fairly localized?

Secretary THOMPSON. To the best of our knowledge, it is what we have seen so far. We have no intel that is saying this is going to be a wider spread thing. But we have to be prepared for it, Congressman.

Mr. KUCINICH. I understand. But when we're speaking of threat assessment, we're speaking of something that at this point is localized?

Secretary THOMPSON. That is the best of our information at this point in time. But we are preparing for something much more dramatic.

Mr. KUCINICH. And you're in contact with obviously the FBI concerning threat assessments and being able to analyze, so that you can prepare accordingly?

Secretary THOMPSON. That is correct. There are two paths currently going on, the criminal path and the public health path. We are responding to the public health path and the FBI is doing the criminal investigations in Florida, in New York and in Trenton and Washington.

Mr. KUCINICH. But you don't see anything, or do you see anything, which would favor a mass stockpiling or prophylactic consumption of Cipro or any other drug that's related?

Secretary THOMPSON. We feel that to be on the prudent side, it is imperative for us to increase the amount of purchase from antibiotics that would treat 2 million people for 60 days up to 12 million people. We feel that it's also advisable, even though we have no knowledge or basis at this point in time for any kind of smallpox to have 300 million doses of smallpox vaccine, just in case it ever did break out, because it's so contagious.

Mr. KUCINICH. There's no connection, though, between that and a threat assessment?

Secretary THOMPSON. No, there is not.

Mr. KUCINICH. This is just you saying, well, you know, what if this happens, we have to be prepared.

Secretary THOMPSON. Let's be prepared.

Mr. KUCINICH. Let's be prepared, but you don't have any information that suggests that there's any kind of a reason for the American people to be concerned that suddenly smallpox is going to be a reality in their communities.

Secretary THOMPSON. That is correct.

Mr. KUCINICH. OK.

A few weeks ago when the first discussion began to surface about anthrax, I remember a report, I think I'm pretty sure this is what I heard, that there was a theft of some anthrax from a Government lab. Had you heard of that at all?

Secretary THOMPSON. We have heard of it. But we have also found out that there's a lot of rumors going on, and a lot of the rumors we found, we do not know about that.

Mr. KUCINICH. Let's go back to threat assessment and the role of Health and Human Services. Are you aware of where any biological agents that could be used against people anywhere are in the control right now of various Government laboratories?

Secretary THOMPSON. We are absolutely certain that there are biological agents in Government laboratories, because they're doing research on them, Congressman.

Mr. KUCINICH. Right. OK. Do you ever talk to the people who are doing research on these, on anthrax, on smallpox, on botulism or any of these others about the security of that and the connection between that security and public health concerns?

Secretary THOMPSON. I certainly have. In fact, I went down to CDC and went through the laboratories down there, and I'll be spending a couple of days next week down at CDC, Congressman, doing just that. We also looked at the IG report, which I had done, to take a look at laboratory security. We have increased the laboratory security in all of CDC and NIH labs, and we're asking for some more money in this appropriation to improve it even more so.

I am not satisfied, if that's what you're asking, with the laboratory security presently. It's much better than it was 3 months ago, and it will be much better if we get the necessary money to do so.

Mr. SHAYS. Could we have that report submitted for the record?

Secretary THOMPSON. Sure.

Mr. SHAYS. Thank you.

Mr. KUCINICH. Since we're talking about threat assessment here, we should be aware of what the Government itself may possess that could create some problems. So I'd also like to ask you, Mr. Secretary, you articulated a number of agencies you've been in touch with. Have you been in touch with, for example, the Department of Defense, relative to any research that's going on in the Department of Defense, and the security of those defense related matters where they might be looking into different types of warfare?

Secretary THOMPSON. We have—let me answer in two ways. First of all, we have the most virulent viruses in the world in our laboratories.

Mr. KUCINICH. That's what I'm concerned about.

Secretary THOMPSON. We're the only ones that are really, we and the Russians are the only ones that are supposed to have smallpox, the smallpox virus. I said we are supposed to.

Mr. KUCINICH. Have there been any discussions about maybe destroying these viruses that we have currently within our own control, so that they don't get into wrong hands?

Secretary THOMPSON. There have been many discussions, but while somebody else has the virus, we do not feel that it is the proper thing to do to destroy our virus. And in regard to the intel, Congressman, we have intel coming in from all sources into our room downstairs. I hope you will avail yourself to go downstairs and take a look at this after the hearing. We have intelligence coming from the Department of Defense, from CIA, FBI, on a daily basis, on an hourly basis.

Mr. KUCINICH. I want to go back to something now. You know, as some of the wonderful work we do in this committee, we have the opportunity to see that sometimes the Department of Defense, which does the best job it can, can't account for various defense material. It's just so big, it's hard to keep track of rocket launchers and boats and airplanes and things like that.

So I want to go back to something you said about the biological and chemical agents, which as you said might be some of the most powerful, something to that effect, in the world. Why, if we have reports that some of this material, anthrax, has been spirited away or suspected to be spirited away, or reports indicate it has been spirited away from a Government lab, in addition to security, why don't we destroy these? Unless—we're not certainly intending to use them against some civilian population somewhere, I would imagine. I don't believe anybody's ever suggested that.

So why don't we destroy, and why don't you as the Secretary, who is concerned about public health, lead the effort to destroy any kinds of agents which may exist right now within our own country that if they got out of control would be like opening Pandora's box?

Secretary THOMPSON. We are confident that the smallpox virus we have is all there and accounted for on a regular basis, and there's none been missing.

In regard to why——

Mr. KUCINICH. If I may, Mr. Secretary, and I appreciate that answer——

Mr. SHAYS. Let him answer.

Mr. KUCINICH. Please.

Secretary THOMPSON. The reason we haven't is because other countries—at least one other country has it. And we need that virus in order to do the necessary research, in order to be able to build an antibiotic or a vaccine for the mutation that may take place in other viruses.

So if we had destroyed ours, and another country had the smallpox virus, they could mutate it and produce a smallpox that we could not have a vaccine. Therefore, we need this to protect America and protect our citizens, to develop a counter-balancing vaccine to a mutated virus that may come from a foreign country.

Mr. KUCINICH. You said Russia is the other country, is that what you said?

Secretary THOMPSON. When smallpox was eradicated, there were two countries that had a deposit of smallpox virus, the USSR at that time and the United States.

Mr. SHAYS. Would the gentleman yield just for a second?

Mr. KUCINICH. Sure.

Mr. SHAYS. We had testimony before our committee, Mr. Alibek for one, who said that North Korea in his judgment has it and was experimenting with it. And there is no certainty that other institutes and so on that might have had the virus destroyed theirs and just left it with the United States and Russia. So we have some real uncertainties here.

Secretary THOMPSON. We have some uncertainties. We do not have conclusive proof that North Korea or Iraq has it. We think that there's a 50–50 chance that they do.

Mr. KUCINICH. OK. I'm going to, I thank the chairman, I thank the Governor. I just want to say, this might be something we might want to get into further discussions about.

Secretary THOMPSON. I would like to go into a closed session, if you want to get more in detail.

Mr. KUCINICH. Sure. And since we're meeting with Russia and talking about a new era of relationship with Russia, this might be a good time to take some major steps here.

Thank you.

Mr. SHAYS. Thank you.

Mr. Lantos, you have 10 minutes.

Mr. LANTOS. Thank you very much, Mr. Chairman.

Let me commend you for a very fine testimony, Mr. Secretary.

Secretary THOMPSON. Thank you.

Mr. LANTOS. And let me sort of put my questions and comments in some kind of perspective. This country has never been more united and more determined, there is no doubt in my mind that we shall prevail. We have the capability intellectually and the resources materially to prevail. And the question we are debating is how we go about it.

Now, in a $10 trillion economy, which is what we have, no one could argue that we do not have the resources to provide the American people, all of them, the maximum possible safety against all hazards, whether it's bioterrorism, whether it's any other type. Yet I find that the people in the public health field are extremely critical of the budget proposed by the administration. Today's Washington Post has a story, I presume there are similar stories across the country, let me ask you to react to some of the issues that your critics have raised.

The administration's proposal, says the executive director of the American Public Health Association, in this field of fighting bioterrorism, is not adequate. You are proposing $300 million, the executive director of the American Public Health Association says he needs $1 billion. An Ohio health scare consultant, public health officer, says antibiotics and vaccine without staff and basic infrastructure is like putting Band-Aids on a huge wound. You can't just rent some people and drop them into a department that doesn't have the training or technology to handle a biological or chemical attack.

The dean of the Public Health School at Columbia University says, there's a whole bunch of things we need, and this $300 million doesn't begin to do all of these things. Now, at a time when every single poll and every fiber of our common sense indicates that safety and security is at the top of the agenda of the American people, how do you respond to these charges coming from people who have no personal interest in seeing these budgets doubled or tripled or quadrupled? These are people operating in the non-profit sector, like Columbia University's School of Public Health. Serious people who have spent a lifetime studying these issues, and they say that the administration's approach is woefully inadequate.

Secretary THOMPSON. I would say to those individuals, some of whom were in the previous administration——

Mr. LANTOS. What does that mean, Mr. Secretary? Does that mean that a professional, a physician who was in the previous administration has his credentials to be questioned?

Secretary THOMPSON. No, no, I'm just saying that the person that you first quoted was an individual that was in the previous administration, and I don't believe that in the previous administration there was enough investment in the public health system. And I'm not being critical. I'm just stating a fact. I think that a lot of people, including those that you mentioned, including people in this Department, recognize the importance of strengthening the local and State public health system.

I think you agree, and I agree with you, that we have some holes, some weaknesses. Our local and State public health system has been stressed. And it's being stretched right now. What we need to do is invest in it. And the $300 million is the first giant step forward.

Now, I am still working——

Mr. LANTOS. $300 million, Mr. Secretary, is $1.10 per person in this country per year. That's what it is.

Secretary THOMPSON. I understand. I do not want to argue with you, because I think you and I are on the same page. I think we both realize that we need to put more resources into our State and public health system. The $300 million is a giant step forward from where we have been.

Does this mean that this is going to cure all evils? Absolutely not. Does this mean that we're going to have to invest more in the future? Absolutely. If we want a strong, coordinated local and State public health system, we're going to have to invest in it.

And as I said yesterday to the same group that's criticizing me and that you quoted today, and I said yesterday to those individuals, there is a consequence. There's some good that came out of the terrorist attack on September 11th. And the good consequence of what came out of that is, I think we now recognize the importance and the need to invest in our local and State public health system.

This is a huge step forward. Is it enough in the future? No. Is it enough for this particular year? I think it's adequate. And I think that's what is important for this committee to know. It is much more than we've had in the past. Do we need more in the future? Absolutely.

Mr. LANTOS. Well, the reference to the future is somewhat intriguing, in view of the earlier testimony that we really don't know when the next terrorist attack comes. We don't have unlimited time to prepare for it. And what your critics are saying, Mr. Secretary, with all due respect, is the future is now, that this is not a leisurely period in American history. September 11th put an end to the age of frivolity and the age of seriousness is now with us.

Secretary THOMPSON. Yes, it is.

Mr. LANTOS. The age of maturity is now with us. And this gradual approach which clearly reflects the way this budget was put together, your critics say is not responsive to the crisis the American people face.

Secretary THOMPSON. I think that my critics are being too harsh. This is a huge step forward, and we are investing money in the places that they would like us to invest, maybe not as much as they would like. And I continue to work with Senators Kennedy and Frist and hopefully with you, Congressman Lantos, to maybe increase that. But that is something that Congress is going to have to make the determination right now, this is the administration's proposal, and I am fairly comfortable that if you increase that in these areas, I'm certain the President will strongly endorse it.

Mr. LANTOS. But Mr. Secretary, could I just ask you an economic question?

Secretary THOMPSON. Sure.

Mr. LANTOS. An increase of $300 million, which amounts to $1.10 per person per year, can that be viewed as a serious way of addressing a woefully inadequate public health capability in responding to bioterrorism?

Secretary THOMPSON. It's not only the $300 million that the administration is asking for, it's asking for an additional $1.6 billion against for our fight against bioterrorism. So it's not just the $300 million. The $300 million is just that portion dealing with the local and State health——

Mr. LANTOS. That's right.

Secretary THOMPSON [continuing]. On this. But the total package, $1.6 billion, which is a lot of money, and it's a lot more than we've had in the past. Could we use more? Absolutely. But is this a tremendous, legitimate step forward? Absolutely.

Mr. LANTOS. Well, let me just say, if I still have time, Mr. Chairman——

Mr. SHAYS. About 1 minute.

Mr. LANTOS. I appreciate that. One of the things that this horrendous and monstrous event on September 11th did to the American economy, it dramatically increased the cost of doing business. Just ordinary business. The airlines are putting in new cockpit doors. The costs across the whole transportation system will be astronomical.

We have to adjust ourselves psychologically to being willing to pay for these things just as during the generations of the cold war, the American people were prepared to pay for security. Now we will have to learn to pay for domestic security, and public health is the front line of domestic security. And I very much hope that you and the President will be open to significantly increasing these proposed amounts.

Secretary THOMPSON. Congressman, I would just like to point out that this President and me personally are passionate about strengthening the local and State public health system. I flew down to Atlanta to give that message yesterday to several thousand public health workers. I asked them for their cooperation and their input in order to improve it and to make it better.

I applaud you for suggesting that we do that. And hopefully we will be able to come up with a bipartisan package that's going to continue to move forward to improve the quality and the ability to give public health services to every American.

Mr. LANTOS. Well, you have my full commitment, as does the President, to improve the public health capabilities of this country.

Secretary THOMPSON. And you have my dedication, my passion to do so, Congressman.

Mr. LANTOS. Thank you. Thank you, Mr. Secretary.

Mr. SHAYS. I thank the gentleman.

Mr. Putnam.

Mr. PUTNAM. Thank you, Mr. Chairman, and thank you, Secretary Thompson.

We have heard considerable testimony on this topic over the course of a number of hearings. To paraphrase Churchill, we may have a woefully inadequate public health system, but I'll take ours over all the rest. I have tremendous confidence in your abilities and in the administration's commitment to combating biological terrorism. All of us are learning a lot as we go along. We have had some hints in the past and we have made some preparations, but obviously we have much more to do.

I have every reason to believe that when you and your very qualified, very professional, very dedicated team of scientists and researchers come up with the magic number per capita, that would keep us all safe and give us the maximum possible safety from all hazards, that you will share that with us.

But in the meantime, I would like to followup on some of the proposals that you have outlined. You mentioned your desire to put one State epidemiologist, to fund them in every capital. How many States have the epidemiologists with the credentials that you believe are needed?

Secretary THOMPSON. Thirty-five.

Mr. PUTNAM. So we're well on our way to meeting that goal of having one in every State.

On the health alert network, in this age of rapid communication and instant connectability, what are the barriers to having an e-mail system or rapid notification system, not just every county health department, but to every hospital and clinic in the Nation, that on a moment's notice, a message could go from Atlanta or from Washington and make these hospitals aware? What are the barriers to us having that now?

Secretary THOMPSON. The resources in order to make the connections, and the equipment in the hospitals and clinics to receive that. It's certainly a giant step forward. We have approximately 68 percent of the counties connected right now. We need to increase that considerably. And we need to make sure that the resources are available to hook up hospitals and clinics and local health departments with CDC.

We have ways in order to get the information out right now. But it would be nice to be able to be hooked up on the Health Alert Network.

Mr. PUTNAM. So it is a separate network?

Secretary THOMPSON. Yes, it is.

Mr. PUTNAM. But to get critical information to hospitals and clinics, surely there is a data base of e-mail addresses that with several keystrokes you could get critical information out?

Secretary THOMPSON. Oh, absolutely. We have dial-up communication, we have fax and we have e-mails and everything like this going in there. But the Health Alert Network is not connected to every hospital or every county. And if you want the best system, that would be the best for CDC in order to communicate quickly and correctly to every health officer in America.

Mr. PUTNAM. Mr. Kucinich raised some important points about laboratory security, and I know that CDC and NIH have taken steps. Are there other private sector or academic institutions that have access to pathogens or biological weapon potentials that need to beef up security and what's being done to address those particular situations.

Secretary THOMPSON. I don't know about the latter part, but they have pathogens and they have some bacteria in the State laboratories. We had requested some legislation for this Department, for our Department, it's moving through the House today to give our Department more authority to regulate the private labs, which contain many biological agents that could be mobilized, besides smallpox. We are looking for that legislation to pass. We know it's got bipartisan support, and hopefully it will.

Mr. PUTNAM. But absent that legislation, so status quo is that——

Secretary THOMPSON. We do not have the power. We can encourage them to do so, and to beef up their security. And they have been wiling to do so. But we don't have the authority to go in and direct them to do so, Congressman.

Mr. PUTNAM. Do you license those facilities or have any kind of a certification, any kind of regulatory oversight at all?

Secretary THOMPSON. No, we don't.

Mr. PUTNAM. That is troubling. I look forward to working on you with that legislation.

Dr. FAUCI. Not with regard to the security that you referred to, Mr. Putnam, but what has happened over the past several years is that prior to 1996, when it was relatively easy for academic institutions to get material that might ultimately be utilized, if it was used nefariously, to have a bioterrorism potential, now is very strictly regulated as a select agent. So I'm not addressing your question of security once the microbe is in an academic center. But over the last several years, it has become much, much more difficult for someone to get an access to a microbe without having a strict connection regulation with the CDC.

In other words, there are select agents now that fall into that category that you can't just call up and get somebody to send something to you.

Mr. PUTNAM. We've heard testimony where some people have taken their handy dandy computer and printed up a letterhead on

Acme Laboratories and sent off for microbes, and you're telling me that——

Dr. FAUCI. Right now that would not be allowable under a law that was passed. And it was stimulated by someone who tried to get an agent from the American Type Culture Collection. And that now, since I believe 1996—is that right, Scott?

Dr. LILIBRIDGE. Correct, about that time.

Dr. FAUCI. About 1996. But that doesn't address your question, which the Secretary just mentioned is something that we need to improve on.

Mr. PUTNAM. Is there some kind of information sharing, so that local health departments and local health departments and local first responders are aware that in the facility in their back yard, those microbes are in that community?

Dr. FAUCI. I can't answer that question from my vantage point.

Mr. PUTNAM. As a farmer, I have to let the fire department know when I buy fertilizer, as part of the community right to know law. And I know that applies to toxic chemicals. I don't think it applies to microbes. Is there a similar law that applies to microbes or other pathogens?

Dr. LILIBRIDGE. No. Not at this time.

That information is not automatically shared with health authorities. It is shared with law enforcement authorities who have connections at the local level.

Mr. PUTNAM. Thank you.

We've heard testimony from Mr. Alibek, who's become world famous now for his work in anthrax as part of the Soviet Union's biological program, and I think everyone's taken great interest in some of the horrifying things that he shared with us. In his testimony last week, he outlined a strategy for broad spectrum and prophylaxis with less emphasis on vaccinations. The purpose of this hearing is obviously to talk about vaccines, which predominantly addresses the issues of anthrax and smallpox.

But if you follow the method of operation from these terrorists who switch on a dime from Embassy bombings to using commercial aircraft to blowing up ships in port to using anthrax, we have, I think, a reasonable expectation that the anthrax will pass soon and there will be a very different threat. So to broaden this a little bit, in addition to stockpiling the vaccine for smallpox, what are we doing from a broad spectrum perspective, akin to what Mr. Lantos was saying, to improve our public health surveillance, to improve the education of all of our health workers, and what are we doing on a broader level beyond just the disease of the day?

Dr. LILIBRIDGE. Let me mention a few things and then turn to Tony Fauci to round up some of the research agenda, looking over the horizon. What we've been doing for the past 3 years is begin to build public health infrastructure around the issues of disease surveillance, laboratory capacity, training, both for clinical recognition but for laboratory recognition at the State and local level. This has been in effect well before the events of September 11th, and has been accelerated to a great extent since that time.

What this allows local practitioners to do, both in the public health community and in the medical community, is to have early recognition, either through training, seminars, collaborations with

guilds like the American Hospital Association [AMA], the American Public Health Association and those kinds of forums, as well as combined Department of Defense, HHS educational programming for clinical disease recognition to get beyond that disease of the day kind of thing.

It has included a wide range of critical agents for public health awareness and continues to accentuate those things that are critical to an understanding of the State and local level for disease detection and control.

With that, let me turn to Tony Fauci for a little more about the research on the horizon.

Dr. FAUCI. Mr. Putnam, what Alibek was referring to specifically was the medical approach of a highly specific approach, like a smallpox vaccine, an anthrax vaccine or an anthrax drug, that boosts what we call the innate or somewhat non-specific immune system. He was referring to research on inducing a component of the immune system that only over the last few years has come under intensive study. We refer to it as the innate immune system. It's innate because it has the capability that a first responder. It's an evolutionary component of when mankind evolved to protect itself against different types of infections. The first line of defense is the innate immune system.

So it has a much broader, non-specific capability of attacking a microbe. So the point he was making is that if you put your money with smallpox vaccine, this vaccine, that vaccine, while you're doing that, he doesn't say don't do that, and we totally agree with that, that you should also be pushing for something that's more broad. And that gets into the category of what the Secretary was referring to as the basic research as well as the applied and the research that you can use, for example, with a vaccine.

There is considerable amount of research going on at the NIH, specifically in my institute, which is the institute that studies the immune system and infections. It is that interface between the immune system and infection that I believe over the next several years will lead us to a more comprehensive approach toward microbes. But that's not something that's going to address the question tomorrow or next month. But it's the research that's going to give us a greater capability 5, 6, 7, 8 years from now.

Mr. PUTNAM. Thank you very much, Dr. Fauci, and Secretary Thompson. You and your people are very much on the front lines of this new war, and are patriots for that, and probably under-recognized for the tremendous responsibility that you bear, and we appreciate what you're doing.

Mr. SHAYS. I thank the gentleman. Mr. Sanders.

Mr. SANDERS. Thank you, Mr. Chairman.

And Mr. Secretary, thank you very much for your important and informative remarks. This is a serious crisis and you are attempting to deal with it seriously. We're just going to have to work together and share the ideas that we have as best we can.

I am especially delighted, in response to Mr. Lantos, your strong commitment to significantly improve our public health systems. I have always believed that it is a national disgrace that in the richest country on earth, 44 million Americans have no health insurance and many more are inadequately insured. But given a health

care crisis as a result of a terrorist attack, I remain concerned that there are many, many millions of Americans who will not know where to turn, that there will not be health care facilities in their community that they can access.

Now, during the campaign, President Bush, Candidate Bush then talked about federally qualified health centers, which seemed to me to be an extraordinarily cost effective mechanism, not only to provide health care to all Americans, but to deal with this current crisis. I come from a rural State. There are people who live 100 miles away from a hospital. They may not know who their doctor is. It would be of real value to people all over this country to know that there is at least one health care clinic in their area that they can walk into, regardless of their income, and get care during an emergency, get the medicine they need, etc.

I would hope that in the midst of this crisis, we raise again the issue of federally qualified health clinics, and we adequately fund them and we set them up in every county in the United States.

Second of all, let me reiterate my concern about the power of the drug companies. It is no secret, I think, as you may well know, that the pharmaceutical industry is the most powerful lobby on Washington. They always win, which means we end up paying the highest prices in the world.

Now, I understand that Bayer has indicated to you that it will take 20 months to produce all the Cipro that you have requested. Yet the FDA has tentatively approved five generic manufacturers to make Cipro. And they have indicated that it will take 3 months to produce the same amount. And I wonder if, in a moment, you can comment on that, why we would not go with five companies who produce what we need in 3 months rather than Bayer in 20 months.

The last question that I wanted to ask is the following. I think as we have all indicated, nobody here is happy about raising nightmarish situations, but it is important that we do, that we get it out on the table and we do our best to be able to respond. Let me throw a nightmare at you.

I am concerned, and I hope that you people can tell me that my concerns are not justified, I fear very much the possibility that on some windy Saturday morning, a half a dozen small Cessnas will take off in different locations in this country, each with a couple hundred pounds of anthrax, and that simultaneously they will be released. And if that is the case, it would mean, given the weather and the temperature and the wind, that tens of millions of people could be exposed to anthrax.

Now, my question is, go through that scenario and tell us our capabilities in responding for a stock, as I understand it. The good news is that if we know we are exposed to anthrax, we can treat it with antibiotics. That's very important and very good. How will you, will the U.S. Government, will our local public health authorities be able to tell the American people before they develop the symptoms, guess what, we've got a crisis, get to the hospital, get your medicine right away? Do we have that capability to detect anthrax in the air? Do we have—you asked for 12 million doses, as I understand, for Cipro. Maybe you could tell us why 12 million and why not 100 million and so forth and so on.

But I fear, I appreciate that's a nightmarish situation. But all over this country, every health resource is strained to the utmost degree. Can we and are we moving to try to deal with that scenario, understanding that the good news is, if we have our act together, that we can perhaps minimize the death and suffering that might take place? Because as you have indicated, anthrax is treatable if we get to it soon enough.

So those are my—I wanted a specific response, if you could, about Bayer and 20 months as opposed to the other companies, federally qualified health clinics and this nightmarish scenario.

Secretary THOMPSON. Thank you very much, Congressman Sanders. Let me try and go through many of the things you've said, and then Scott Lilibridge will want to respond and I'm sure Tony Fauci will as well, to your nightmarish thing that hopefully will not happen.

First off, in regards to community health centers, federally qualified centers, as you know, the President put in his proposal enough money to increase that from 2,200 to 3,400, an additional 1,200, and go from 11 million people to 20 million. In regards to every county, I am not opposed to that. As you can probably recognize, I think that is a way to deliver good quality health care in America. And also, coming from a rural area, I know the importance of community health centers and federally qualified health centers. So I recognize that. Whether or not the resources are there, whether or not Congress is going to pass it, I don't know.

Mr. SANDERS. But you recognize this is a very cost effective way to provide quality care?

Secretary THOMPSON. It's one of the best. And I think it is, I think they get very good quality health care there. I have spoken to them, been involved and raised some money for them personally and been very much involved. It's a very cost effective way.

Mr. SANDERS. And they could play a role, if, God forbid, we need them.

Secretary THOMPSON. They could. Second, I want to point out that once again, how do we notify people? What we do is we have 7,000 medical professionals throughout the United States divided into 90 teams. So we would move very quickly. We have CDC sending out epidemiologists and we would also have NIH, we also have our Commission Corps, if it was a vast thing. We would be able to call those people up within hours.

Mr. SANDERS. Yes, Mr. Secretary, here was my question, though. Can one detect anthrax in the air before one develops the symptoms? In other words——

Secretary THOMPSON. No.

Mr. SANDERS [continuing]. The problem would be that if it takes you 3 days, by the time you've got a symptom, you've got a problem.

Secretary THOMPSON. We haven't been able to determine that.

Mr. SANDERS. Are we working on trying to develop a mechanism?

Secretary THOMPSON. Yes, we are. But we haven't found it yet. But the third thing is that, in regard to Bayer, that you are concerned about, I'm not here to defend Bayer. I'm here to tell you that we're negotiating with them, and once negotiations are done, I would like to sit down and show you what we are. They have in-

dicated to me that they can provide 200 million pills within 90 days and they can adequately wrap up and produce it within weeks, whatever we need.

But the price is the question, not the supply. And that is something we're going to be negotiating and debating. I can assure you that we are not going to pay the price that they ask.

Mr. SANDERS. Let me ask, am I incorrect in saying that they have told you that it would take them 20 months to produce all the Cipro you have requested?

Secretary THOMPSON. I think you're wrong, because they told me they could produce 200 million pills within the next 60 days.

Mr. SANDERS. And if you are unhappy with their performance either in terms of speed of delivery or in price, are you prepared to go to generic companies?

Secretary THOMPSON. I am prepared to ask Congress for that authority.

Mr. SANDERS. Do you know the Canadians have done that?

Secretary THOMPSON. I know, but I know that we have a different law than the Canadians.

Mr. SANDERS. But you are prepared, if Bayer does not cooperate with you, to do that?

Secretary THOMPSON. Yes, I am.

Now, the third thing, in regard to your nightmare thing, let's hope it doesn't happen. But I think Scott Lilibridge is better able to deal with that.

Dr. LILIBRIDGE. Sir, let me make a few comments. First, as we've gone to this new kind of war, we've developed a game plan. We developed this game plan as we refined it over the last couple of weeks. And let me just tell you what's emerging in this.

While we had a basic public health commitment to build infrastructure in certain areas, we've been on that for the past 3 years, we've also been readying our clinical response. Let me tell you some of the key elements of this game plan. There are clearly preventions, and we are networking with the intelligence community to try to interdict, understand, get early warning about such events. We do that on a daily basis.

Mr. SANDERS. Do you get early warning in other ways than somebody just suddenly seeing a rash of illness in a given community and saying, we've got a problem? Can you get early warning in other ways before that?

Dr. LILIBRIDGE. You can. You can get early warning in terms of helping you gauge your likelihood of one, prioritize your efforts in one pathogen versus another, you can get early warning in terms of where to put your resources, and you can get early warning to put your detection out and look in certain areas.

We are working with the intelligence, law enforcement communities on a daily basis and coordinating in a way we haven't done before.

The second part of the game plan is clearly detection, early detection. That involves clinical awareness, picking up cases, sentinel networks for surveillance, laboratory kinds of information. The third area of the control is disease control. That involves the steps to corral and contain the disease, keep it from spreading in the population, interdicting steps like prophylaxis.

Mr. SANDERS. Would you agree with the Secretary that at this point, there is no way of doing air detection and knowing if there's something in the air?

Dr. LILIBRIDGE. Sir, currently, my understanding is that real time technology to detect aerosol assault is not available.

Mr. SANDERS. Is that something we're working on?

Dr. LILIBRIDGE. It is something multiple agencies and departments are working on in a collective fashion.

Dr. FAUCI. What I can address, sir, is the research component of it. What we can do in the future for having capabilities of detecting. There obviously are molecular means that are research tools right now. You can detect a microbe by using what we call a microchip that might be able to determine if there's a certain concentration in the atmosphere. That's in the research phase right now. That is not going to help tomorrow or the next day.

From the standpoint of research related to better ways of addressing anthrax, I think it's important to bring out, the public health components of it as Scott mentioned very well. I can't add to that. The research that's going on right now is trying to address much more specific ways to combat the anthrax microbe over and above the question of antibiotics. In fact, today, this afternoon there will be a press conference downtown by the the Journal Nature talking about some very exciting new research about really being able to specifically block the toxins of anthrax. I think that's something that we should pay attention to. Because we're going to try and translate that from the fundamental basic research to something we can try in humans very rapidly.

Mr. SANDERS. I think my time has run out. Thank you.

Mr. SHAYS. Mr. Secretary, this is probably the only time you'll appear before our committee this term. If you don't mind, we'd like to do one last pass, and then you can walk across the hall to your office. [Laughter.]

Mr. Kucinich.

Mr. KUCINICH. Thank you very much.

We heard from the media, the public, Government as they interact throughout this——

Secretary THOMPSON. Excuse me, can I just interrupt? Senators Kennedy and Frist are over here to meet with Dr. Fauci. Do you mind if we—do you have another question for Dr. Fauci?

Mr. SHAYS. I will tell you that I do want to get into the whole issue of new vaccines and to what extent do we push FDA and so on. But I'm not inclined to have you keep Senators waiting. So we'll try to wrestle throughout with Dr. Fauci.

Secretary THOMPSON. I have somebody from FDA here.

Mr. SHAYS. OK. I'll need to swear them in, but that's OK, that's fine.

Dr. FAUCI. Thank you very much, sir.

Mr. SHAYS. Would you let the Senators know we were eager to have you meet with them? [Laughter.]

Dr. FAUCI. I will convey that message.

Mr. SHAYS. Could I ask you to stand and just identify yourself?

Dr. EGEN. Dr. William Egen, Deputy Director, Office of Vaccines, FDA.

Mr. SHAYS. Thank you. Will you raise your right hand?

[Witness sworn.]

Mr. SHAYS. Thank you very much. Nice to have your participation.

The gentleman can start over.

Mr. KUCINICH. I thank the Chair.

In the last few weeks, we've seen from Government, the media, the public, people are experiencing and articulating some of their deepest fears. And for that reason, it's a very challenging time in the life of our Nation. And with many people, when you start to experience your deepest fears, you go into a survival mode. And I would just like to suggest that such a condition, which has its analog in science and in terms of a general stimulus response, is not necessarily conducive to maintaining a democracy.

And that is that we need to meet these challenges as they arise and try to prevent them as best we can. We need to take great care that as we explore these various public health challenges that could come up, that we do not create hysteria or induce a panic among the American people. Because panic is not a good place from which to make decisions.

Now, I think we're starting to redefine what are public health issues here. I'm certain the Secretary has come up with some new definitions of public health since September 11th. And one of the things that occurs to me, with this dialog we had a few moments ago about biological weapons that may be present on our own shores, with the Government, with the private sector in some way, that for the first time, the biological weapons treaty becomes a public health issue. Because if we can find a way to start to control biological and chemical weapons, it's quite possible that such weapons will not be used against mass publics, therefore occasioning the kinds of concerns which HHS is very busy about these days.

So I wanted to share that view with you, Mr. Secretary, because I know that based on your interview with 60 Minutes that, and based on your experience as a Governor, you try to maintain a confident outlook, you try to communicate to the public that we're going to do everything we can to protect them, you're also aware of all the different variables.

Secretary THOMPSON. That's right.

Mr. KUCINICH. And I think that you're trying to do the best job you can, and I respect that and I appreciate your service. Now, one of the things that we need to look at, I believe, is to focus resources more and more on the National Medical Response System, which is intended, as you know, to help every city, locality or metropolitan area design a disaster plan for public health emergencies. Now, it's operated through contracts awarded through HHS and FEMA has estimated that it would cost approximately $2.5 million per city to develop and coordinate these plans.

And actually, those kinds of plans make sense. It gets people working together in the event of any contingency. So there is a sense through that work, people gain a sense of security that we're ready, we're prepared. And then they can go about their life a little bit easier.

Now, currently, according to my information, HHS has been giving about $600,000 to each city. And your new proposal provides only $50 million more for local and State plans. According to my

calculations, this would be enough to only bring about 25 cities up to the minimum level recommended by FEMA. And of course, there are more than 25 cities that need full funding for public health emergencies.

What can you do as the Secretary to help local communities get the resources to prepare for public health emergencies and begin the process of trying to bring some peace of mind to communities that at least are working to deal with eventualities whether or not they in fact ever materialize?

Secretary THOMPSON. Several things. First, I can use the bully pulpit of my office. Second, we are expanding it from 97 to 122 cities, as you've indicated, 25. It's important. I think that stretches us to about, with everything else going on, I think that's about as much as we can handle in this particular year, Congressman. It would have been nice if we could do more, but we want to, what we do we want to do correctly and be able to develop the best systems, the best plans.

No. 3, I am trying to be confident in outlook, because I think it's very important for the American people to know that we are not going to allow the terrorists to defeat us through terror. We've feared the bio, but the second part of that, the terror, is what you talked about, and it's important.

Fourth, we do need the supplemental plan approved by Congress. It's important for us to get those extra dollars into the local and State public health systems. If Congressman Lantos is successful in getting more, we will be able to put that to good use. I think it is important for all of us to realize that this is a bipartisan thing. I think that in the past, I don't think we've invested in our public health system very adequately. And I think we've actually disinvested.

I think it's important for us to realize that and now move forward on a bipartisan basis to strengthen and coordinate our local and public health systems, develop disaster plans, develop educations, put epidemiologists in our health departments wherever we possibly can, expand our Health Alert Network and be able to get that kind of education and information to our local health departments, our hospitals, as well as educating our emergency ward people, our doctors and nurses, how to diagnose and how to look at things. Because they've been trained in medical school, but since they've never seen anthrax poisoning, they probably could miss it.

So it's important for us to do all of these things in a cooperative and collaborative fashion, through the Department of Health and Human Services, NIH and CDC and with Congress.

Mr. KUCINICH. Well, I'm glad to see the Secretary articulating, it's brought a vision of involvement of HHS working cooperative with government at all levels to try to make sure that our public health institutions will be up to the challenge. Not only the challenge that we find as a result of the events of September 11th, Mr. Secretary, there are, Mr. Sanders alluded to it earlier, there are 43 million Americans right now who don't have adequate health coverage. It may be with insurance companies bringing a parade to Congress looking for bailouts of their very industry, which is supposed to be about risk, that we may find your department achiev-

ing a larger and larger role in the functioning of public health in this country, even beyond what you do.

Secretary THOMPSON. I never expected when I came out here to become an expert in embryonic stem cells and bioterrorism. So I would like to get back to public health. [Laughter.]

And I never expected to have to the Capitol under an anthrax scare, and I'll tell you, we'll never do it again.

Now, I want to conclude with this discussion, again, that Mr. Sanders started. This is about this generic manufacturer of Cipro. It's possible, since you have five generic companies that have already tentatively been approved to manufacture Cipro, and it's legal, because the Government has, as you know, both the authority and the precedent to act under the TRPPS Agreement, Article 73, security exceptions clause, "nothing construed to prevent a member from taking any action which it considers necessary for the protection of its essential national security interest, taken in time of war or other emergency in international relations."

So we have a legal precedent there. We also have 28 U.S.C. Section 1498, which allows the Government to purchase products for official use from alternative sources, with payment to patent holder of a royalty fee to be determined by a judge. And I might say, as Mr. Sanders has repeatedly stressed, it's cheaper, for the U.S. Government, the purchase price is nearly $2 per pill, generic versions are 20 cents or less per pill. That means with $643 million, of the $1.5 billion HHS requested, the United States could buy enough generic doses to treat 31.5 million people instead of merely 2.6 million people, if we were paying top dollar.

So these are considerations, I'm sure, that you're going into because you want to make sure that you can, if we need to deal with this, or if we have it stockpiled, at least to have the ability to respond to help more and more people. I'm confident, Mr. Secretary, that these are things you're considering.

Secretary THOMPSON. You're absolutely correct.

Mr. KUCINICH. Do you feel that you'll be able to look at trying to lower the cost to the Government for these?

Secretary THOMPSON. You don't know me that well, but I negotiate very tough and well.

Mr. KUCINICH. I'll accept that. Thank you.

Mr. SHAYS. I just again want to thank the Secretary for participating here. We have allocated 10 minutes to each of the Members. For the remaining time we've been joined by Mr. Tierney as well.

I just would say to the Members that they don't need to use the 10 minutes. We do have three other panels that will follow.

But at this time we're going to go to Mr. Lantos, then we're going to go to my colleague, the ranking member, then to Mr. Sanders, then Mr. Tierney, and then I'll finish up.

Mr. LANTOS. Mr. Chairman, I'd like to ask unanimous consent to place in the record that brilliant article on germ bank security which appeared in today's New York Times.

Mr. SHAYS. Without objection, so ordered.

Mr. SANDERS. I'd like to raise some questions.

Mr. SHAYS. What date is that?

Mr. SANDERS. Today's. The president elect of the American Society of Microbiology estimates that there are about 250 scientific

centers in the United States that have anthrax stocks and about 1,000 sites abroad. And clearly, security at many if not most of these is singularly inadequate. And obviously, determined terrorists are fully capable of obtaining anthrax at all of these facilities.

As a matter of fact, they don't even have to be terrorists engaging in criminal acts. Let me remind all of us that a fellow by the name of Larry Harris, with a history of affiliations with hate groups, managed to buy plague bacteria from an American germ bank by mail, paying $100 each for three vials. And after he was caught, Congress rewrote the Nation's terrorism laws and tightened germ security, imposing tough rules on the acquisition and transfer.

But we have had very little success in having overseas facilities follow the procedures that need to be followed in this country. I would be grateful if the Secretary or either of your colleagues would comment on what steps we are taking to see to it that globally this does not happen in the future.

Secretary THOMPSON. We haven't done enough, Congressman, but I'm going to defer the answer to the question to Scott Lilibridge.

Dr. LILIBRIDGE. Thanks. Sir, there's a number of things that we're doing. We have ongoing collaborations internationally with groups like the World Health Organization that include issues like laboratory safety, training, global surveillance and other things that can provide early detection. It falls short of interdiction in terms of legal ability to detain, acquire.

But there is a growing international movement, the WHO director was at CDC just yesterday, and there is growing concern in international circles, both in ministries of health, which have been contacting us, as well as WHO, that bioterrorism preparedness needs to be a regular part of ministry of health activity, and that it needs to be a substantial component of the infectious disease control effort at WHO. We're going to participate in those efforts.

Mr. LANTOS. I realize, Mr. Secretary, that this is not in your bailiwick, but in Colin Powell's bailiwick, but I would like to ask you to join me in discussing with Secretary Powell that we direct all of our Ambassadors in every country where we have diplomatic relations that this issue be raised with the appropriate authorities at the highest levels. Because you can have the most incredible security here in this country, if this security is not present elsewhere, we will face the problem. And I would be grateful for your help and cooperation on this.

Secretary THOMPSON. That's a very valid suggestion and I would enjoy joining with you in that discussion. I think it's a discussion that should be taken, Congressman.

Mr. LANTOS. Thank you very much. Before I yield my time, let me just say, Mr. Secretary, you have done an outstanding job here, and we all appreciate your commitment to this issue.

Secretary THOMPSON. Thank you very much, Congressman.

Mr. LANTOS. I yield back.

Mr. SHAYS. I thank the gentleman for yielding back. We'll go to Mr. Putnam.

Mr. PUTNAM. Thank you, Mr. Chairman.

I want to change gears just slightly. As part of your request for supplemental, you have asked for 410 new FDA inspectors to deal with food safety issues. Would that be at the retail level only, the finished product, grocery store level? What is being done to coordinate with USDA to deal with agriterrorism and bulk goods?

Secretary THOMPSON. We are coordinating very effectively with agriculture. But the problem we have, Congressman, is that we have 750 agents in FDA. We have 56,000 establishments that we're supposed to inspect. And we are inspecting them, we're supposed to inspect them once a year. And those who have not caused problems we'll inspect maybe once every 4 years, once every 5 years.

There are 132 ports of entry into the United States that food is imported into the United States. And we at the present time only have 150 agents that are inspecting the food that comes in from 132 different ports. We are not even scratching the surface as far as monitoring and inspecting foods. The 410, 200 goes to the border and goes to airports to buttress the 150, so we would have 350. The other 100 would go to the laboratories to give the background checks and to be able to improve what we have as our OASIS system. And the remaining 100 would go to help improve the inspections on the 56,000 sites.

So FDA has not, FDA is like the public health system, it has not been able to get the resources in food inspection like we have not invested in our public health system in America.

Mr. PUTNAM. Well, you have APHIS under USDA at the ports, looking for invasive, exotic pests, plants and diseases.

Secretary THOMPSON. That is correct.

Mr. PUTNAM. How does FDA overlap with that, if it is a bulk container of a perishable fruit or vegetable, is that USDA, but if it's meat, is it FDA? Where are the jurisdictional lines there?

Secretary THOMPSON. They're pretty cloudy. There's really no rational reason for it. Agriculture is supposed to inspect the beef and poultry and we are supposed to inspect the manufactured goods. But in the case of eggs, we inspect the raw eggs and they inspect the manufactured eggs, which makes no sense whatsoever. And there needs to be further cooperation and collaboration with the Department of Agriculture.

I think that we're working in that regard. Am I satisfied? No. Am I satisfied with the inspection we're doing? No. Is this going to help? Tremendously. And we have to do a much better job. I am more fearful about this than anything else.

Mr. PUTNAM. Well, I am, too, and I have been talking about this in a variety of committees on the ag side and on this side, and even in the legislature, trying to beef up our airport and seaport inspection teams. But FDA only deals with the finished, processed food product, is that an accurate statement?

Secretary THOMPSON. That's correct. Yes.

Mr. PUTNAM. So all of the raw goods coming in, including meat, is USDA's responsibility, not yours?

Secretary THOMPSON. That is correct.

Mr. PUTNAM. And they have the same inadequate system as you?

Secretary THOMPSON. Agriculture, I believe, is down to nine ports. We have 132 ports of entry.

Mr. PUTNAM. Food only comes into—I don't understand.

Secretary THOMPSON. Agriculture, the ports that agriculture comes in I think are down to nine.

Mr. PUTNAM. That sounds a little low.

Secretary THOMPSON. I think it's only nine that they come in.

Mr. PUTNAM. That is an area of great concern. We have highlighted, in the frivolous, as we've heard earlier, in the frivolous pre-September 11th days we were dealing with things like hoof and mouth disease, which would have a huge impact on food safety——

Secretary THOMPSON. Tremendous.

Mr. PUTNAM [continuing]. And food safety in the level of quality and healthfulness of our food supply.

Mr. SHAYS. Would the gentleman yield a second? Given that you have staff here, if they could confirm that so we could put it on the record as to how many points of entry.

Secretary THOMPSON. I'll get that for you.

Mr. SHAYS. Before we adjourn, before the Secretary leaves, if someone could find that out.

Secretary THOMPSON. We'll get that from FDA and also get it from Agriculture.

Mr. PUTNAM. So we have these other things that were out there prior to September 11th that we used to think were scary.

Secretary THOMPSON. Like mad cow disease.

Mr. PUTNAM. Mad cow, hoof and mouth and all those things can be harnessed and weaponized or contained and channeled into a particular direction. We have testimony again from Mr. Alibek that indicates that he had as many people working on agricultural terrorism threats to the economy and livestock and crops as he did working on threats to the humans, the casualties. So this is of great concern to me, and I hope that the coordination will improve between the agencies.

Secretary THOMPSON. You know what we should do? We should be able to allow agriculture inspectors to be able to inspect our stuff and we should be able to inspect agriculture. We should have cross-certification. I mean, it's a radical idea, but it makes common sense to me. Instead of having two inspectors go in the same building, one inspector should be able to do it and maximize the time and effort. And it hasn't been able to have been worked out, and I hope with this kind of a problem, that's one positive thing that may come out of this.

Mr. PUTNAM. No question about it, jurisdictional fights. And it's not just between FDA and USDA. Because you have Fish and Wildlife, you have Customs, you have Border Patrol. And all these things didn't have the momentum behind them to be seriously addressed by the Congress until September 11th.

I would hope that all of us will harness this new momentum to bring about the radical change that will be necessary to establish a safety net at our airports and seaports that we just haven't had in the past. There is no cross-training, there is very little communication. And even with the best of coordination, we're still only hitting a tiny fraction of the containers that are coming into these seaports.

Secretary THOMPSON. You're absolutely correct, and Congressman Putnam, I'm so happy you brought it up. This has been a concern of mine for a long time, and I'm so appreciative that people

like you are concerned about it. I hope that you will take a look at our proposal dealing with food safety. It is still not enough, but it is a tremendous step in the right direction and I would hope that we would be able to get it passed in this session of Congress.

Mr. PUTNAM. Thank you, Mr. Secretary.

Mr. Chairman, I yield back.

Mr. SHAYS. I thank the gentleman for yielding back.

Mr. Sanders, and then Mr. Tierney, we'll go to you.

Mr. SANDERS. Thank you, Mr. Chairman.

Mr. Secretary, I would like you, if you would be so kind, to comment on an article that appeared in the New York Times October 18, 2001. Let me quote from parts of the article.

"Although Bayer, a German pharmaceutical company, is tripling production of Cipro, it will take the company 20 months working 24 hours a day to produce what Mr. Thompson says the Government needs, enough pills to treat 12 million people for 60 days. The Government currently has enough Cipro for 2 million people. Five drug companies that have received initial approval to make generic Cipro pending the expiration of Bayer's patent in 2003 say they could produce the same quantity in 3 months—not 20 months, 3 months. One official close to the Administration's negotiations with Mr. Shumer said that the White House had 'clearly made a political decision.' White House officials did not respond to requests for comment on the issue," which is why I'm going to give you the opportunity now.

"Mr. Thompson acknowledged that there were other considerations. 'We haven't been in the process of breaking patents,' he said today. Bush Administration officials and other Republican administrations have long been philosophically opposed to meddling in the private marketplace. President Bush also has close ties to the pharmaceutical industry, which contributed heavily to his Presidential campaign and Republican election committees. Two of the President's Cabinet members are former drug company executives," etc.

So bottom line here is, it seems that if we went to other companies, we might likely have more Cipro quicker and perhaps at a lower price. So I would like for you to tell me and the American people why we are not moving in that direction and also, the issue about treating 12 million people for 60 days. God forbid there is a real tragedy, we may need more of that. So can you please respond to that article.

Secretary THOMPSON. I'll try and respond, Congressman, to your satisfaction. First off, it is my understanding directly talking to the company that they can produce the number of pills that we need in regard to this anthrax outbreak within 60 days, not 20 months. That's what they have told me as recently as of last week.

Mr. SANDERS. So the New York Times said 20 months and you believe it is 2 months?

Secretary THOMPSON. That is what the company has responded to me when I raised that question to them.

Mr. SANDERS. Would you be so kind as to confirm that later on, after you talk to Bayer, with this committee, and see if the New York Times is accurate?

Secretary THOMPSON. Sure. I'm going to be negotiating with Bayer this afternoon, Congressman, and that's one of the questions that's on my itinerary that I'm going to be talking about, OK?

Second, in regard to the patent issue, I have indicated to Bayer that they'd better sharpen their pencil very sharp before they come down here, and if they don't sharpen the pencil, they don't need to come. Third, if I can get the same price or similar price or save the taxpayer dollars, considerable dollars, and not break the patent, I see no problem with that.

Fourth, my lawyers tell me, unless Congress changes the law further, that we would have to pay damages to them if they brought a lawsuit against us. And that is, I know you're smiling, but——

Mr. SANDERS. I'm not smiling——

Secretary THOMPSON. Well, that's what my lawyers say, Congressman, and I have to rely——

Mr. SANDERS. Well, Mr. Kucinich—if I may——

Secretary THOMPSON. Sure.

Mr. SANDERS. Mr. Kucinich raised this issue a moment ago. Common sense dictates and international law dictates that when you have a national crisis, we do not have to give enormously profitable pharmaceutical companies the price they want. That's why we're here, to protect the American people. And if they want profits rather than serving the people, I think the law is very clear that we have a right to go outside of their company. Do you disagree with that?

Secretary THOMPSON. I do not disagree. In fact, I agreed with you earlier. I also told you that, wait until I get done negotiating, then I'll sit down and we will discuss whether or not I made a good deal.

Mr. SANDERS. But you are not at this point ruling out——

Secretary THOMPSON. I am not ruling out——

Mr. SANDERS [continuing]. Going outside Bayer and getting it generic?

Secretary THOMPSON. I answered Congressman Kucinich that if in fact I could not reach an agreement that was advantageous to the American public, I would come and talk to this committee and to Congress and ask for more authority to do so. And knowing your passion for this, you'll be the first one I'd come to see and ask you to support the legislation.

Mr. SANDERS. I think, Mr. Secretary, this is an enormously important issue.

Secretary THOMPSON. It is.

Mr. SANDERS. In this sense, also. It's not only a moral issue, but it is very clearly a health response issue. The American people would be very disappointed if they believed that an industry which has spent hundreds of millions of dollars on campaign contributions and lobbying, all that stuff, was able to prevail upon the Congress or the administration in reaching a decision that only works for the company and not the American people.

Secretary THOMPSON. And I agree with that. Could I finish my answer?

Mr. SANDERS. Please.

Secretary THOMPSON. Also, everybody, Congressman, Senators, is just concerned about Cipro. But of all the anthrax that we've tested, and I want to make this crystal clear, the anthrax that's been

tested, all of the anthrax that's been tested is sensitive to all the antibiotics, Ciprofloxin, penicillin, Doxycycline and several other ones. And those are generic drugs.

We think that since they can treat anthrax just as effectively as Cipro, and that's what CDC has indicated and FDA has approved that, we should start talking more not just about Cipro but talk about penicillin and talk about Doxycycline. Some of them in some cases are more effective. Some individuals have reactions to Ciprofloxin. Some mothers that are pregnant should not be taking Ciprofloxin. So we put them on other antibiotics.

And what we're saying is, not only are we purchasing Cipro, we are purchasing other antibiotics, such as penicillin and Doxycycline to treat anthrax. It is not only Cipro. And those are generic drugs and those are going to be purchased.

I would like to leave this committee and the American public with the understanding and knowledge that they can also purchase penicillin and Doxycycline if they need to in order to prevent and to be able to prevent the infection from taking place, if they encounter anthrax. They should not go out and hoard it, that's what I'm saying.

Mr. SANDERS. Mr. Secretary, last question on this subject. I have heard differently than what you have just indicated, that while it is true that penicillin and other antibiotics can work effectively, that the product of choice would be Cipro.

Secretary THOMPSON. For the first 5 days.

Mr. SANDERS. OK. That is your understanding?

Secretary THOMPSON. Correct.

Mr. SANDERS. So if, God forbid, there was an emergency, we would turn to that particular drug, Cipro. And then the question is, how do we get that product inexpensively, how do we produce it? You didn't also yet tell me what's holy about the word 12 million, 12 million people rather than more.

Secretary THOMPSON. Because it's not contagious, we felt that 12 million is an ample supply, if in fact the nightmarish thing that you mentioned would come about. We thought that we could treat it.

Mr. SANDERS. Let me just ask you again, this is a God forbid scenario——

Secretary THOMPSON. And we didn't pull this figure out of the air, I want you to know, Congressman. This is a scientific panel that reviewed this and made this recommendation to me.

Mr. SANDERS. All right. If an aerosol was dropped on our three largest cities, you would have more than 12 million people. Wouldn't all of those people want to go——

Secretary THOMPSON. We also have the 12 million for 60 days and we would go back into the market and purchase more during the 60 days.

Mr. SANDERS. Thank you very much.

Mr. SHAYS. I thank the gentleman.

Mr. Tierney, thank you for your patience.

Mr. TIERNEY. Thank you.

I've only got two or three questions, following up on my colleague, Mr. Sanders' on Cipro, there are press accounts that Cipro struck a deal with one of the generic manufacturers, and basically

received millions of dollars from that generic manufacturer to not go into competition on that. What are your feelings about that specifically?

I also understand the FTC may be bringing action against them for an antitrust violation. But what are your specific feelings about that incident, but also on a broader scale, what ought we do to do about that in terms of the whole marketplace?

Secretary THOMPSON. I really have no knowledge of that lawsuit. I've heard about it, I have not investigated it myself, Representative Tierney. And I will, now what you've mentioned it, but I haven't had time to delve into it.

I do know that those individuals want to come and talk to me about that lawsuit, and I intend to do so. But at this point in time, I do not have the background information in order for me to properly respond to your question.

Mr. TIERNEY. During the first Bush administration, Mr. Bush, Sr., there was a public health representative on the National Security Council. My understanding is that President Bush stopped that practice. What's your recommendation with regard to that? Do you favor having a public health representative on the National Security Council?

Secretary THOMPSON. Yes. But I have not been asked about it.

Mr. TIERNEY. You've not even been asked? Let me say, we had an occasion over the last weekend to meet with most of the first responders in the District, police officers, firefighters, EMTs, public health people. One of the major topics that they had was communication, in terms of getting the message from people at the Federal or State level and getting it themselves and then being able to disperse it to the public so that it was consistent, it didn't cause confusion, didn't cause panic.

What do you propose for information sharing for the CDC and the public health people on through that will sort of help that process, be one that's a message of consistency that flows all the way down to the local level so that people have some appreciation and feeling of security that they're getting accurate information and that they can rely on it?

Secretary THOMPSON. We've been tempted to rectify that problem. In the last 10 days I have had a telecommunications conference with the head of CDC, Jeff Koplan, and myself, with all the State health directors on a Saturday afternoon. And it went very well. Since then, we've had a teleconference with the State legislative leaders, the National Governors organization, the American Hospital Association and the American Medical Association. Every day in the last 5 days we've been holding teleconferences with the press from my office, with health officers and myself.

So we are reaching out, getting as much information as possible. We've also put up on the Web site at CDC how to handle anthrax and information that you need to know. We also opened up the 24 hour hot line for anybody that wants to call into CDC. We also have a 24 hour hot line going into our war room downstairs on the sixth floor. So there's plenty of ways that you can get information, and we're trying to educate the American public, and we're trying to give as much information as we possibly can about public health.

That's why we're reaching out with these teleconferences, these press conferences and these 24 hour hot lines that we set up at CDC and here in the Humphrey Building.

Mr. TIERNEY. The feedback is that those hot lines have been extraordinarily helpful. So I want to thank you and your staff for that, but ask you, that 24 hour, 7 days a week hot line, is that something you intend to continue?

Secretary THOMPSON. For the foreseeable future, I don't know when this terrible thing is going to——

Mr. TIERNEY. You have no plans of taking it down, or whatever, because it has gotten a great response, people are receptive to it.

Secretary THOMPSON. We're trying to. We're trying to do more. We're reaching out, you know, wherever we possibly can, and other groups, now we're looking into the specialized medical groups, especially the emergency wards, being able to have a teleconference with them. A lot of those were on the American Medical Association, I think there were 50,000 doctors on that teleconference hookup that particular day that Jeff Koplan and I did it. So we know that there's an interest out there, and we're trying to do more of that, Congressman. And if you've got any suggestions, we'll be more than happy to take them up and try to implement them.

Mr. TIERNEY. Thank you very much.

I yield back the balance of my time.

Mr. SHAYS. I thank the gentleman.

We have another new member, Dr. Weldon, and then I'll finish up.

Dr. WELDON. Thank you, Mr. Chairman.

Secretary THOMPSON. I've tried to get hold of you and return your call. I had my deputy secretary call you.

Dr. WELDON. Well, thank you for trying to get back. And certainly I want to thank you for all the work that you're doing in this arena. I've been listening to you and you're sounding less like a lawyer and more like a doctor when I hear you on television. [Laughter.]

Mr. SHAYS. That may not be a compliment. [Laughter.]

Secretary THOMPSON. In this case I'll take it as one.

Mr. SHAYS. You should.

Dr. WELDON. And I just got here, so I apologize if I cover some territory that maybe already has been covered.

But the two postal workers that died, I understand one of them had been in the emergency room and had been sent out and then came back. And as I'm sure you know, the nature of inhaled anthrax is, it's very fulminant and in its very early hours of presentation mimics the flu or a cold. I heard you mention in response to one of the questions a very high level of interest amongst the medical profession. Can you just briefly outline some of the things HHS is doing to educate the medical profession, particularly in the Washington, DC, area, to look for certain indicators that they may be dealing with anthrax?

Secretary THOMPSON. I'd rather have Scott Lilibridge answer that question, because he's in charge of that particular portion of it.

Mr. LILIBRIDGE. Just a few things, sir. Some of the things that they've done to help educate the medical community actually start-

ed over the past several years. They've included work with the American College of Emergency Physicians to help develop a curriculum that could be used to help educate their staff, their officers, their physicians that work in that guild.

The other things that are going on presently in town, and more of a real time effort, is our work with HHS with the Department of Health, the District Department of Health. It has involved quite a bit of information, health alerts, it's involved some of the disease recognition activities and a number of continuous press briefings to update the public on different aspects of cases as they emerge and information about how they may present and what to be on the lookout for.

On a more long term basis, and a national basis, things like the Health Alert Network are beginning to send out things, particularly during this event, on a more real time event with clinical information about sensitivity to the drugs, updates on clinical findings in terms of States and locations, and beginning to help people piece together the national mosaic and how this is fitting together.

Dr. WELDON. I'm curious about the level of cooperation from DOD. I was in the Army for several years, and there were some fairly knowledgeable experts on these issues, anthrax, bioterrorism in general. Are you finding the level of cooperation to be very good, are you getting a lot of data and help from the experts in the various branches of the military that are working in this arena?

Secretary THOMPSON. Congressman, we really have. We're cooperating very nicely. What I did is I took a hearing room down on the sixth floor of the Humphrey building and turned it into a huge room, a clearinghouse, a conference room. And we have people there from the Department of Defense, and from FEMA and from the Public Health Service. That is open 24 hours a day.

We also have meetings every morning, somewhere around 7:30, 8 a.m., to get intel, which is from the CIA, Department of Defense, from the FBI and from the Public Health. Those meetings are very good because we're exchanging information. That exchange of information is going on throughout a 24 hour day. Our hearing room downstairs is open 24 hours a day, 7 days a week. And Scott Lilibridge is in charge of that, and he's pulled together a great team. It's right across the corridor from my office, so I get over there very frequently to find out what's going on.

We also have meetings from the various agencies, almost on a daily basis.

Dr. WELDON. I'm sure you've probably covered this already, but being a physician myself, I've had Members of Congress approach me about just putting everybody on antibiotics and I've had to explain that may not be the appropriate thing to do. People can have side effects, occasionally you get rare, serious side effects, occasionally life threatening side effects. And at least in the case of the House and Senate exposure, the surveillance of testing the nasal swabs on the employees, staff, has shown that the original number of 28 or 30 people——

Secretary THOMPSON. Thirty-one today.

Dr. WELDON [continuing]. It's limited to them, as I understand it. It would be inappropriate to take all the thousands of people who work in these buildings and put them on antibiotics. And ditto

for the postal workers, that it's appropriate for the ones at high risk who have been exposed to be put on antibiotics. But for the others, to do the surveillance and determine if there has been an exposure level.

Secretary THOMPSON. I addressed that in my statement, Congressman Weldon. I indicated we're going to be much more aggressive dealing with postal workers. And when we find that there has been an exposure, we're going to go in there and treat them with prophylactics much more aggressively than we have in the past, just because we have found that it needs to be done.

Dr. WELDON. I totally support that, particularly the ones in that Brentwood facility. I understand that part of the problem there was, those letters came through a letter sorting machine that they clean at the end of the day with a compressed air gun, and it may have just thrown the anthrax up in the air and these poor souls may have inhaled lethal amounts right at that time.

Secretary THOMPSON. That is being examined. We do not have conclusive evidence that's what took place, but that is part of the speculation that took place.

Did you want to answer that, Scott?

Mr. LILIBRIDGE. No, I just wanted to add, that's exactly correct. Those individuals at Brentwood are being prophylaxed at this time, and an ongoing environmental investigation is in progress.

In lieu of having all the results, we've gone ahead and erred on the side of caution, and began to prophylax that population as well as looking at the substations that drain or relate to Brentwood.

I do want to mention two things, one, compliments to the Mayor and the District health officer for their continued stewardship of this issue and keeping the message clear, informing the public and playing a key leadership role in this response.

Dr. WELDON. Well, thank you very much. Before I yield back, I want to thank all of you for the hard work you're doing, particularly you, Mr. Secretary. I certainly thank the President for the leadership role he is providing our Nation in this arena. By him putting all the resources of agencies like yours to work to combat this terrorist attack that we will be able to be victorious in the end, and America will be able to get back to business.

Thank you so much, and I yield back.

Mr. SHAYS. I thank the gentleman very much.

Mr. Secretary, I'm last, and I have a number of questions. I'd like to see if I can get through them.

And I want to say to you that besides what our committee has done for the last 2½ years, basically the members here were on a committee that oversaw HHS for 4 years before that, and we've seen the Department of Veterans Affairs for now 8 years, and have gotten into issues like Gulf war illnesses and the whole military anthrax program.

So one of the questions I'm going to be asking is how your program differs in terms of anthrax to the needs of the military. But before I do that, I want to come back to the original question I had asked. It's clear that you are not advocating at all dealing with smallpox, that all Americans be vaccinated.

Secretary THOMPSON. That's right.

Mr. SHAYS. But that you are looking to have a greater supply. And it's clear that we have 15 million, 12 million of the finest quality and 3 million that's a little lesser quality and you can dilute that.

I just want to be very clear, though. In terms of the dilution, the five to one, will this be a sign-off by FDA or an acknowledgement that you've done it, and how—I don't need to know about how we're going to determine the trial now, because I'm going to get to other questions. But I need to know, really, whether FDA signs off on this, are you going to overrule FDA and so on?

Secretary THOMPSON. FDA is working in collaboration with us. But I think Dr. Egen should respond directly to that question.

Dr. EGEN. I think the dilution studies are being conducted under IND. So it's with the approval of the FDA. The FDA will oversee the trial.

Mr. SHAYS. So if they're successful, FDA will acknowledge that they're—and sign off?

Dr. EGEN. Oh, absolutely. And that's being done now.

Mr. SHAYS. In terms of the production of new smallpox vaccine, I'm interested that you have to go through the trials, you have basically three phases after you've dealt with the animal side of the investigation. And I'm not talking about the typical argument that the pharmaceutical industry can say FDA takes too long. We're not talking about that kind of 12 years and sometimes the pharmaceutical companies can be at fault. Here we're talking about wanting it, agreeing to speed it up as quickly as possible.

But you still are going to do all three phases, correct?

Secretary THOMPSON. Correct.

Mr. SHAYS. Do you still want to respond?

Dr. EGEN. Yes. I think you're starting off at a better point. You're starting with a virus, a vaccine virus that you've already worked with and you know is effective against smallpox. It's eradicated smallpox in the world. So it's not like we're taking a disease, isolating the disease——

Mr. SHAYS. It's a new vaccine?

Dr. EGEN. It's a new vaccine in one way, in a sense, it's going into a different cell substrate. And there is the possibility of change there. For example, using a human cell or an animal derived cell, nobody's going to make the vaccine on the skin of calves any more. We're going to do it in cell substrates.

And then look for or use the surrogate markers that we've got. Dr. Fauci talked earlier about looking at the take rate. So that's certainly one of the things——

Mr. SHAYS. And we would do that with a new vaccine?

Dr. EGEN. We'll look at that, we'll do that with the new vaccine, again, under IND, looking for take rate, looking at immunological responses to the vaccine, comparing those to the currently licensed vaccine, the current vaccine, the dry vaccines, from Wyeth Lederle, and looking for similarity of immunological response, whether those immunological response are cross-neutralized——

Mr. SHAYS. That's going to tell you about the efficacy, but it may not tell you about the safety, correct? In other words, with the old vaccine, 1 out of 1 million would literally die. Somewhere, I heard the number 200,000 would have very serious, 1 out of 200,000

would have a very serious adverse reaction, which raised the question of the vaccinia immunoglobulin which we are producing now, which is to deal with those adverse effects. We have to go through a study, a trial on that as well, with VIG?

Dr. EGEN. I think if you're going to be licensing new sources, going through studies to compare them with the currently licensed material.

Mr. SHAYS. And are we in the process of trying to get additional VIG as well?

Dr. EGEN. Yes.

Mr. SHAYS. But we won't have to do more studies for that?

Dr. EGEN. Well, to compare those new sources or new preparations with older, existing preparations. So there are some studies, yes.

Mr. SHAYS. Going back to, just now going to anthrax, our committee has taken exception to the mandatory program that the military had for anthrax for a variety of reasons, but one was it was sole-sourced. Another was that it was an old vaccine and we had wasted many years developing a new vaccine, six shots. They arbitrarily decided to give three shots instead of six, even though the protocol doesn't allow for that. They did it because ultimately they started to run out.

We literally have a few, 10,000 of it, I mean, we don't have a lot. That's public record. And the issue is, what kind of pressure ultimately, how are we going to respond to BioPort? They have 11 lots of it, around 200,000 a lot, I don't understand.

Secretary THOMPSON. There are about 5 million.

Mr. SHAYS. But some of it is their new batch, and the other is old batch that has lost some of its efficacy, its potency. So you all are going to have to make a decision on the new production, and you're going to have to make a decision on the 2 to 3 million of old lots vaccines. And I'm interested to know whether you are basically going to just allow them to use it, I want to know what's happening here. I want to have a sense that we aren't pressuring FDA into saying, OK, let's move forward because we have a national emergency.

Dr. EGEN. Are you asking the Secretary if he's pressuring FDA to do things?

Mr. SHAYS. I'm asking about the real concern. Let me just be real clear about it. This is not new territory for us. During the Gulf war, we decided to have 700,000 of our troops take peritostigmine bromide [PB], and we used it as a prophylactic. It was an approved drug, but we used it in a prophylactic way.

And there are some real questions as to whether that was advisable, and there were some real questions about whether the FDA shouldn't have stepped in, and there were some real questions about whether protocol was followed. The troops weren't told about how they should take it, when they should take it, records weren't kept on who took PB and so on. So this is a history that goes well beyond any Secretary.

And I'm just concerned we are in a warlike condition, and I would just like to know what the policy will be of the Department.

Mr. SHAYS. Let me answer that. They have about 5 million samples of vaccine, 3 million of which is licensable and 2 million of

which is going to have to be inspected. FDA is going to have to do the inspection, FDA is going to have to go and inspect their new building that they're remodeling, or reconditioning a new building, but reconditioning and remodeling it. They have just filed, as of last Friday, an application for certification, and FDA will be going in there as soon as its completed. If it's completed and it's up to the specification that FDA approves, they should be operational by November 22nd. It was originally going to be the 15th, now it looks like it's going to be the 22nd.

But I can assure you, Congressman, nobody is pressuring FDA to approve this. There's been an ongoing conflict between FDA and BioPort for some time. That conflict has been brought on mainly by BioPort for not performing a good manufacturing system.

They are improving that and modernizing and cleaning their plant and now we go in and be inspected by FDA. And FDA will give it a very close and scrutinize very carefully all the problems they've had in the past to make sure that it's up to speed before it introduces and starts manufacturing again.

As far as the 5 million, most of that will have to be reinspected, yes.

Mr. SHAYS. Let me just say that this, we are also asking the same question of DOD as well, because in this case it becomes an investigatory type drug. And I would want to know if we will require informed consent by those who will be taking the drug. Smallpox, if we move forward—I'm sorry, I've moved to smallpox.

Dr. EGEN. Will it be done under IND?

Mr. SHAYS. Yes, OK. And that will require informed consent?

Dr. EGEN. When it's done under IND, it does require informed consent, absolutely. The dilution studies——

Secretary THOMPSON. No, he's talking about the new stuff. You will have to be informed, and the person, before he receives the smallpox, would have to be informed and would have to give his or her consent.

Mr. SHAYS. Mr. Secretary, is there a question we should have asked that you want to respond to?

Secretary THOMPSON. No, I think—[laughter]—you've done a very effective job and I'm very happy to have you here. I hope you stop down and see our room before you leave.

Mr. SHAYS. We will stop down.

Secretary THOMPSON. And I want to thank you.

Mr. SHAYS. And I want to thank you, and say the President and the country is fortunate to have you as Secretary.

Secretary THOMPSON. Thank you very much, Congressman.

Mr. SHAYS. We'll have a 1-minute break and then we'll call our next witnesses up.

[Recess.]

Mr. SHAYS. Thanks to the courtesy of the Deputy Assistant Secretary of Defense, she's waiving what we have as a typical protocol and allowing our next three panels to meet as one panel. And so I'm going to be asking all three panels, I'll be calling them all up at once. We have Dr. Anna Johnson-Wineger, Deputy Assistant to the Secretary of Defense for Chemical/Biological Defense Programs, Department of Defense.

We have Dr. Nancy Kingsbury, Managing Director for Applied Research and Methods, General Accounting Office. And you'll be accompanied by, and behind you will be Janet Heinrich, Dr. Sushil K. Sharma, and Jack Melling. I'd like to swear them in as well.

And then Stephen G. Sudovar, thank you, who is president and chief executive officer of EluSys Therapeutics, Inc., and Dr. Una S. Ryan, president and chief executive officer, AVANT Immunotherapies, Inc.

I need to swear you all in, and I would ask you to stand. Do we have everyone here?

Dr. KINGSBURY. Dr. Melling seems to have taken more than 1 minute.

Mr. SHAYS. Well, if he doesn't get back soon, we won't be able to hear from him. We'll take a minute here. He is such a delightful gentleman, I do want to make sure he's sworn in.

I will now ask all of you to stand and I'll swear you all in.

[Witnesses sworn.]

Mr. SHAYS. Note for the record that our witnesses have responded in the affirmative.

Dr. Wineger, I do want to thank you for your flexibility in the protocol issue. I think it will make it easier for all of you to make your statement and easier for us to question all of you. You won't all—it will make it go by a bit quicker and more efficiently. So thank you.

I'm going to tell you, you'll have 5 minutes and then you'll have another 5 minutes to roll over. Given that you've been so generous, I'll even give you a bit more than the rest.

STATEMENT OF ANNA JOHNSON-WINEGER, DEPUTY ASSISTANT TO THE SECRETARY OF DEFENSE FOR CHEMICAL/BIOLOGICAL DEFENSE PROGRAMS, DEPARTMENT OF DEFENSE

Ms. JOHNSON-WINEGER. Thank you, distinguished members of the panel. I'm honored to be here today to address your committee and to try to answer any questions that you might have.

As a matter of introduction, my name is Anna Johnson-Wineger. I am currently the Deputy Assistant to the Secretary of Defense for Chemical/Biological Defense Programs. I have a Ph.D in microbiology and have spent 35 years working for the Department of Defense.

At your request, I will focus my remarks today on force protection and in particular, on our current and planned capacity to immunize against outbreaks of disease that may result from intentional exposures to biological warfare threat agents. As you know, these include a number if etiologic agents and you asked specifically that the Department address anthrax, smallpox, tularemia, plague, hemorrhagic fevers, etc.

I am also prepared to address my understanding of the current FDA regulatory environment for the developmental testing and licensure of vaccines for protection against biological warfare threat agents and the role of the private sector in the development of these needed vaccines. I believe the vaccines are and will remain a cornerstone of force protection against biological warfare threats for the military.

I will focus my testimony on the medical aspects of force protection, realizing all the while that the Department of Defense does indeed have a comprehensive program of which medical is one component. Each year we have a technology area review and assessment. This last year that TARA group characterized our medical biological defense research program as a "well-balanced, strategic road map focused on warfighter requirements."

I would also like to mention that in accordance with the Government Performance and Results Act, which I know you support strongly, we have developed performance metrics in the form of technology readiness levels and exit criteria have been developed in support of our medical biological defense research program.

Finally, I wanted to point out that all aspects of our program are encompassed without our joint future operational capabilities for the military. Clearly, the discovery, development and production of FDA licensed vaccines for biological warfare defense embodies a very challenging undertaking for us.

With specific regard to anthrax, the FDA licensed anthrax vaccine represents old, well established technology. Each of us is familiar with the difficulties encountered in the FDA compliant production of the anthrax vaccine in BioPort, so it is not my intention to review these problems at this point. However, I am prepared to answer any questions that you might have.

I think that one of the things the Department of Defense learned from this experience, and indeed, there are many things, is that while successful vaccine research and development is necessary, it alone is not sufficient to meet our force protection needs. FDA compliant production capability, with sufficient capacity, is essential for our force protection. Establishment and licensure of vaccine production facilities, whether public or private, is a relatively expensive, technically complex, and long lead time project for each and every vaccine and procurement program that we support.

As you are well aware, the former Deputy Secretary of Defense, in his July testimony concerning anthrax vaccine, before the Subcommittee on Military Personnel of the House Armed Services Committee, testified that he had directed that an independent panel review and report on DOD's overall management of acquisition of vaccines. The report of that panel was submitted to the Congress this year as part of DOD's response to Section 218 of the Floyd Spence National Authorization Act for Fiscal Year 2001, Public Law 106–398. This report addresses a number of issues concerning acquisition of biological defense vaccines and I'd like to point out just a few of those to you.

This independent panel pointed out that the DOD has been unsuccessful in attracting large, established vaccine manufacturers to support our biological defense needs. The independent panel found that participation by the pharmaceutical industry is an essential element in securing FDA licensed, safe and effective vaccines. They found that barriers to industry participation include the size and scope of the vaccine requirements, episodic DOD production requirements that lead to idle manufacturing, industry concerns about program stability and political considerations, DOD procurement practices and acquisition regulations that are inconsistent with the vaccine industry's best practices and model for success.

The panel recommended that application of a combined, integrated approach by the Department of Defense and industry would enable a successful program.

Three key findings of the independent panel included the following points. No. 1, the scope and complexity of the DOD vaccine requirement is too great for either the DOD or the pharmaceutical industry to accomplish alone. Two, the resources do not match the requirements. Using an eight scale vaccine as a target, the panel estimated that the DOD acquisition of vaccine production would require between $2.4 billion and $3.2 billion in R&D costs over a 7 to 12 year period.

Additionally, when considering a Government owned, contractor operated or a contractor owned, contractor operated facility, with an initial capacity to produce three or four vaccines, including pilot production and scale-up, would require approximately $370 million in construction. This is in close agreement with the DOD estimate of $386 million.

Finally, the independent panel pointed out that vaccine acquisition is indeed different from weapons acquisition, and success within the Department of Defense will require different procedures. The panel recommended a lean, streamlined, technically competent vaccine acquisition management organization. Strong technical leadership is imperative at all levels, from the laboratory to senior management. Stable, long term funding with full flexibility to move resources to match these requirements is essential. Procurement practices need to move to closely approximately industry practices. And vaccine programs must be fully integrated from discovery through licensure.

I have hosted several meetings of a Federal interagency working group on vaccine acquisition. Participants in that group have included representatives from the Department of Human Health and Services, such as CDC, FDA, NIH, the Public Health Service, the Office of the Surgeon General of the United States, as well as representatives from the Department of Agriculture, USAID, the National Security Council, the Office of Management and Budget, and the Office of Science and Technology Policy. That group generally agreed that an approach and the need for GOCO or a COCO vaccine production facility to complement the private sector capacities is what is required.

In the interest of time, I will ask that the rest of my statement be entered into the record as written, and would just like to conclude with a few comments. Because I know that you're particularly interested in our work on a new anthrax vaccine and a new smallpox vaccine, so just let me add a few more comments here.

We do have indeed an approach for a new anthrax vaccine. And we have a candidate vaccine, which is a recombinant protective antigen product. At present, the joint program office projects attainment of a baseline amount of this material in the year 2007. And we are working with the DynPort vaccine company to make this happen. And in accordance with your questions earlier, that will be done under the full jurisdiction of the FDA with phase one and phase two studies for safety and immunogenicity and will be administered under written informed consent during those early phases of the study.

With regard to smallpox, as was mentioned in previous testimony, prior to 1972, smallpox vaccination was routine. Wyeth Laboratories produced the licensed vaccine and the remaining stocks are, as you know, under the control of CDC. The DOD has an R&D program to identify potential new vaccines and new anti-viral drugs as well. A smallpox vaccine is one of our highest priorities, and the DOD has contracted with Bioreliance to make small amounts of good manufacturing practices production. And we have a phase one clinical trial scheduled for January 2002.

We hope to be able to accelerate production of that material, and we are currently evaluating ways to accelerate our time line for a new smallpox vaccine.

As you are aware, we have a comprehensive program looking at many other vaccines. I think that addresses the comments from this morning, that while anthrax and smallpox are our No. 1 and No. 2 priorities today, the threat is indeed much broader than that.

And I would just like to mention that we do have ongoing research and development programs looking at such things as multi-agent vaccines, medical counter-measures for a number of other threat agents, and needle-less delivery methods for some of the recombinant protein vaccines. I think that you would agree that the DOD vaccine program is technically very complex.

Our requirements are diverse and challenging. And for the near term, our vaccine dependent medical readiness for force protection against biological weapons and the terrorist use will be limited. Over the long term, we are committed to effective immunization as one cornerstone of force protection for the military. Realization of this goal will indeed require changes in our business practices, expanded participation by the pharmaceutical industry, hopefully complemented by a dedicated vaccine production facility, and indeed, a long term national commitment to the success of this program.

[The prepared statement of Dr. Johnson-Wineger follows:]

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SECURITY, VETERANS AFFAIRS, AND INTERNATIONAL RELATIONS
HOUSE COMMITTEE ON GOVERNMENT REFORM

STATEMENT OF

DR. ANNA JOHNSON-WINEGAR

**DEPUTY ASSISTANT TO THE SECRETARY OF DEFENSE
FOR CHEMICAL/BIOLOGICAL DEFENSE**

**DEPARTMENT OF DEFENSE
BIOLOGICAL WARFARE DEFENSE VACCINE RESEARCH & DEVELOPMENT
PROGRAMS**

ON

**TUESDAY
OCTOBER 23, 2001**

BEFORE THE

**SUBCOMMITTEE ON NATIONAL SECURITY, VETERANS AFFAIRS,
AND INTERNATIONAL RELATIONS
HOUSE COMMITTEE ON GOVERNMENT REFORM**

FIRST SESSION 107th CONGRESS

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NATIONAL SECURITY, VETERANS AFFAIRS, AND
INTERNATIONAL RELATIONS
HOUSE COMMITTEE ON GOVERNMENT REFORM

Good afternoon, Mr. Chairman and distinguished members. I am honored to appear before your committee today to discuss the near-term and long-term role of vaccines in preparedness against biological warfare and terrorism. I am Dr. Anna Johnson-Winegar, Deputy Assistant to the Secretary of Defense for Chemical and Biological Defense.

At your request, I will focus my remarks on force protection and, in particular, on current and planned capacity to immunize against, or contain, outbreaks of disease that may result from intentional exposures to biological warfare (BW) threat agents. These may include a number of etiologic, or disease-causing, agents and you asked that the Department address anthrax, smallpox, tularemia, plague, and hemorrhagic fevers, et cetera. I am also prepared to address my understanding of the current Food and Drug Administration (FDA) regulatory environment for developmental testing and licensure of vaccines for protection against BW threat agents and the role of the private sector in the development of needed vaccines.

Vaccines are and will remain the cornerstone of force protection against BW threats for the foreseeable future, near and far-term. Prevention of the devastating and life-threatening health effects posed by BW threats by prior immunization is the quintessential element of our comprehensive strategy that also includes detection, avoidance, diagnostics, therapeutics, individual and collective protection, and decontamination. The DoD Technology Area Review and Assessment (TARA) has characterized the medical biological defense research program as a "well-balanced strategic roadmap focused on warfighter requirements." I will focus my testimony on the medical aspects of force protection, emphasizing the DoD vaccine program and capacity in preparedness against BW and terrorism.

I should also mention that in accordance with the Government Performance and Results Act, performance metrics in the form of Technology Readiness Levels and exit criteria have been developed in support of the medical biological defense program. All aspects of the program are encompassed within the Joint Future Operational Capabilities.

Defense Acquisition of Vaccine Production

We are all familiar with the difficulties, complexities, and frustrations encountered in FDA-compliant manufacturing of sufficient quantities of the anthrax vaccine. I don't intend to review these at this point. Rather, it is important to understand that anthrax vaccine represents an old, well-established technology. For many, the "lesson-learned" has been that research and development of a vaccine technology, though necessary, is not by itself sufficient to fulfill our force protection needs. FDA-compliant production capability and sufficient capacity are essential for force protection. Establishment and licensure of vaccine production facilities, whether public or private, are relatively expensive, technically complex and long-lead time projects within every vaccine research, development, licensure, and procurement program.

In his July 13, 2000 testimony before the House Armed Services Committee, Subcommittee on Military Personnel, concerning anthrax vaccine, the Deputy Secretary of Defense testified that he had directed that an independent panel review and report on DoD's overall management of acquisition of vaccine production. The report of the Independent Panel was submitted to the Congress this year as part of the Department's response to Section 218 of the Floyd D. Spence

National Defense Authorization Act for Fiscal Year 2001, Public Law 106-398. The Section 218 report addresses a number of issues concerning acquisition of biological defense vaccines.

The Independent Panel found that vaccines are the lowest risk, most effective protection against BW threats; better than antibiotics and enable force projection. As we have previously testified, the Department has not been successful in attracting large, established vaccine manufacturers to support our biological defense vaccine needs. The Independent Panel found that participation by the pharmaceutical industry is an essential element of success in securing a ready and reliable access to FDA-licensed, safe, and effective vaccines for protection against BW threat agents. Barriers to industry participation include the size and scope of our vaccine requirements, episodic DoD production requirements that lead to idle manufacturing that is contrary to both industry practices and efficient and effective FDA compliance, industry concerns about program stability and political considerations, Defense procurement practices and DoD acquisition procedures that are inconsistent with the vaccine industry's best practices and model for success. The Panel recommended that application of a combined, integrated approach by Defense and industry will enable a successful program.

Specific findings of the Independent Panel include the following key points that are presently under review and consideration by Defense Department leadership.

- *The scope and complexity of the DoD vaccine requirement is too great for either the DoD or the pharmaceutical industry to accomplish alone.*

Presently in the United States, the FDA has licensed vaccines that protect against approximately 20 diseases having substantial public health consequences. The DoD biological defense vaccine program has requirements approaching that number. The pharmaceutical industry, as evidenced by recent shortages in flu and tetanus vaccines, is at full capacity. The Panel recommended establishment of a government-owned, contractor-operated (GOCO/COCO)[1] vaccine production facility and that long-term, up-front government commitment would be essential to pharmaceutical industry support.

- *Resources do not match requirements.*

Using an eight-vaccine scale, the Panel estimated that the DoD acquisition of vaccine production would require between $2.4B to $3.2B in research and development costs over a 7- to 12-year period. Furthermore, resources for a GOCO/COCO with an initial capacity of three to four products, pilot production, and production scale-up would require approximately $370M in initial construction; this is in close agreement with the Department's estimate of $386M.

- *Management Organization.*

The Panel recommended a lean, streamlined vaccine acquisition management organization. Vaccine acquisition is different from weapons acquisition and success requires different procedures. Strong technical leadership is imperative, both throughout the workforce and at all levels of management. Personnel practices must enable hiring and retaining highly qualified and experienced people. Stable, long-range funding with maximal ability to move resources to

[1] Discussed as an option but not recorded in the Independent Panel's report, a contractor-owned, contractor-operated (COCO) capability is equivalent to a GOCO and going forward the abbreviation GOCO/COCO is used.

match requirements is essential. Procurement practices need to more closely approximate industry practices. The programs must be fully integrated from discovery through licensure. Private sector advisory boards are required to support strategic planning at the executive level and program execution at the program manager level.

Over the past 2 years, I have hosted regular meetings of a federal interagency working group on vaccine acquisition. Participants have included representatives from the Department of Health and Human Services (DHHS)—including the FDA, the National Institutes of Health, the Public Health Service and the Office of The Surgeon General of the United States, the National Security Council, the Office of Management and Budget, and the Office of Science and Technology Policy. These meetings have been productive and general agreement has been reached on approaches such as recommended above and the need for a GOCO/COCO vaccine production facility to complement private sector capacity and capabilities for public health and Defense vaccine needs.

In November 2000, as addressed in the Section 218 report, a concept study was conducted to develop a new conceptual cost estimate and schedule for design, construction, fit-up, and qualification to FDA regulatory requirements for vaccine development, licensure, and manufacturing as promulgated in Title 21 Code of Federal Regulations, Food and Drugs. The first eight DoD-critical products planned included:

- Anthrax vaccine, adsorbed (AVA)
- Smallpox vaccine
- Plague vaccine
- Tularemia vaccine
- Multivalent botulinum vaccine
- Next generation anthrax vaccine
- Ricin vaccine
- Multivalent equine encephalitis vaccine

As noted, the preliminary costs for designing, building, and validating the GOCO/COCO facility are estimated to be $386M. The life-cycle cost for operations is estimated at approximately $915M over the 25-year life cycle; other government life-cycle costs are estimated to be $259M.

The Surgeon General of the United States, by letter dated January 31, 2001, supported establishment of a GOCO/COCO vaccine production facility. He noted that the list of DoD-required vaccines is very similar to those that would confront U.S. public health. The Surgeon General also observed that civilian participation could contribute to the successful planning and operation of the GOCO/COCO and that it is important that the GOCO/COCO have sufficient flexibility to accommodate evolving production requirements, both for new vaccines and for fulfilling future civilian sector needs.

Regulatory Process Governing Vaccine Development and Licensure

As requested in your October 9th letter, and before discussing the DoD biological defense vaccine R&D programs, I would like to describe the FDA processes governing these vaccines. This survey should facilitate review of the R&D programs.

The vaccine approval process is long and complex. From discovery to market can take 15 years, although the vast majority of vaccine candidates do not get into clinical, that is human, trials let alone approved. The Pharmaceutical Research and Manufacturers of America reports that for every 5,000 drugs discovered in the research and development laboratories 20 drugs will go on to preclinical trials. Of these 20 drugs, only 5 will undergo human clinical trials and only 1 will eventually get approved. We do not have information on whether the numbers related to vaccine discovery are the same as those related to the drug discovery process. It should be noted that FDA regulates drugs and vaccines in a similar manner. Since most biological products also meet the definition of "drug", I have generally used the term drug to encompass both drugs and biological products.

Below is a discussion of the stages of drug development as they relate to vaccines to protect against BW and terrorist use of BW agents. Included in the discussion is the way the current Guidelines issued by the FDA would apply to this class of vaccines. The important difference is that it is not ethically possible to demonstrate through controlled clinical testing, the current standard, that a vaccine is safe, effective, and will protect against BW agents.

Preclinical Testing. Pharmaceutical companies conduct laboratory and animal studies to determine if the vaccine under study affects the targeted disease. In addition to efficacy, the safety of the vaccine candidate is also evaluated. This process usually takes 3½ to 6 years. It is during these studies that for vaccines intended to protect against BW threats, that the animal models for surrogate efficacy are developed and validated.

Investigational New Drug Application (IND). If the preclinical testing demonstrates that the vaccine has efficacy in the surrogate model, an IND is made to the FDA. The IND becomes effective if the FDA does not place the IND on clinical hold within 30 days and it is only once the IND is in effect that human clinical trials may legally begin. The initial IND must include the method of manufacture (this can be, and usually is, refined during the drug development process); the proposed mechanism of action in humans; the results of the preclinical testing, including any toxic side effects and the surrogate model; how, where, and by whom the human clinical studies would be performed; and some information on the chemical structure of the vaccine.

Phase 1 Clinical Trials. Phase 1 studies for vaccines usually involve 10-30 healthy adult volunteers. This initial phase of clinical study is designed to test for safety by determining what happens to the drug in the human body – by studying its pharmacological and toxicological actions in humans. Dose-ranging studies are also performed during Phase 1 studies to determine the maximum tolerated dose and the minimum dose that will result in a measurable effect. About two thirds of drugs that enter clinical trials complete Phase 1 studies.

Phase 2 Clinical Trials. Phase 2 studies usually involve 30 to 100 healthy adult volunteers. This phase is designed to test for preliminary evidence of efficacy (i.e., does the drug do what it is supposed to do – produce effects that mimic the surrogate efficacy model). During Phase 2 studies, formulation buffers are studied and the final formulation buffer is determined. About one-third of the experimental drugs tested complete Phase 1 and 2 studies.

Phase 3 Clinical Trials. Phase 3 studies usually involve 1,000-3,000 patients in clinics and hospitals. These large, multicenter clinical trials are designed to prove conclusively that the drug works better than the standard treatment for the disease in question and/or a placebo. Most Phase 3 studies are randomized to the various arms of the study and double-blind, neither recipients nor test scientists know whether the study compound or a placebo is being administered. It is usual to discuss the design of the Phase 3 trial with the FDA prior to commencing the trial. By obtaining the agreement of the FDA, it is more likely that the product will ultimately be approved. All of the patients are asked to list any side effects that occur while they are in the study. Phase 3 testing usually takes around 3 years and approximately 80% of the drugs that enter this phase successfully complete the testing.

It is prior to this Phase, and to a lesser extent the other Phases, that FDA's 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 Humans Ethically Cannot Be Conducted" would guide these discussions. These discussions take place at a meeting with the FDA called "End of Phase 2/pre-Phase 3 meeting." At this meeting, agreement is reached between the FDA and the drug company on the design of the Phase 3 clinical trial.

The proposed rule can be summarized as described below:

Scope. (1) Drugs and biological products that reduce or prevent serious or life-threatening conditions caused by exposure to lethal or permanently disabling toxic chemical, biological, radiological, or nuclear substances; (2) products are expected to provide meaningful therapeutic benefit over existing therapies; (3) traditional human efficacy trials are not feasible or ethical; and (4) use of animal efficacy data when scientifically appropriate.

Proposed Rule. FDA has proposed to amend its new drug and biological products regulations so that FDA may approve a product for which safety has been established and requirements of 21 CFR 601.60 have been met based on adequate and well-controlled animal trials when results of those animal studies establish that product is reasonably likely to provide clinical benefit in humans. The FDA will rely on evidence from animal studies only where there exists reasonably well-understood mechanism of toxicity of agent, how the product prevents the toxicity, the effect is independently substantiated in multiple species, and studies include species expected to react with a response predictive for humans. The proposed rule would continue to require clinical testing data on product safety and immunogenicity.

Areas of ongoing discussion include issues such as agents that are only relevant for primates; animal study endpoint clearly related to desired benefit in humans; generally, enhancement of survival or prevention of major morbidity; selection of an effective dose in humans; and kinetics and pharmacodynamics and other relevant data, in animals and humans.

New Drug Application (NDA). Once the Phase 3 clinical trials are completed, the drug manufacturer compiles and analyzes all the data. If the data demonstrate the safety and effectiveness, as defined prospectively in the Phase 3 study design, of the drug, an NDA or Biologic License Application (BLA) is filed with the FDA. The average review time for an NDA/BLA is 2 years. However, this time can be reduced by about 1 year if the product is given priority review. Priority review means that the FDA must complete its initial review of the application within 6 months. FDA approval gives the manufacturer the right to market the drug exclusively under a trademark name for the period of exclusivity remaining for the drug.

Approval of the product based on the proposed rules is subject to three requirements. The first is postmarketing studies to verify and describe the product's clinical benefit when feasible and ethical. Such postmarketing studies may not be feasible with biological defense vaccines until an exigency arises. The second requirement provides restrictions to assure safe use and distribution. The third requirement requires labeling for users that explain that product's approval based on efficacy studies conducted in animals alone.

The proposed rule does not apply if product approval can be based on standards described elsewhere in FDA's regulations. For example, accelerated approval based on human surrogate markers or clinical endpoints other than survival or irreversible morbidity.

Phase 4 Studies. Phase 4 studies (when required) are designed for any additional data collection from patients after the drug has received FDA approval. These studies are normally required for products approved using FDA-accelerated approval rules for products approved using surrogate markers for efficacy. The data collected would confirm the efficacy of the product in long-term studies. For example, FDA currently approves cancer drugs based on evidence that the drug causes a tumor to shrink; the Phase 4 study would confirm that tumor shrinkage is correlated with long-term survival. Once the results of the Phase 4 study are analyzed and they demonstrate that the approval based on the surrogate marker are confirmed, the product is given a full approval. If however, the results of the Phase 4 study show that the surrogate marker for efficacy does not reflect efficacy, approval of the product could be withdrawn. Products for protection against BW threats would be approved using this mechanism.

The Vaccine Technology Discovery, Development, and Licensure Pipeline

I will now focus my remarks on those medical biological defense subprogram areas of immediate concern as identified in your letter of October 9, 2001. There are three major and integrated components of the medical biological defense Research, Development and Acquisition program - diagnostics, vaccines, and therapeutics. Vaccines and therapeutics are also subdivided into three areas: bacterial (e.g., anthrax, tularemia, and plague), viral (e.g., smallpox and hemorrhagic fevers), and toxins (botulinum, staphylococcal enterotoxins, and ricin).

Diagnostics. The DoD continues to actively pursue the development of diagnostic capabilities. It has developed the reagents and applied the technology to sample and detect the presence of BW agents in biological fluids. As new capabilities are developed and verified, they are inserted into existing, fielded systems.

There is an ongoing Defense Technology Objective (DTO) to develop a common platform/ device capable of diagnosing rapidly and early-on the presence of infectious disease and BW agents in clinical specimens. Two leading technologies are immunologically based membranes to detect host immune response to antigens (including their products) of biological agents, and miniaturized polymerase chain reaction (PCR) to detect and identify the nucleic acids of biological agents. An integrated specimen processing/gene amplification cartridge for rapid identification of anthrax spores has been designed and technical data package for a second generation portable PCR system is being completed in preparation for transition to advanced development this fiscal year.

The DoD TARA assessed the program as "Green" and characterized it as comprehensive and aggressive, with good collaboration and leveraging of technology and expertise, noting a need for intra-DoD and Federal Interagency standards for diagnostic reagents, sampling, and processes.

Anthrax (*Bacillus anthracis*) Vaccine. As you are aware, the DoD has a contract with Bioport Corporation to manufacture an anthrax vaccine licensed by the FDA since 1970. This contractor is the sole source of the licensed product, a matter of continued concern to the Department that is reflective of the factors limiting vaccine production and success that I mentioned earlier. Bioport has filed its response to the FDA pre-approval inspection. This is an important step in FDA approval of the Bioport BLA and resumed, FDA-compliant production of anthrax vaccine.

We are maintaining an aggressive R&D program to identify ways of enhancing the immunogenicity of vaccines through immunomodulators, as well as pursuing the development of a replacement anthrax vaccine using recombinant technology. This recombinant protective antigen (rPA) anthrax vaccine is a DTO that is showing considerable promise. Safety and efficacy studies are ongoing in laboratory models, and a potential surrogate marker of vaccine efficacy is being evaluated. In nonclinical studies, the rPA candidate demonstrated protection against inhalation exposure to anthrax. A major advantage of this technology is that resulting products and manufacturing processes are generally reproducible, yielding a consistently pure, potent, and safe product. Further, it does not have the associated facility containment problems seen with AVA production. A Technical Data Package has been prepared to support transitioning this candidate to development. The candidate rPA anthrax vaccine has transitioned to advanced development in FY01. At present the Joint Vaccine Acquisition Program (JVAP) Project Management Office projects attainment of baseline stockpile quantities in FY07 and BLA submission in FY10. The JVAP added this next generation anthrax vaccine to its prime systems contract with DynPort Vaccine Company (DVC) in FY01.

The DoD TARA assessed the rPA DTO as "Green," noting the industrial partnering for the production and purification under FDA current good manufacturing practice (cGMP) regulations.

Tularemia (*Francisella tularensis*) Vaccine. A tularemia vaccine candidate was one of the three vaccines in the JVAP base contract with DVC. This candidate is in advanced development and is completing process definition at Cambrex BioScience, Inc., in Baltimore. New assays will be required before clinical trials may be initiated and DVC has subcontracted with the Defense Science and Technology Laboratory (DSTL), UK to develop a new potency assay and assays for identity. Phase 1 studies are planned for FY03 with baseline stockpile quantities planned for FY06 and BLA submission scheduled for FY07.

Plague (*Yersinia pestis*) Vaccine. A plague vaccine was first made by Miles Cutter who then sold this line of business to Greer Laboratories. Greer then became the sole manufacturer of a licensed plague vaccine and provided DoD with the vaccine for several years. Greer apprised DoD of the impact of limited sales and required facility upgrade costs before determining it was no longer fiscally sound to continue production of the vaccine. Although this vaccine was effective against transdermal exposure to plague, it was relatively ineffective against aerosol challenge in animal studies.

The DoD has an ongoing R&D effort focused on developing a recombinant vaccine, immunomodulators, and treatment modalities for plague. There is a DTO for the recombinant plague vaccine that demonstrates efficacy in laboratory models, even against aerosol exposure. The U.S. Army Medical Research Institute for Infectious Diseases (USAMRIID) and DSTL, UK, are conducting research programs on a recombinant plague vaccine. The purification process is well under way and protective antigens, besides F and V, are being pursued. The JVAP is in the process of exercising its DVC contract option to add a plague vaccine and a Phase 1 clinical trial is planned for FY04.

The DOD TARA rated the status of the DTO as "Green," noting the potential vulnerability of a single antigen vaccine to genetically altered plague.

Smallpox (*vaccinia*) Vaccine. Prior to 1972, smallpox vaccination was a routine practice. The licensed vaccine was produced by Wyeth Laboratories and the remaining but extremely limited supply is under the control of the Centers for Disease Control and Prevention (CDC). Due to the potential problem of severe cutaneous reactions to the vaccine, vaccinia immune globulin, which is also in limited supply, should be available to treat this adverse reaction in the event of its occurrence.

The DoD has an ongoing R&D program to identify potential antiviral drugs, alternatives to vaccinia immune globulin, and a new smallpox vaccine. A model of human smallpox has been developed in nonhuman primates. The dose and schedule of the lead antiviral drug for treating smallpox have been initially established.

A smallpox vaccine was included as one of the three vaccines in the JVAP base contract with DVC. DVC subcontracted with BioReliance where the product is in cGMP production, a Phase 1 clinical trial is planned for January 2002, and a Milestone C consistency lot production decision is scheduled early this FY. The JVAP schedule is to have established baseline stockpile quantities in FY02 and the BLA submission is scheduled for FY04.

A Phase 1 clinical trial has been completed for vaccinia immune globulin and a manufacturing capability is being developed. DoD and DHHS are discussing how best to produce smallpox vaccine.

Hemorrhagic Fever Vaccine. There are a number of hemorrhagic fever (HF) viruses (e.g., Ebola and Marburg) for which the Department has an ongoing R&D effort to develop vaccines and treatment modalities. Progress has been made in characterizing HF virus infections, identifying potential surrogate markers of immunity, and establishing laboratory models for evaluating the safety and efficacy of candidate vaccines and therapeutics. Initial studies testing prime-boost candidate vaccines for HF (Marburg) have been completed and the results show promise. The DNA of the antigen of interest "primes" the immune system and the antigen serves as a "booster," stimulating the immune system to rapidly respond to the antigen. The candidates are in advanced development. A DTO for a HF virus (i.e., Ebola) vaccine is planned for FY03.

Q-Fever (*Coxiella burnetii)* Vaccine. A Q-fever vaccine was included as the third vaccine in the JVAP base contract. That development effort that was being conducted in collaboration with an Australian company was terminated. Foremost among many concerns with the candidate product was the need to conduct skin test screening for potential allergic reactions among recipients. We are evaluating other approaches.

Toxins. We have an ongoing R&D effort to develop safe and efficacious countermeasures against toxins, such as SEB, botulinum, and ricin. Monoclonal antibodies that neutralize botulinum neurotoxin serotype A and staphylococcal enterotoxin serotypes A, B, C1, and D have been generated. Recombinant vaccine candidates for botulinum serotypes D and G have been initially produced and are undergoing early efficacy evaluation. Reagents and assays to support development of candidate recombinant ricin vaccines are planned for completion this FY. Formulation studies of lead inhibitors of botulinum and SEB are ongoing. A recombinant botulinum, bivalent (AB) vaccine is in development as an exercised option on the JVAP contract with DVC. This candidate vaccine is in process definition at Diosynth-RTP, Princeton, NJ. Clinical trials are planned for FY04, and baseline stockpile is planned to be obtained in FY08 with BLA submission planned for FY11.

There is no DTO for toxins. A DTO, Medical Countermeasures for Staphylococcal Enterotoxins, has been successfully completed and a pre-IND meeting has been held with the FDA.

Other Medical Biological Defense DTOs. The Department has ongoing R&D supporting four other DTOs - Multiagent Vaccines for Biological Threat Agents, Medical Countermeasures for Brucellae, Medical Countermeasures for Encephalitis Viruses, and Needleless Delivery Methods for Recombinant Protein Vaccines. The DoD TARA recommended completion of the multivalent Venezuelan equine encephalitis (VEE) work and termination of the associated DTO. A VEE vaccine is undergoing demonstration and validation studies and the JVAP is in the process of exercising an option on its DVC contract to include a VEE vaccine. The JVAP schedule is to establish the baseline stockpile for VEE vaccine in FY08 and submit the BLA in FY11. There were no specific recommendations regarding the other three DTOs.

Finally, the Defense Advanced Research Projects Agency (DARPA) conducts high risk, high payoff research for the DoD. Genetic vaccine technologies and novel approaches to immunization are among the areas of the DARPA biomedical research portfolio that could contribute important capabilities to our long-term readiness posture.

In summary, the DoD vaccine program is technically very complex and our requirements are diverse and challenging. For the near-term, our vaccine-dependent medical readiness for force protection against BW and terrorist use of BW agents will be limited. Over the long-term we are committed to effective immunization as our cornerstone of force protection. Realization of this goal will require changes in our business practices, expanded participation by the pharmaceutical industry complemented by a GOCO/COCO vaccine capability, and a long-term national commitment to the program's success.

Mr. SHAYS. Thank you very much, Dr. Wineger.

Dr. Kingsbury.

STATEMENTS OF NANCY KINGSBURY, MANAGING DIRECTOR FOR APPLIED RESEARCH AND METHODS, GENERAL ACCOUNTING OFFICE, ACCOMPANIED BY JANET HEINRICH, DIRECTOR, HEALTH CARE-PUBLIC HEALTH ISSUES; SUSHIL K. SHARMA, ASSISTANT DIRECTOR FOR APPLIED RESEARCH AND METHODS; AND JACK MELLING, CONSULTANT

Ms. KINGSBURY. Thank you, Mr. Chairman, and I want to thank you for inviting us here today to report to you on this specific work we've done at your request that well pre-dates our current adventures with bioterrorism, to examine the changes in the manufacturing processes at BioPort and what FDA did or did not do with respect to those. And I'll get to that in just a moment.

You chose to swear in my colleagues, and that's fine. I want to be sure that you understand why they're here. Jan Heinrich is responsible for our recent work on the capability of State and local governments to respond to bioterrorism, that the health care group did. Dr. Sharma worked with me and did most of the work on this manufacturing changes job. And Dr. Jack Melling is one of our consultants, and in fact, was responsible for the production facility in the UK that produced anthrax vaccine, was on their licensure entity and also has run a biologics project in the United States. So we rely very heavily on him for his expertise.

Mr. SHAYS. I think what we'll do is, since they'll need a microphone to respond, we'll have two sit on this side and one sit on this side, and you can come on up.

Ms. KINGSBURY. Report to the front, as the gentleman suggests.

I think this committee is very familiar with the process that FDA uses for regulation under normal conditions. You asked us to look at certain changes that took place to the vaccine manufacturing process, beginning in 1990. In 1990, BioPort, or it was actually the Michigan facility owned by the State of Michigan at the time, introduced two new fermenters. They shifted from a glass fermenter to a stainless steel fermenter in 1990. That was reported as required under regulation to FDA in December 1990 and FDA approved those changes in 1993.

However, in 1993, the Michigan facility also introduced two other similar, but not identical, fermenters. And despite some advice from DOD and others that they were required to submit to notify FDA about this, they did not do so until 1999. They did report the fermenter change in 1999 and FDA approved that change in May 2001.

With respect to filters, the Michigan facility also changed filters in 1990, and the principal change was to move from a ceramic filter to a nylon filter. They changed the type of filters again in 1996 and 1997. When you asked us to do this work, we could find no evidence that these changes had been reported to FDA. And in December 2000, we met with FDA to discuss the matter with them. They admitted at the time that they were not aware of those changes, and about 2 months later, in February 2001, they wrote a letter to BioPort asking them to provide information about the impact of those changes. But of course, this is nearly a full decade

after the initial changes were made, and so BioPort submitted information to FDA in April 2001. That information was what they could reconstruct from their records. It had been the tests that were available, they seemed to be fairly straightforward.

FDA did approve the filter changes in July 2001. But I think it's important to recognize that the data provided by BioPort were not the sort of data that might be provided today if a license amendment were filed about that sort of change. And we know from, or at least Dr. Melling advises, that nylon filters absorb less protein than ceramic filters, so there is perhaps a theoretical reason to want to explore the question of whether the vaccine produced after these filter changes is different from the vaccine produced before these filter changes. That issue has not been fully explored.

When we couldn't find very much information about the actual nature of the vaccine changes, we did look for other evidence that might suggest that this issue of whether the vaccine changed should be examined. And we found two different kinds of evidence. One was a study that the U.S. Army had done at USAMRIID to apply a new methodology to attempt to measure the level of protective antigen, which is one of the components of the vaccine toxin in lots produced before and after the filter changes. That study suggested that there was a much higher level of protective antigen in the vaccine produced after the filter changes.

The author of that study, which has never been published, was quite cautious about what could be read into this information. But we have been trying to see whether that doesn't suggest that other studies might be warranted.

In addition, as you know, we have done a survey at GAO and we have been looking at the epidemiological research that others are doing on the health conditions of people who served in the Gulf war and who did or did not take the anthrax vaccine. Our study suggests, which will be published shortly, that the levels of people reporting, at least in our sample, of fairly serious systemic reactions to the vaccine are considerably higher than the levels that we are led to expect by looking at the product insert for the vaccine, which admittedly were estimates that were made during the clinical trials in the late 1960's, so it's old information. But it's the best we have.

So we think that these two things also suggest that a little more study of the impact of the filter change might be good medical practice.

We note in closing that public health vaccines that are in common use worldwide are soft of self-monitoring. If a problem arises, people tend to find out about it, they tend to look into it. Biodefense vaccines are in a different category, because the disease against which they are created is not commonly experienced until we have an emergency, and we think that suggests that both the manufacturing practices and the surveillance of people who take the vaccine ought to be somewhat more rigorous than what might otherwise be the case. And we leave you with that thought, and we'll be happy to accept your questions.

[The prepared statement of Ms. Kingsbury follows:]

United States General Accounting Office

GAO

Testimony
Before the Subcommittee on National Security, Veterans' Affairs, and International Relations, Committee on Government Reform, House of Representatives

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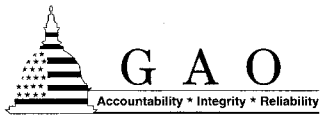
ANTHRAX VACCINE

Changes to the Manufacturing Process

Statement of Nancy Kingsbury, Ph.D., Managing Director, Applied Research and Methods



GAO-02-181T

Mr. Chairman and Members of the Subcommittee:

We are pleased to be here today to contribute to your hearing on biological warfare defense vaccine programs. This topic is of considerable urgency today in light of the terrorist attacks of September 11 and the exposures to anthrax in recent weeks. Our testimony today is limited to the work we have done in response to your October 2000 request to review the changes to the manufacturing process for the anthrax vaccine that has been produced by the BioPort Corporation and its predecessor entities. As you know, BioPort is the sole facility in the U.S. currently capable of producing anthrax vaccine.

My testimony today will address the changes that occurred in the manufacturing process for anthrax vaccine since 1989, and the status of the approval of those changes by the Food and Drug Administration (FDA). It is, of course, FDA's responsibility to determine that the anthrax vaccine is safe and efficacious, and it is our understanding that FDA officials will be undertaking a review in the near future to determine if vaccine production can be resumed. We appreciate the opportunity to provide information that may be relevant to that determination.

A brief summary of our scope and methodology is provided in appendix I. A list of related GAO products is presented in appendix II.

Background

The original anthrax vaccine was developed by George Wright and others in the 1950s and was first produced on a large scale by the pharmaceutical company Merck Sharp & Dohme (Merck).[1] A clinical study in 1962 evaluated the safety and effectiveness of the Merck vaccine in mill workers.[2] The results of this study formed the basis for subsequent licensure of the vaccine in 1970. The original license for the production of anthrax vaccine was issued to the Michigan Department of Public Health by the Division of Biologics of the National Institutes of Health.[3] In 1995, the facility changed its name to the Michigan Biologic Products Institute.

[1] Merck Sharp and Dohme is currently known as Merck and Co., Inc.

[2] The most common occurrence of anthrax infection has been in industrial settings like wool mills where workers may be exposed to infected animal products.

[3] Prior to the establishment of FDA as the licensing authority for vaccines, the National Institutes of Health was responsible for licensing.

In 1998, the facility was sold, and its name was changed to BioPort Corporation.

Today, FDA, through the Center for Biologics Evaluation and Research (CBER), licenses biological products (that is, biologics) and the facilities in which they are produced. The manufacturer is required to comply with current Good Manufacturing Practices (cGMP) regulations, which regulate personnel, buildings, equipment, production controls, records, and other aspects of the vaccine manufacturing process. [4]

When there is a major change in the manufacturing process—defined as a change determined by FDA to have a substantial potential to adversely affect the identity, strength, quality, purity, or potency of a product in relation to safety or effectiveness—the manufacturer must submit evidence to FDA demonstrating that the change does not have any such adverse effects. This requirement is particularly important for vaccines since the quality of biologics cannot be ensured solely from final tests on random samples. Instead, the quality of biologics can be determined only by a combination of strict control of the entire manufacturing process, in-process tests, and end-product tests. When significant process changes are made, the onus is on the manufacturer to ensure that the quality of the product is maintained after such changes are introduced. Depending on the changes made, this may require trial studies (with animals or humans) to evaluate the impact of the new process, followed by comparison of pre- and post-change lots before releasing the post-change lots for use.[5]

As our testimony today reports, in the case of the anthrax vaccine, the Michigan facility did not notify FDA of a number of changes made in the manufacturing process in the early 1990s and no specific studies were undertaken to confirm that vaccine quality was not affected. FDA inspectors did not inspect the Michigan facility's anthrax production room

[4] cGMP embodies a set of scientifically sound methods, practices, or principles that are implemented and documented during development and production to ensure consistent manufacture of safe, pure, and potent products. Such principles apply to the manufacturing process as well as to the facilities in which products are manufactured. (21 C.F.R., parts 600 through 680.)

[5] FDA guidance states that, if significant changes to the manufacturing or formulation of a vaccine are made after the original clinical trial, bridging studies may be used to demonstrate that immunogenicity and the occurrence of common adverse events have not been affected adversely by these changes. Anthony, B.F. and A. Sutton, "The Role of the Food and Drug Administration in Vaccine Testing and Licensure," *New Generation Vaccines*, New York, Marcel Dekker, Inc., Ch. 73, p. 1191.

until 1993. According to FDA, access was not granted because its inspectors had not been vaccinated against anthrax. FDA inspectors were able to perform some aspects of inspection—for example, reviewing records—but not equipment and production.[6]

The inspections that FDA ultimately was able to conduct over time found a number of deficiencies, many of which were not corrected in a timely manner. For example, the deficiencies that FDA identified it its February 1998 inspection fell broadly into two categories: (1) those that, although serious, might affect only one or a limited number of batches that were produced when the deficiency was extant and (2) those of a generic nature that could compromise the safety and efficacy of any batch or all batches. Vaccine production was suspended after these findings, and BioPort has been attempting since then to bring the facility and manufacturing process into compliance. We understand from recent testimony by the Secretary of Health and Human Services that BioPort has recently submitted an application for an FDA inspection to approve its facility and manufacturing process.

Changes to the Fermenters and Filters in the 1990s and FDA's Approval of Those Changes

Beginning in 1990, the Michigan state-owned facility (the Michigan facility) that was later sold to BioPort changed both the fermenters and the filters it used in manufacturing the anthrax vaccine.[7] With regard to fermenters, it replaced the original glass fermenter with two 100-liter stainless steel fermenters in 1990, and installed two similar fermenters in 1993. With regard to filters, the facility changed from ceramic to nylon filters in 1990. After the 1990 change, the facility changed the types of filters two more times, in 1996 and 1997. According to Michigan facility officials, changing the filters reduced processing time for the production of a single lot of anthrax vaccine, while changing and adding additional fermenters increased its production volume. We were informed that both changes were made to increase production before the onset of the Gulf War.

[6] The purpose of FDA's inspection is to determine that the products are manufactured in compliance with cGMP as described in the license application. Manufacturers who fail to meet product standards or who make unreported or undocumented changes in manufacturing methods may have their license suspended or revoked.

[7] A fermenter is used to grow the bacteria. A filter is one of the processing stages after the fermentation. The filter removes whole bacteria and other biochemical components.

Under FDA regulations, changes to a vaccine manufacturing process are to be reported to FDA and significant changes may require the manufacturer to submit a license application amendment.[8] In December 1990, FDA was notified of the replacement of the original glass fermenter with two 100-liter stainless steel fermenters. FDA approved that change in 1993. Although the Michigan facility installed two additional stainless steel fermenters in 1993, it did not notify the FDA about the additional fermenters at that time. Inspection records indicate that FDA was aware of the additional fermenters and encouraged the facility to submit a license amendment application for them in 1993[9] and again in 1995[10]. In January 1999, BioPort submitted a license amendment application with supporting documentation to FDA concerning the two additional fermenters. In May 2001, FDA approved these additional fermenters.

Because we could find no evidence in BioPort or FDA records that the filter changes had been reported to FDA, we contacted FDA officials in December 2000 to discuss the filter changes. They told us that they had not been notified and were not aware of changes to any filters used to produce anthrax vaccine. In February 2001, FDA wrote to BioPort, raising questions about the changes to the filters. In April 2001, BioPort submitted documentation, primarily in-process tests and lot release data, to FDA to demonstrate that the filter changes had not had a significant impact on vaccine quality. FDA reviewed and accepted the data and approved the filter changes in July 2001. Although the lot release data included lots produced immediately before and after the filter changes, the data submitted did not include the type of data that, according to FDA officials, would normally have been required if a license amendment application had been filed contemporaneously with the changes, that is, a direct

[8] Prior to 1997, FDA regulations required that "important" proposed changes in the vaccine manufacturing process be reported to FDA at least 30 days prior to implementation. Since 1997, FDA regulations have required that "major" changes be reported to FDA at least 30 days prior to implementation and that FDA approve such changes prior to distribution of vaccine made using them.

[9] The FDA inspection report (May 26, 1993) stated that "any changes to the manufacturing [process] that have the potential to affect the safety, purity, or potency of a biologic must be submitted and approved by CBER prior to implementation."

[10] In April 1995, Michigan facility officials told FDA that the additional fermenters installed in 1993 were similar, although not identical, to those installed in 1990 and approved in 1993. In response, FDA officials explained that "a different fermenter may cause change in the product, even if the fermenter is similar to the existing fermenter, and would most likely require agency approval." (FDA/CBER Conversation Record, Apr. 21, 1995.)

biochemical analysis of vaccine samples from before and after the changes. FDA officials told us that such a direct comparison is not possible now, because appropriate pre-1990 vaccine samples no longer exist.

Studies Suggest Possible Changes to the Anthrax Vaccine After the 1990 Manufacturing Changes

Because it is not now possible to definitively resolve the question of whether the anthrax vaccine produced after the filter changes is the same as that produced before the changes (a demonstration that is normally required in a license amendment application), we have reviewed other studies to see if evidence suggests that the question may need to be further examined. We have found two types of such evidence.

First, in an unpublished study performed in 1990, the Department of Defense (DOD) found up to a hundredfold increase in the protective antigen levels in lots produced after the filter change that year.[11] (Anthrax toxin is composed of protective antigen, lethal factor, and edema factor. The individual toxin components are not toxic. A protective antigen and lethal factor combination produces lethality, and a combination of protective antigen and edema factor cause swelling.)

In a subsequent article published in 1994, DOD researchers, referencing the earlier study, hypothesized that the filter change altered the composition of the vaccine by increasing the level of protective antigen in the finished product.[12] According to the authors of this article, when DOD questioned the Michigan facility about this increase in 1990, the responsible Michigan facility official attributed it to the change in the filter from ceramic to nylon.

[11] J.W. Ezell and T. Abshire, "In Vitro Analysis of Michigan Department of Public Health Human Anthrax Vaccine", U.S. Army Medical Research Institute of Infectious Diseases, Bacteriology Division, Fort Detrick, MD, Oct. 25, 1990. This unpublished study applied a then-new methodology to measure protective antigen that had not been separately validated at the time but is widely used today, and Dr. Ezell told us that the results should be interpreted cautiously as a result. We have had the study reviewed by two experts in anthrax vaccine issues who did not see any evident reasons to question the study methodology. We believe at best, however, it is an indicator that protective antigen levels may have changed after the filter changes. Since it cannot be replicated, it is the only evidence available on this point.

[12] B.E. Ivens and others, "Efficacy of a Standard Human Anthrax Vaccine Against *Bacillus anthracis* Spore Challenge in Guinea Pigs," *Vaccine*, vol. 12 (1994), pp. 872-874.

There are no studies to show what the effect of a significant increase in protective antigen may be on safety or efficacy of the vaccine. However, because the tests that could have demonstrated that the product was not changed in a material way in the context of a timely license amendment application were not done, and cannot now be done, there is potential merit in evaluating the findings of the 1990 DOD study further. We discussed the DOD study further with FDA officials on October 15, 2001, and they told us that they had not evaluated the study because they did not have it. At their request, we have provided the study to them.[13]

Second, we have reported several times in earlier work that, before 1990, anthrax vaccine was used by a small number of at-risk individuals (for example, wool mill workers), and FDA did not have any system to report adverse reactions associated with drugs and vaccines. Safety data, as reported in the product insert, were limited to the information from studies done in the 1960s, long before the fermenter and filter changes discussed here. Published and unpublished data on anthrax vaccine use during the Gulf War and since 1998 show a significantly greater incidence of both local and systemic adverse reactions compared with rates reported in the product insert. For example, the product insert says that the following should be expected: (1) 30 percent of recipients should experience a mild local reaction; (2) 4 percent should experience a moderate local reaction; and (3) 0.2 percent should experience systemic reactions characterized by malaise and lassitude with chills and fever reported in only a few cases. This indicates that some reaction should be experienced by a total of 34.2 percent of recipients. By comparison, in a survey we conducted in calendar year 2000, 85 percent of National Guard and reserve forces in our survey who were given the anthrax vaccine reported some reactions, with local reactions experienced by 76.2 percent of recipients and systemic reactions experienced by 23.8 percent. Chills and fever were reported by between 9 and 11 percent of our surveyed

[13] Because we had earlier discussed this study with both DOD and BioPort, we had assumed that one or both of them had referred the information to FDA. We had also asked FDA about the study in December 2000 but they did not request a copy from us at that time.

vaccine recipients.[14] These results are consistent with unpublished DOD studies and other published epidemiological work we are aware of.[15]

Because there are no data to evaluate the effect of the filter change on the characteristics of the vaccine product, it is difficult to determine whether these greater levels of adverse reactions could be related to changes in the vaccine associated with the filter changes. Ceramic filters (used before 1990) absorb proteins more than nylon ones, and the change to nylon filters in 1990 could theoretically have resulted not only in more protective antigen coming through but also other proteins. The end-product and in-process tests that BioPort submitted to FDA in 2001 in support of the filter changes may lack the capability to evaluate this possibility. Additional biochemical tests would have been required. For example, a filter change could have allowed more edema factor to pass through. The Michigan facility did not routinely test for edema factor in the product. We note that, since 1997, United Kingdom (U.K.) regulations have required the anthrax vaccine produced by the U.K. Center for Applied Microbiology and Researchto be tested for both protective antigen and edema factor. [16]

Observations

General public health vaccines are produced according to cGMP and are in constant, routine use worldwide. This use permits real-time monitoring of whether the vaccines are performing properly. In contrast, bio-defense vaccines have no such ongoing reality check because of the absence of natural disease and relatively limited use. Thus, only in emergency situations are bio-defense vaccines subjected to the evaluations that public health vaccines undergo all the time. Accordingly, the stringent application of cGMP by FDA in its approval of the resumption of vaccine manufacture at BioPort, as well as subsequent monitoring of the manufacturing process, is vital to ensure that vaccines produced are safe, pure, and of high quality.

[14] The full results of our survey will be reported in the near future.

[15] We reported on the results of several DOD studies in *Anthrax Vaccine: Safety and Efficacy Issues* (GAO/T-NSIAD-00-48, Oct. 12, 1999.) See also Lea Steele, "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, 2000, pp. 992-1002.

[16] The Center for Applied Microbiology and Research is the manufacturer of the U.K.'s only licensed anthrax vaccine.

In view of the increasing importance that will be given to the anthrax vaccine in the current environment and whether or not the anthrax vaccine is approved for production in the near future, it is important to ensure that studies continue to evaluate the vaccine's safety and efficacy, particularly with respect to the effect of higher levels of protective antigen and possibly other proteins. If FDA reinstates BioPort's license to manufacture and distribute vaccine, such studies would be strengthened by the implementation, by FDA or DOD, or both of an aggressive active surveillance program to ensure the early identification and analysis of adverse reactions.

Mr. Chairman, this concludes my statement. I will be happy to answer any questions you or Members of this Subcommittee may have.

Contacts and Acknowledgments

For further questions regarding this testimony, please contact Nancy Kingsbury, Ph.D., at (202) 512-2700. Other individuals making key contributions to this testimony include Sushil K. Sharma, Ph.D., DrPH; Jack Melling, Ph.D.; George Bogart; and David Gootnick, M.D.

Appendix I: Scope and Methodology

To conduct our work, we reviewed documents provided to us by FDA, DOD, and the Michigan facility/BioPort Corporation pertaining to the anthrax vaccine. In addition, we reviewed published and unpublished scientific reports on anthrax vaccine and on the safety and efficacy of the vaccine. In addition, we interviewed officials of FDA, DOD, the Michigan facility/BioPort, and experts in anthrax vaccine in U.S. and the U.K.

Appendix II: Related GAO Products

Gulf War Illnesses: Questions About the Presence of Squalene Antibodies in Veterans Can Be Resolved (GAO/NSIAD-99-5, Mar. 29, 1999).

Medical Readiness: Safety and Efficacy of the Anthrax Vaccine (GAO/T-NSIAD-99-148, Apr. 29, 1999).

Contract Management: Observations on DOD's Financial Relationship with the Anthrax Vaccine Manufacturer (GAO/T-NSIAD-99-214, June 30, 1999).

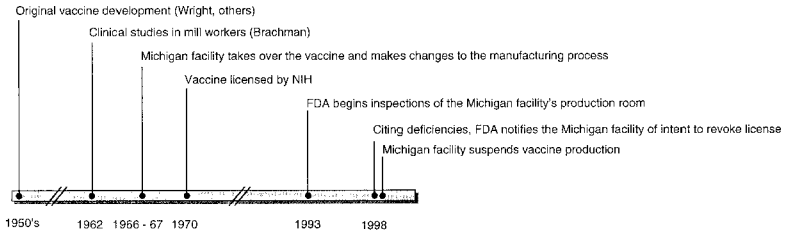
Medical Readiness: Issues Concerning the Anthrax Vaccine (GAO/T-NSIAD-99-226, July 21, 1999).

Anthrax Vaccine: Safety and Efficacy Issues (GAO/T-NSIAD-00-48, Oct. 12, 1999).

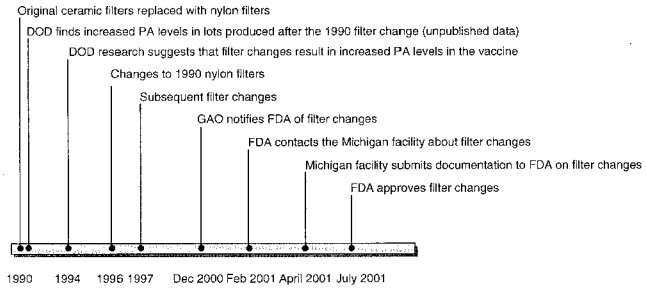
Medical Readiness: DOD Faces Challenges in Implementing Its Anthrax Vaccine Immunization Program (GAO/-NSIAD-00-36, Oct. 1999).

Medical Readiness: DOD continues to Face Challenges in Implementing Its Anthrax Vaccine Immunization Program (GAO/T-NSIAD-00-157, Apr. 2000).

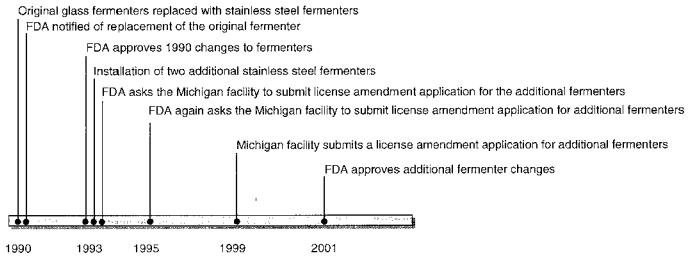
Gulf War Illnesses: Questions About the Presence of Squalene Antibodies in Veterans Can Be Resolved (GAO/NSIAD-99-5, March 29, 1999).



Changes to Filters Used in the Production of Anthrax Vaccine



Changes to Fermenters Used in the Production of Anthrax Vaccine



Source: GAO-02-181T

Mr. SHAYS. Thank you. We've heard from the Department of Defense and from GAO and now we have two people from the private sector. Mr. Sudovar, we'll be happy to hear from you.

STATEMENTS OF STEPHEN G. SUDOVAR, PRESIDENT AND CHIEF EXECUTIVE OFFICER, ELUSYS THERAPEUTICS, INC.; AND UNA S. RYAN, PRESIDENT AND CHIEF EXECUTIVE OFFICER, AVANT IMMUNOTHERAPEUTICS, INC.

Mr. SUDOVAR. Thank you, Mr. Chairman and members of the committee. It's indeed my privilege to be here today, and I thank you very much for inviting us.

I'll try and be brief in my comments and not cover ground that's already been covered by others who have testified before me. So I'll try and move fairly swiftly through reading and focusing on those points I think might be germane to the conversation that we have in the aftermath of this.

One of the key points I'd like to address today is that it is just as important to pursue other biomedical and biotherapeutic solutions in addition to vaccines that can protect the American people from a variety of pathogens and an increasingly sophisticated enemy. The biotechnology industry is engaged in a tremendous research and development effort dedicated to that end.

Another key point that I'd like to make and discuss today is the critical importance of Government support of this industry, largely made up of small companies that have no base of marketed products or revenues to fund research. I'm here today representing BIO, that is the biotechnology industry organization, whose role in American health care, safety and security is becoming more apparent, I believe, every day. BIO represents 1,000 biotech companies, academic institutions, State biotech centers and related groups in all 50 States of America. BIO's members are involved in research and development of products for health care, agricultural industry and the environment. BIO members recently formed a special biodefense task force, of which I am a member.

I also am president and CEO of EluSys Therapeutics, Inc., and before that held leadership positions with the global pharmaceutical manufacturing industry for almost 25 years. My company, and the biotechnology industry, are engaged in cutting edge science that is uniquely poised to benefit Americans; 125 approved biotechnology products and vaccines have helped some 250 million people worldwide; 75 percent of these medicines have been approved in the past 6 years.

EluSys is an example of how the biotechnology industry works. We are a fledgling company that has licensed early stage technology from academia and are developing safe, effective and marketable therapeutics for a wide range of medical needs. Since the company's founding back in 1998, we have worked collaboratively, first with academia, and now with the U.S. Army Medical Research Institute of Infectious Diseases [USAMRIID], to pursue development of our unique therapy against potential biological weapons of mass destruction, such as anthrax, hemorrhagic fever, the Ebola virus, plague and smallpox. We've done this without financial assistance from the Government.

I'd like to take a moment just to explain, at least from my perspective, the therapeutic options our Nation needs to explore in connection with biological weapons and the diseases they may cause. There are actually three levels. We've heard about vaccines, of course. We've talked a great deal this morning about antibiotics. What I'd like to talk a little bit more about are therapeutics.

Each of these approaches, other than the antibiotic course, each of these approaches is critical. All are necessary and none of them is in a stage where we can rest easily.

Let me explore each of these treatment options in a little more depth so you can understand how they differ and how they complement each other. I believe we can skip over the vaccine section, since we've talked a great deal about it. I think that the vaccines obviously have a major role to play within the crisis, particularly that we're facing now, against numerous pathogens. I think Dr. Wineger has covered both the vaccines most important to us, the smallpox vaccine and the vaccine for anthrax.

There are, I think, additional considerations that we should consider, especially in regard to military versus civilian populations. As we've talked about, the anthrax vaccine requires some six injections over about 18 months, plus booster shots to provide full immunity. While this may be conceivable in the military population, it's clearly unrealistic, I believe, in the civilian population.

We are fortunate to have effective antibiotics already available. In addition, there are anti-viral therapies currently available for cytolomegalovirus, HIV-AIDS and herpes that may or may not be effective against viruses used in biowarfare. Biotech and biopharmaceutical companies are working to find new alternatives.

Antibiotics inactivate or kill bacteria, including anthrax. But they can't help, at least they have not proven to help, someone who's experiencing symptoms. If the bacteria already has released toxins into the bloodstream, there is little that can be done. It is too late. That is where blood cleansing technologies like the one EluSys is working on can come into play.

The unique heteropolymer system which we have discovered at EluSys is developing uses for two monoclonal antibodies chemically joined together like biological double sided tape. One of these antibodies sticks to the toxin, in this case, anthrax. The other bonds to a receptor found on the human red blood cell. Red blood cells then carry the pathogen to the liver for destruction and return unharmed to the normal blood circulation. This whole process happens within minutes.

Unlike vaccines, antibiotics and anti-virals, the HP system can be engineered to be activate against anything that circulates in the blood stream, such as bacteria, toxins and viruses.

To help the public, we need more post-exposure options. It is not feasible or practical to vaccinate the entire population. There are side effects to these vaccines, and the benefits probably would not outweigh the risks in most cases. Nor would antibiotics protect people from a possible scenario in which a pathogen is released through a building's air system, for example. Many people could be exposed and infected without knowing it. There would be no telltale signs of white powder in an envelope. A few days later, when

they started experiencing symptoms and went to their doctors, it may in fact be too late.

Once a toxin has been released into the blood stream and symptoms have appeared, there's no evidence that a course of antibiotic therapy will be effective in preventing death. The EluSys heteropolymer system, however, by removing the toxin from the blood stream, has the potential to do just that. Since it works against the toxin, it may buy the crucial time to allow for later stage antibiotic treatment. Companies in this field have identified a variety of needs and barriers that hinder quick, large scale development and production of several products. We at BIO have identified some 20 companies that are working on bioterrorist and biowarfare agents.

But there are barriers, and let me provide you with my view, at least the prevailing view, I believe, among many industry leaders, of how to overcome these barriers. No. 1, the market for these agents, biological toxins, is small and it is uncertain. There's no guarantee that the vaccines or therapeutics we develop will ever be needed, and hopefully they will not.

Because of that uncertainty, support from the venture capital and financial markets, which we depend upon, is limited. That is why we and other companies need the support of the Government to continue the development of these important drugs and devices and by that, I mean targeted funding by the Government, which will enable small and innovative companies, like my own, to significantly expedite the development of important agents against biological toxins.

We've discussed our technology with many Congressman and Senators up here on the Hill. The single most often-asked question of me is, what would it take to expedite the development of your drug product. For example, normally it would take 4 to 6 years, in many cases, as long as 10 years, to get the EluSys antidote ready to treat human beings exposed to anthrax. Government funding on the order of about $50 million will enable us to develop the antidote in roughly 2 years, and we've laid a program out to do that, which we'd be glad to submit to the record.

In addition, biodefense companies need long term Government contracts. This will help maintain consistent revenue streams so our companies can continue to draw support for biodefense and commercial applications of our products and technologies.

The biotechnology industry also needs support from Government that goes beyond funding and includes the following. No. 1, some protection from liability. The biotechnology industry needs Government to indemnify our companies. Fear of liability has clearly prevented many companies from even considering the development of vaccines, and in fact, many companies have discontinued programs for this very reason.

No. 2, support for security measures. The nature of our research, to develop protection from those who want to harm people, puts our laboratories, our researchers and other personnel at increased risk. We ask the Government to support the additional security measures that we need.

Third, FDA support. We talked a little bit about this today, but perhaps from a little different perspective. FDA needs to expedite

the product review and approval process by allowing us to demonstrate efficacy through non-human, animal data only. I mention this because one of the problems we have is there is no naturally occurring disease called anthrax. It's a bioterrorist-created disease, which is inhalation anthrax. There is no way to do a well controlled clinical trial with human beings. There are very few people that will step to the control group in a trial of that kind, and particularly if they're in a control group without the benefit of our technology.

So there needs to be an alterative means of approving products that can be utilized in this fashion for disease that are literally created. We believe that the FDA's regulations, which we've commented on and discussed with them, and we will submit for the record also our comments on those and not go into those now, that only human testing would be necessary, and of course, we do safety testing on large numbers of human beings.

Let me just close by saying that I hope you have a better understanding of the array of approaches. It's clear that the use of biologicals in warfare and home land terrorism, which we've talked a great deal about, is a great threat to Americans. I want to say on behalf of the industry that we stand ready to work side by side with Government to stamp out this threat.

Thank you very much for your time.

[The prepared statement of Mr. Sudovar follows:]

Biotechnology Industry Organization
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TESTIMONY OF

STEPHEN G. SUDOVAR

PRESIDENT AND CEO

ELUSYS THERAPUETICS, INC.

ON BEHALF OF THE
BIOTECHNOLOGY INDUSTRY ORGANIZATION
(BIO)

BEFORE THE

COMMITTEE ON GOVERNMENT REFORM

SUBCOMMITTEE ON NATIONAL SECURITY, VETERANS AFFAIRS AND INTERNATIONAL RELATIONS

OCTOBER 23, 2001

Testimony of Stephen G. Sudovar, Oct. 23, 2001

Mr. Chairman and Members of the Committee:

Thank you for the opportunity to testify before your committee on "Biological Warfare Defense Vaccine Research and Development Programs." I will review the status of vaccine development as well as the technological, financial, regulatory, and other challenges facing us. One of the key points I will address today is that it is just as **important to pursue other biomedical and biotherapeutic solutions** – in addition to vaccines – that can protect the American people from a variety of pathogens and an increasingly sophisticated enemy. The biotechnology industry is engaged in a tremendous research and development effort dedicated to that end.

Another key point I will discuss today is the **critical importance of government support of this industry,** largely made up of small companies that have no base of marketed products and profits to fund research.

I am here today representing BIO, the Biotechnology Industry Organization, whose role in American health care, safety and security is becoming more apparent every day.

BIO represents more than 1,000 biotechnology companies, academic institutions, state biotechnology centers and related organizations in all 50 U.S. states and 33 other nations. BIO members are involved in the research and development of health care, agricultural, industrial and environmental biotechnology products, and have recently formed a special biodefense taskforce, of which I am a member.

I also am president and CEO of EluSys Therapeutics, Inc. and before that, held leadership positions with a global pharmaceutical manufacturer for almost 25 years. My company and the biotechnology industry are engaged in cutting edge science that is uniquely poised to benefit Americans in many ways.

Biotechnology is one of the most research-intensive industries in the world. The US biotech industry spent $10.7 billion on research and development in 2000. And in many cases, the benefits already have been realized. Close to 120 FDA-approved biotechnology drug products and vaccines have helped some 250 million people worldwide. *Seventy-five percent of these medicines were approved in the past six years.* Clearly, biotechnology endeavors have made a significant contribution to the nation's health.

EluSys is an example of how the biotech industry works – we are a fledgling company that has licensed early-stage technology from academia, and are engaged in the process of developing safe, effective and marketable therapeutics for a range of unmet medical needs. Since the company's founding in 1998 we

have worked collaboratively, first with academia and now the US Army Medical Research Institute of Infectious Diseases, to pursue development of our unique therapy against potential biological weapons of mass destruction, such as anthrax, hemorrhagic fever, Ebola virus, plague and smallpox. We have done this without financial assistance from the government.

Therapeutic Options

I'd like to take a moment to explain the therapeutic options our nation needs to explore and understand in connection with biological weapons and the diseases they cause. There are actually three levels of treatment:

- Prophylaxis – that is, vaccines to prevent people from becoming ill before they are exposed
- Antibiotics and antivirals that need to be given immediately upon diagnosis or exposure, and
- Antidotes and other therapeutics that can cleanse the blood of toxins once the disease has developed.

Each of these approaches is critical, and all are necessary. None of them is at a stage where we can rest easy.

Let me explore each of these treatment options in a little more depth so you can better understand how they differ and how they complement each other.

Vaccines

We now have two vaccines for biowarfare pathogens, one for anthrax and one for smallpox, and there are others in development. The major challenges in vaccine technology are to improve their safety, to develop vaccines against a variety of pathogens and strains, to shorten the time needed to inoculate people, to be able to mass produce them and to determine how and when – and to whom – to administer them.

Those are the major technical challenges. There are, however, added considerations, especially in regard to military vs. civilian populations. The current anthrax vaccine requires six injections over 18 months, plus booster shots, to provide full immunity. While this may be conceivable in the military population, it is clearly unrealistic in the civilian population. If you think of the logistics of tracking a five or six vaccination series and boosters for 280 million people for anthrax, you can easily visualize problems. Potential improvements in vaccine regimens notwithstanding, it is important to have post-exposure options for both the military and civilian populations. Therapeutics that can be administered post-exposure are obviously more desirable for civilians, but also necessary for the military.

Antibiotics and Antivirals
We are fortunate to have effective antibiotics already available. In addition, there are antiviral therapies currently available, for CMV (cytomegalovirus), HIV/AIDS and herpes that may or may not be effective against viruses used in biowarfare. Biotechnology and pharmaceutical companies are working to find new antibiotic and antiviral alternatives in anticipation of the development of strains that are resistant to available drugs.

Antibiotics inactivate or kill bacteria, including anthrax. But they don't protect against viruses, and they can't help someone who is experiencing signs and symptoms of anthrax or another such disease. If the bacteria already have released toxins into the bloodstream, there is nothing that can be done. It is too late. That is where blood-cleansing technologies like the one EluSys is working on comes in.

Therapeutics and Antidotes
The unique Heteropolymer System that EluSys is developing uses two monoclonal antibodies chemically joined together, like biological double-sided tape. One of these antibodies sticks to the target to be removed (such as the anthrax toxin); the other binds to a receptor found on human red blood cells. The red blood cells then carry the pathogen to the liver for destruction and return unharmed to the normal blood circulation. This whole process happens within minutes.

Preliminary test results show that the EluSys Heteropolymer (or HP) System works like a temporary vaccine in that it confers an instant but temporary state of immunity to pathogens that are carried in the bloodstream, whether bacterial or viral.

Unlike vaccines, antibiotics and antivirals, the HP System can be engineered to be active against anything that circulates in the bloodstream – bacteria, toxins and viruses.

Post-Exposure Options
For the general public, we need more post-exposure options; it is not feasible or practical to vaccinate the entire population against anthrax or other toxins. There are side effects to these vaccines and the benefits probably would not outweigh the risks.

Nor would antibiotics protect people from a possible scenario in which a pathogen is aerosolized and released through a building's air system. Many people could be exposed and infected without knowing it – there would be no telltale white powder. A few days later, when they started experiencing symptoms and went to their doctors, it would be too late.

Inhalation anthrax involves exposure to anthrax spores that enter cells in the lung and become the bacteria that can produce toxin. The toxin and the bacteria then enter the bloodstream and circulate through the body.

While antibiotics are effective against the bacteria, they are not effective against the toxin, and it is the toxin that can rapidly cause widespread inflammation and cell death in multiple organs, including the brain, liver and spleen. Once the toxin has been released into the bloodstream and symptoms have appeared, there is no evidence that a course of antibiotics will be effective in preventing death.

The EluSys HP System, by removing the toxin from the bloodstream, has the potential to fill an unmet need in the armamentarium against anthrax. Since it works against the toxin, it may buy crucial time to allow for later-stage antibiotic treatment.

The Need for Government Support

EluSys is one of almost two dozen American companies involved in the development of biodefense vaccines and therapeutics. These companies are addressing a range of products we fervently hope we never need. Avant, in Massachusetts, is developing anthrax and cholera vaccines. Genelabs, in California, is working on broad-spectrum antimicrobial and antiviral drugs. Luminex, in Texas, is exploring biodetection systems. Inotek, in Ohio, is researching a product to fight inflammatory biowarfare agents such as plague and Ebola virus.

Companies in this field of research and development have identified barriers that hinder quick, large-scale development and production of these products. While there may not be unanimity about how to specifically overcome all these barriers, let me provide you with my view – a prevailing view among industry leaders. EluSys and other biotechnology companies rely heavily on venture capital to support our work, and at this juncture, we need the support of government as well to move forward as quickly as the science allows.

The normal drug-marketing paradigm assumes that research will lead to drugs that can be marketed to certain patient populations. However, the market for agents against biological toxins is small and uncertain: there is no guarantee that the vaccines or therapeutics we develop will ever be needed. And since biowarfare is an area of national defense that may or may not have a market, support from the venture capital and financial sectors for this research is limited That is why we and other companies need the support of the government to continue to develop these important drugs and devices.

Aggressive government funding will enable companies like mine to significantly expedite the development of important agents against biological toxins. For example, in the normal course of development, it would take four to six years to get the EluSys antidote ready to treat human beings exposed to anthrax.

Government funding of $50 million will enable us to develop the antidote in roughly two years.

Long-Term Financial and Administrative Considerations

In addition to supporting our research on an accelerated schedule, the government must provide support in the form of long-term contracts. This will help maintain consistent revenue streams so our companies can continue to draw support for both biodefense and commercial applications of our products and technologies.

The biotechnology industry also needs support from government that goes beyond funding and includes:

1. Protection from liability. We are in somewhat uncharted territory, dealing with toxins that pose significant danger of harming people. All drugs carry the potential for side effects – some serious, some not – and drugs to protect or counter the effects of these toxins may cause some negative side effects. However, in order to focus our efforts on developing agents for the broad population, the biotechnology industry needs government to indemnify our companies to protect them from lawsuits. In fact, fear of liability has prevented many companies from even considering the development of vaccines.

2. Support for security measures. The nature of our research – to develop protection for people against an agent that is deployed by those who want to harm people – puts our laboratories, researchers and other personnel at increased risk of danger. We ask the government to support the additional security measures we will need

3. FDA Support: In 1999, the Food and Drug Administration issued proposed regulations on efficacy data for products to prevent toxicity. In essence, the regulations would allow the data showing that the agent is effective against a certain biological, chemical, radiological or nuclear substance to be demonstrated through animal data only. The only human testing would involve the evaluation of safety to the drug without exposure to the noxious agent. FDA needs to adopt measures that will clarify and expedite the product review and approval process. This will help those of us who are pursuing countermeasures to toxins plan the further development of our agents.

In conclusion, I hope I have been able to give you a better understanding of the array of approaches we can bring to biodefense, and a sense of urgency about some broader issues of funding and administrative support. It is clear that use of biologicals in warfare and homeland terrorism is a great threat to Americans and the biotechnology industry stands ready to work side by side with the government to stamp out this threat.

Testimony of Stephen G. Sudovar, Oct. 23, 2001

Thank you for the opportunity to testify today. I'll be happy to answer any questions you may have.

# # #

Mr. SHAYS. Thank you for your time.

Dr. Ryan.

Ms. RYAN. Mr. Chairman and members of the subcommittee, I'm delighted to be here and very grateful for the opportunity to testify. I understand that time is short and so if I may, I'd like to enter my written testimony into the record and I will simply speak to the issues that haven't been covered in detail.

I'm going to take it as a given that we need a vaccine. I could elaborate on that, but I believe both as a preventative and as a treatment, post-exposure, one needs the power and memory of the immune system to have been activated. So I'm simply going to talk about vaccines.

I'm going to talk about those that we have and I'd like really to tempt you with what we could have if we were to make a wish list. I believe that the biotech industry is absolutely ideally part of the solution. We are not the pharmaceutical industry, we're small, we're nimble, we're unencumbered by profits. And we are extremely highly motivated to——

Mr. SHAYS. You have no profits.

Ms. RYAN. Exactly. The halo.

Let me just start with a very brief review as an example the way I see the anthrax vaccine technology. Dr. Johnson-Wineger has mentioned the BioPort, which I see as mark one vaccine. It's a complex mixture, the toxins are released into the broth, they have to be inactivated and an adjutant has to be added to make the vaccine more immunogenic. You know the disadvantages, multiple injections have to be given to get protection. It takes a matter of months, even up to 18 months, and we simply cannot anticipate terror attacks by that period of time. And it's expensive and difficult to make.

On October 10th, AVANT—we don't need to go into the immunotherapeutics, just AVANT—licensed to DynPort a recombinant PA vaccine that you mentioned. I believe that this is much more precise. It should therefore be safer, meaning I think it will have fewer side effects. And it should be easier to manufacture. It's made in E. coli, a bacterium that replicates very quickly.

But I believe that it will still be an injectable, and most people don't like shots. It will probably require multiple doses, and it will, as you've heard, take time to manufacture. So I consider that the second generation. But now, I think we need to talk about fighting this war and using the technology that's available now. I'd like to focus my testimony on what I believe would be much more rapidly protecting, single dose, oral, much more cheaply manufactured vaccines that I believe we could leapfrog into development very rapidly.

Let me give you some examples. AVANT is an immunotherapeutics company. We make vaccines. We're experts at modern vaccine technology. We don't make the mass small margin vaccines of childhood prevention. We, for example, have a vaccine that raises your good cholesterol, but I digress.

Let me get back to the program that I want to talk to you about. One of the things that we're doing in our peace time activities is producing single dose oral vaccines that very rapidly would protect travelers. This is to protect travelers against serious causes of bac-

terial diarrhea, things like cholera, typhoid fever, shigella, which is dysentery, E. coli and campylobacter. Now, those are things that can ruin a vacation, they can ruin a war, but they kill a lot of people in countries where they're endemic. Although we're focusing on the top five bioterrorism agents, I just want you to know that we have vaccines against these diseases under development now, two of them quite late stage.

I don't want to go into the fact that they're there. If we were called upon for the country's defense, we would provide them. But what I want to talk about is something that I think could bring that user friendly technology to bear on anti-biowarfare agents. So let me take the example of cholera and show you how that can be a launching pad for what I believe is a very rapid development of an anti-bioterrorism series of vaccines that have the same rapid protection and other useful characteristics.

Let's take cholera. Our single dose cholera vaccine protects very rapidly, in a matter of days, not weeks or months. We know that you can get very high protective titres in 7 days. And since they're on a curve going up after, just a few days there are probably protective titres. We simply haven't measured it earlier than a week.

You see, what we're trying to do is have people get on a plane, have champagne, orange juice or cholera vaccine and be protected by the time they arrive. So speed is very important. So we call our cholera vaccine CholeraGarde. But because cholera, the vibrio cholera organism is very invasive, it can also be used as what we call a vector. And you might want to think of this as a Trojan horse.

So we have already developed the Trojan horse. We know a lot about it. We can manufacturer it at GMP manufacturing, good manufacturing practice conditions. We will be entering pivotal phase three trials through the peace time FDA scenarios this year, in 2002.

What I believe we can do is take what we call VibrioVec, which is essentially the cholera vaccine, and as if with a cassette, slip into it PA, the same recombinant PA that we have licensed to DynPort. But again, plague or any of the bacterial antigens that would protect against whatever the bioterrorism agent would be.

Now, this is not some pipe dream that is far away. We have this vaccine approach in late stage trials now. You've already heard that there is currently no FDA, no regulatory mechanism for approving an anthrax vaccine. You can't do challenge trials, and you cannot do fail trials in an endemic area. It's just not possible to get one approved.

But where I think I was hearing concern about sort of bypassing safety and efficacy trials at the FDA, I'm not talking about that at all. The Trojan horse itself will have gone through extensive trials, will have been approved, and I think what we would need would be safety and immunogenicity studies in primates or humans that could be quite rapid. This would allow us very rapid protection, single dose, oral, easy and inexpensive manufacturing, and the versatility to address a very large number of biowarfare agents.

Now, when I picked cholera I was thinking of bacterial biowarfare agents. I know your next question is going to be, what about the viral agents. There I believe we can use what we call SalmoVec, which is a vector based salmonella typhi, so it would be

the same story. But I don't want to dilute my message on the cholera, because that is still more theoretical. We are extrapolating that we can do that.

But we actually have proof of principle for the bacterial antigens, and we are far down the road in development of these vaccines. They are extremely inexpensive to make. We use a manufacturer called BioSetis in Argentina. But we had bids out to many different manufacturers, and I don't really see why, as long as they can get themselves to be GMP compliant, one couldn't have multiple manufacturers.

But I'm simply trying to say that there is 21st century technology that's available. Although it may seem newer, because you've heard of the other vaccines, I believe it could be up and running more quickly.

[The prepared statement of Ms. Ryan follows:]

TESTIMONY

U.S. House of Representatives

Committee on Government Reform

Subcommittee on National Security, Veterans Affairs, and International Relations

Hearing on

Biological Warfare Defense Vaccine Research & Development Programs

10:00 A.M. – 2:00 P.M.

October 23, 2001

Rayburn House Office Building

Room 2154

Una S. Ryan, Ph.D.

President & CEO

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AVANT VACCINE TECHNOLOGY TO COUNTER BIOTERRORISM

Mr. Chairman and Members of the subcommittee: I am very grateful for the opportunity to testify today. I plan to provide a brief overview of some of the advances in vaccine technology that we are developing and which, in one case, has been licensed to a Department of Defense contractor. It is my belief that the scientific advances of recent years can, with the cooperation of government agencies, be rapidly developed and brought to the service of the nation in achieving a much broader, safer, and more flexible arsenal of vaccines to enhance biosecurity.

Prevention is better than cure

It is clear from the current spate of anthrax threats and scares that there is an important place for antibiotics, especially if taken quickly, and in the future this usefulness will continue, as may a role for antidotes and other post-exposure treatments. In addition to logistical difficulties and other drawbacks associated with providing antibiotics to an exposed population is the concern that it would be straightforward for an attacker to produce a strain of multi-drug resistant anthrax. In addition to the same logistical problems, the antidote approach must contend with the fact that the organism that causes anthrax, *Bacillus anthracis*, is in itself not the cause of illness or death, but rather the producer of toxins that ultimately kill its host or rapidly trigger downstream havoc in the body. AVANT's approach has been to develop vaccines that would prevent the establishment of virulence and subsequent toxin production if the bacteria were to be encountered through any of the known routes: inhalation, ingestion or skin contact.

Current thinking on approaches to anthrax vaccines fall into three broad groups.

1. BioPort's subunit vaccine approach employs filtrates from *Bacillus anthracis* that are detoxified with formaldehyde followed by admixture of alum to increase

immunogenicity. This particular approach has the virtue that it already exists, but has some strong disadvantages in that manufacturing is difficult, six or more doses are needed to confer protection, and any attack would have to be anticipated by up to 18 months.

2. On October 10, 2001, we announced that AVANT would license its recombinant PA (protective antigen) subunit vaccine technology to the Department of Defense and its contractor, Dynport. AVANT's role was to provide the technology and know-how for the development of this vaccine, specifically the ability to produce pure recombinant PA in *E. coli*. Further development and manufacturing will be conducted by Dynport. This product is pure, and should, theoretically, have fewer side effects than the BioPort vaccine.

3. A third approach, AVANT's vector technology, is the one where I would like to focus my testimony. This involves the combination of new advances in live attenuated vaccine vector technology. The aim is to induce rapid protection together with flexibility to address a number of different bioterrorism agents, including, potentially, a "third-generation" anthrax vaccine.

Anthrax Vaccine Technologies		
BioPort	**DynPort**	**AVANT's Vaccine Vectors**
Subunit vaccine [Sterile filtrates of *B. anthracis* culture]	Subunit vaccine that is purer and (theoretically) safer than BioPort vaccine	Live attenuated vaccine – PA vectored in proprietary attenuated *Vibrio* or *Salmonella* species
Injectable	Injectable	Oral
6 doses over 18 months to confer complete protection	May require multiple doses to confer protection	Has shown single-dose, protection against cholera
Delayed onset of protection	Probable delayed onset of protection	**Rapid protection**

AVANT is a vaccine company that prides itself on novel approaches to vaccine development. Of pertinence to this committee, AVANT is engaged in the development of oral, single-dose, rapidly immunogenic vaccines for the protection of travelers visiting areas where bacterial diseases are endemic, causing death and disability to residents, discomfort to travelers and, as was seen in Desert Storm, capable of severely incapacitating our troops. AVANT's portfolio includes vaccine candidates against the following diseases:

- cholera
- typhoid fever
- dysentery
- enterotoxigenic *E. coli* (ETEC)
- campylobacter.

The profile of AVANT's vaccines for this market is necessarily one that is user-friendly and rapidly protecting, eliciting protection in a matter of days rather than months. AVANT is currently focused on its core business of protecting travelers. However, the approach is also highly applicable to military uses. Troops could be rapidly protected with all the benefits of systemic and mucosal immunity without enduring multiple painful injections.

AVANT's programs addressing the travelers vaccine market include manufacturing for late-stage clinical trials of single-dose, oral vaccines. We intend to take the travelers vaccines program as a launching pad for the development of potent, single-dose, oral vaccines that should protect rapidly against biowarfare agents.

AVANT's Vaccine Vectors to Counter Bio-terrorism

The use of *Vibrio cholerae* as a live, attenuated vaccine (CholeraGarde™) and as a vector (VibrioVec™) is extremely attractive because the bacterium is non-invasive and rapidly elicits a prominent and long-lasting immune response after a single, oral dose. Clinical studies using clinical-grade vaccine produced at the Walter Reed Army Institute of Research (WRAIR) Forest Glen facility have been conducted under a NIH sponsored Investigational New Drug (IND) application under the direction of Dr. Mitchell Cohen of Children's Hospital in Cincinnati. Thus far, AVANT's cholera vaccine (CholeraGarde™), based on the Peru-15 strain, has been clinically evaluated in over 120 volunteers including a Phase IIb study in which it was well-tolerated, highly immunogenic, and conferred 100% protection against moderate to severe diarrhea following virulent cholera challenge. AVANT is developing CholeraGarde™ as a travelers' vaccine for cholera and is currently producing cGMP (clinical good manufacturing practice) material for pivotal studies.

Live attenuated VibrioVec™ strains have been evaluated pre-clinically as bacterial vectors of assorted heterologous antigens including shiga-like toxin B-subunit (Slt-B), cholera toxin B subunit (CT-B) fused to an *E. histolytica* peptide (SREHP) and *Shigella sonnei* O-antigen. Each vector induced an immune response against the heterologous antigen when administered to mice or rabbits. AVANT is developing the VibrioVec™ vectored *S. sonnei* O-antigen as a vaccine against dysentery.

It is therefore anticipated that vaccinees immunized with VibrioVec™ vectored protective antigens associated with biological threats (e.g. anthrax or plague) would **rapidly** become protected from these pathogens.

AVANT's technology allows the vectoring of Protective Antigen (PA) derived from *B. anthracis* in VibrioVec™ to produce a single-dose, live attenuated vaccine against anthrax. Candidate vaccines will be evaluated preclinically for immunogenicity and protection from toxin challenge in the established germ-free mouse model. With the selection of a suitable strain, cell banking and GMP process development will proceed modeled on current manufacturing practices for CholeraGarde™. The VibrioVec™ vector could provide a platform for the development of a variety of vaccines against bacterial biowarfare agents.

AVANT is also developing other proprietary live bacterial vectors including attenuated *Salmonella typhi* and *S. typhimurium* strains. These vectors, deleted at *phoP/Q* genes that govern virulence, are actively being evaluated both pre-clinically and clinically for their capacity to provoke immune responses against heterologous bacterial and viral antigens. Although less developed, *Salmonella* derived vectors could provide a platform for delivery of viral antigens to combat viral biowarfare agents.

Conclusion

AVANT's live vaccine vectors to counter bioterrorism are:

- orally adminstered
- well tolerated and immunogenic
- shown to elicit high-titer antibodies as early as 7 days post-immunization
- easily and quickly manufactured
- extremely inexpensive compared to subunit-based vaccines
- currently under cGMP production
- potentially usable for a variety of antigens, allowing flexibility to address a range of biowarfare agents

Advances in vaccine technology, including those currently under development by AVANT, will allow us to expand and improve the vaccine arsenal to offer safer, more effective, and more practical vaccine protection against a wide variety of agents that might be employed by those wishing to attack the civilian population and military forces of the United States.

Mr. SHAYS. Thank you very much. What we're going to do is go to Mr. Putnam, and then we'll go to Mr. Sanders, then we'll go to Dr. Weldon and to John and myself. I think we'll do 5 minutes the first round and then go from there. Mr. PUTNAM. Thank you, Mr. Chairman.

Dr. Wineger, how does, you've spent a good time describing your plans for development of smallpox vaccine. How does that vaccine differ for a military population that presumably doesn't include the elderly or the very young, from the civilian vaccine that HHS would be working on?

Ms. WINEGER. In essence, the two candidate vaccines that our departments have worked up thus far are indeed very similar. The production methods are a little bit different, in that we proposed to use what are called nunc cell factories, and the HHS approach uses a bioreactor, with cells actually grown on beads. Other than that, the viruses are very similar. As a matter of fact, we are in continued discussions with the Department of Health and Human Services about collapsing the two individual programs into one nationwide program, which I think would serve both of our purposes very well.

Mr. PUTNAM. So are the time lines essentially the same, then, for production?

Ms. WINEGER. It's a matter of volume. I think the time lines would be very close to being similar, yes. But I would like to go back to the point that you made regarding the population. The requirements for any of the military products that I've mentioned are indeed for a product that could be used in normal, healthy adults between the ages of 18 and 65, because that's what our military population is. We have not had a mandate, nor do we have any expertise in doing the kinds of studies that would show that any of these products would be safe and immunogenic in a pediatric population, or a geriatric population. So that would help to forge an attractive partnership for us with our counterparts in HHS.

Mr. PUTNAM. Have you done a threat assessment on each of the antigens, each of the biological weapons that we talked about, plague, smallpox, anthrax, botox, Ebola?

Ms. WINEGER. There are a number of threat assessments that have been done. We really on the Defense Intelligence Agency and input from the chairman of the Joint Chiefs of Staff to provide us with a prioritized matrix. That is a classified document, but I believe we can provide it to you. I believe you may already have it. If not, we can provide it to the committee for your review.

Mr. PUTNAM. Thank you.

Dr. Kingsbury, your testimony, GAO's previous testimony about the anthrax vaccine used during the Gulf war and since 1998 showing the "significantly greater incidence of both local and systemic adverse reactions compared with rates reported in product insert," how do BioPort and FDA account for the higher rates, and will the product insert be changed accordingly?

Ms. KINGSBURY. To my knowledge, they don't account for it, because they haven't really looked into the question. I would assume that when they are approved to produce additional vaccine, that they will be addressing the issue of what they put in the product insert.

We've actually been quite surprised that what appears to be emerging in the epidemiological literature are some fairly well designed studies looking at the impact or the incidence of various kinds of illnesses in people who have and have not been exposed to the vaccine and haven't been deployed to the Gulf region is not being looked at by BioPort, or at least in our view, FDA. So I can't really answer your question.

Mr. PUTNAM. For anyone on the panel, we have spent the vast majority of our discussion talking about specific treatment protocols and vaccinations for humans who become exposed or infected with these particular diseases. Is any research going on, or how far along may be that research if it is going on in the public or private sector, with regard to decontaminating exposed machinery, buildings and situations of the sort that we find ourselves in here in Washington? How far along are we on that research? How high technology, or is it a low tech approach, with Clorox? What types of things are we doing and how effective is that?

Ms. WINEGER. I'll take the first shot at that, and if anybody else wants to chime in, they can. From the Department of Defense, we obviously had a higher requirement for a number of years for successful decontaminating agents. We currently have in the system something called DS2, which works very effectively. But the problem with it is that it does tend to be caustic and it's not environmentally friendly and requires large amounts of water.

So that doesn't make it very applicable.

Mr. PUTNAM. Won't work on a computer screen, then?

Ms. WINEGER. Won't work on sensitive electronic equipment, doesn't work on people.

We do have a separate kit, a resin based kit, that can be used to decontaminate the skin of individuals, and that is an FDA approved item. We are currently evaluating a number of different technologies, and one that I'd like to bring to your attention was in fact developed by another one of our sister agencies, the Department of Energy, at their Sandia Laboratory. That's a foam. The foam incorporates in it materials which can inactivate chemical and biological agents.

The attractive feature of this foam is that it's something that, for example, firefighters are used to using and they know how to employ a particular kind of foam, so that you wouldn't have to know in advance whether there were a chemical or biological agent there, and it could be a universal type of item.

There's a lot of research ongoing into enzymatic decontamination, which is again a more gentle type of approach. We have some very promising results with regard to the chemical warfare agents, specifically the nerve agents, and have only begun looking at some of the biological agents and some of the more resistant chemical agents.

Mr. PUTNAM. Thank you. My time has expired. I'll followup with the rest of you in my next round.

Mr. SHAYS. Thank you. Mr. Sanders.

Mr. SANDERS. Thank you, Mr. Chairman.

My question is a general question, and I'd appreciate anyone who wanted to respond to it. It is no secret that the pharmaceutical industry is attracted to those areas where they can make a lot of

money. It's not uncommon, for example, for me too drugs to be developed which really aren't very different from the original drug, billions of dollars in research and marketing going into such important areas as baldness or breast enhancement or other types of cosmetic areas.

In your judgment, how do we draw serious researchers into pursuing illnesses and medical problems that you cannot necessarily make a whole lot of money out of, or that is somewhat unpredictable? In other words, but is absolutely necessary? We send the men and women in our armed forces to countries and to situations where they need protection. One may not necessarily make a lot of money by providing that product. One may not necessarily make a lot of money by providing a product that we may or may never need. But we need those products.

The U.S. Government obviously has a serious interest in developing these products. What in your judgment, I know that Mr. Sudovar talked about the need for Federal funds, and I don't think anybody in Congress has an objection to that, if it is based in an approach which benefits the American people or the men and women in our armed forces, and is not designed simply to make profits for the company who is doing the work.

What is, in your judgment, a proper relationship between the U.S. Government and the private sector in terms of developing products which are not in itself profitable, but which are needed by our society? Anyone who wanted to respond.

Ms. RYAN. Well, I think there are some quite good mechanisms in place. One is the SBIRs, the small business research grants, and the other are CRADAs, with the Army. But what I think the Government needs to do in sending a strong message is to support really innovative research. Because as I was trying to say, if you've made advances in a very fundamental way, often it can be used both to make money and to make money in completely different areas. And if the Government is wise, it can leverage that technology into areas that are in the national interest for quite small additional dollars.

Mr. SUDOVAR. If I could comment on that as well, Congressman. I think in my testimony I addressed the issue of targeted Government funding. By that I really meant just what we spoke of a moment ago, and that is, to target that money to truly innovative technologies. Because I think one of the difficulties is that you can run into the problem of financing such endeavors as to bring about me too items which certainly are not useful and necessary for the American people.

I think some of the technologies that we've talked about today, particularly in the biotechnology industry, which it seems to me is part of the solution to the biotechnology problem that we have, which is bioterrorism and biowarfare, is to target those moneys at the most promising technologies. I think that with respect to profit, I think we all believe, and I would hopefully be speaking as well for the large pharmaceutical companies, that the profit motivation alone is not what we're here for. What we're here for is to collaborate with Government at a time of war.

I think the feelings of even a company like my own and my venture capitalists is quite tolerant of us going after areas of business

that may not be as lucrative as alternative therapies in other areas of business. Clearly, there are unmet needs out there of vast size that we could go after with our unique science. Our own technology alone deals with all blood-borne infections. So it need not only be bioterrorist infections.

There are such things as asthma, in our case, and other allergies, autoimmune diseases, which are unconquered today. And I must say, on behalf of the venture capitalists that have worked with us, that they have allowed us really to expend and invest in biotechnology as it relates to biowarfare. I think that there are significant limitations to that.

Mr. SANDERS. Let me interrupt you. They have allowed you. We are working here, the purpose of the hearing is to protect the American people.

Mr. SUDOVAR. Correct.

Mr. SANDERS. Is to protect the men and women in our armed forces. We don't need people to allow to. It has to happen.

So what I am saying is, the function of the U.S. Government is to protect the people of this country and our armed forces. Whether the venture capitalists allow it or not is not of importance to me.

Mr. SUDOVAR. In our current system, whether we like it or not, that's the way it works.

Mr. SANDERS. Well, that's what I'm asking. I don't like that. And I'm suggesting, that's why I want ideas here. What happens if the venture capitalists said no? We could get a baldness cure. I could use that myself, but there are more important issues out there. It's not allow to. We need it. And I'm asking questions of how we are going to get it in a cooperative—and I'm not saying you don't make a profit off of it.

But if the people of the United States need protection from bioterrorism, we don't need the permission of the venture capitalists to happen. I want it to happen, we want it to happen.

Mr. SUDOVAR. I think we've outlined a number of things that get in the way of that happening. One is the fact that there may be more attractive markets, whether it's venture capitalists, whether it's public financing. I think we all know with the condition of the economy and with the condition in private financing through venture capital, there's not a great deal of money available for that. I mean, going public in today's environment doesn't really work very well. We haven't seen biotech companies go public, and the reason is, there's no available funding for it.

So we do need help from Government if we wish to direct our efforts toward bioterrorism and biowarfare. I think that's an important point that I've made in my testimony. I think there are other issues like the ones that I mentioned. Government has a way of being fickle. We could have a disease this month and another disease next year and another disease the year after. If we continue to follow what Government needs in any particular year, we'd never make a profit.

I mean, we're not not-for-profit, we're just not profitable. We do want to make money eventually. I'm not trying to be a Fortune 500 company, and we certainly aren't. But I think if we're going to use the existing system, it needs to be bolstered by Government and we

need some help in areas like liability protection, longer term contracting, some of the things I've submitted in testimony.

Mr. SHAYS. Thank you. We're just doing a smaller 5 minute round now. Dr. Weldon.

Dr. WELDON. Thank you, Mr. Chairman. Dr. Wineger, I just want to followup on the line of questioning in your responses regarding antiseptic agents, or agents that can neutralize these biologicals. I've had some inquiries from constituents in my district regarding a product called Ecasol. Are you familiar with that at all? Evidently it's been—at least I've been informed that the Marine Corps has done some work with it. Do you have any knowledge of this product at all?

Ms. WINEGER. There's a number of different products of a similar nature. I have a limited amount of knowledge about each of those, yes.

Dr. WELDON. I'm just curious, I have constituents asking me about it, I thought you might be able to enlighten me a little bit. Maybe we can followup with some letters back and forth.

Ms. WINEGER. Sure.

Dr. WELDON. The line of questioning I'm getting is, some of these products, as you mentioned, that neutralize these agents, are irritating, corrosive, and this product has been extolled by some people as being very effective but not having those features. So I'll followup with a letter to you and maybe you can get some more information to me.

Mr. Sudovar, I was very intrigued, you talked about your product being one that could be administered to somebody to clear toxins out of their system. As I understand the pathophysiology of inhaled anthrax, that your product would be very useful in that setting, because the agent sort of incubates in the lungs and then gets into the lymph nodes and then proceeds to cause a tremendous outpouring of toxins into the blood stream. People actually die of shock, as I understand.

I'm a little concerned, you say with $50 million you could get your product on the market in 2 years, is that right?

Mr. SUDOVAR. Yes, the assumptions there are clear. One of the assumptions is the regulatory process that we spoke of, expedited approval and the availability of only animal data, not human data, obviously, for the reasons already discussed.

We have worked, this is not a new product, this is not something we've just come upon, we've been working with USAMRIID for well over a year now under contract. The results of those studies have been very promising. So we're not all the way, but we're quite a ways along. We're at the process where we've already screened about 150 antibodies that would indeed be directed at the toxin.

We have very promising results with a small number of those antibodies in terms of their efficacy in vitro. Our next step would be to go to animal models and then on with USAMRIID. If the FDA process were followed that has been proposed in regulation but has not been finalized, it would require us then to turn the product over to USAMRIID, or a containment facility like USAMRIID has, for their experimentation under well defined models, non-human primate models, perhaps other species. That would be the surrogate for what we would normally do as human trials.

Of course, on the safety side, we'd continue to do as we do today with drugs, we'd do safety trials with normal human volunteers.

Dr. WELDON. So what you're saying is, if the normal process were pursued, it would take many more years than 2 years?

Mr. SUDOVAR. I think there's two issues. One is the issue of priority. I think that's something we'd like more guidance from Government on, which agents do we want to develop, in what order and so on. I think anthrax has been talked about a lot today, smallpox certainly. We are focusing on the anthrax issue at the moment, although USAMRIID has also talked to us about the prospect of moving forward with plague and/or smallpox as the next one in line. I think if we were going to truncate the program, we're going to need more resources to do it. Because at the same time we're developing a drug for lupus, we're developing drugs for cancer. We're spread out in a number of disease categories.

Dr. WELDON. I think, Dr. Wineger, you talked about developing a new anthrax vaccine by the year 2007?

Ms. WINEGER. Yes.

Dr. WELDON. Do you think that's an appropriate time line for something like this? Do you think we can accelerate it in a variety of ways to get a product out quicker than 6 years from now? The war might be over in 6 years.

Ms. WINEGER. Exactly. I think we'd all like to identify ways to accelerate the schedule without in any way compromising the safety.

Dr. WELDON. I think Dr. Ryan testified on ways to do that more quickly. Weren't you essentially saying you could get a product out much more rapidly?

Ms. RYAN. The recombinant PA that we licensed to BioPort, we had actually manufactured in 1999 and had provided to USAMRIID, Dr. Friedlander. So we know it can be made. But we licensed the technology. Although the development of the vaccine would be in BioPort's hands, not mine.

Ms. WINEGER. I think you mean DynPort, not BioPort.

Ms. RYAN. I'm sorry. I do mean DynPort. The ones that I'm talking about, again, I don't know what the regulatory pathway would be. But it's a matter of months to do the manufacturing, because we've done it.

So I think the time to approval and use by the American public would depend on what testing would have to be done.

Ms. WINEGER. If I could just elaborate on that, for both our recombinant anthrax vaccine and the next generation smallpox vaccine also, I don't think that production is the limiting factor, at least not at the moment.

I think that indeed, the testing, and if you assume that we have to do the careful scrutiny that we know will be required and that we certainly support and intend to do, of a phase one study with a limited number of people, maybe 25 or 30 people, then take some time to evaluate that data, meet with the FDA to discuss that, and then move into a phase two type of study, which would enroll larger numbers of volunteers, and would be doing such things as optimizing the dose and measuring whatever types of response we can measure, whether it's a toxin neutralization or a virus neutralization for the smallpox vaccine, all those types of studies take

months, if not years, to do. I think that's where we would really have to concentrate on shortening the schedule.

Dr. WELDON. My time has expired. Thank you, Mr. Chairman.

Mr. SHAYS. Mr. Tierney.

Mr. TIERNEY. Thank you.

I think, Ms. Kingsbury, you might be the proper one to address this question. How does the Federal Government actually, or are we actually identifying and making threat risk assessments, so that we can say to manufacturers, this is the priority of remedies that we need, or are we doing it differently in every agency? I heard Dr. Wineger earlier say that she takes her information from Defense Intelligence, and they have a matrix. I know the FBI bases theirs, or I believe the FBI bases theirs on what terrorists would likely use. And the CDC bases theirs on what likely would have the most impact.

So we seem to be coming at it from different angles. Is there any cogent way that the Federal Government is approaching this, or is there anything in the works?

Ms. Kingsbury. We haven't actually looked very much into that, although we did get briefings last week that would suggest that there is finally coming together better coordination across the intelligence agencies and the law enforcement agencies to try to do that. But we haven't actually looked at the results of that work.

Mr. TIERNEY. Do you know if there is a process that has been in place, and how formal is it?

Ms. KINGSBURY. We were told there are daily meetings where all the right people are in the room. I have, at this point in the aftermath of September 11th, I suspect it's probably working better than it ever has before. But I don't know that for a fact.

Mr. TIERNEY. Where would we get that information? What would be our best source on that? Would it be back to the Secretary of Health?

Ms. KINGSBURY. I don't know if it would be the Secretary of Health or the Secretary of Defense.

Mr. TIERNEY. OK. We'll pursue that.

The other thing I'm not real clear on is, if we have no way of testing any of these new products that may come out on humans, effectively what we're saying is that we're going to have an approved product, if that part of it is set aside, that we'll never know if it's going to work or not, we'll never have any real confidence in its reliability until there's a crisis and we use it and see what the results are. Is that pretty much what the situation is?

Ms. RYAN. I think that we can't ever do the efficacy trial with a life challenge or in an endemic area. But I do think it can be tested in humans for tolerability, that actually giving the vaccine doesn't make volunteers, for example, sick. And for measuring a titre, which is a very good surrogate for protective immunity.

So one would have to use a surrogate marker that's served very well in vaccines over the years. In fact, that's how you test if somebody is protected, is do they have the right level of antibodies. So you wouldn't be able to do the kind of trial that you are nowadays required to do in peace time that take 6, 7, 8 years. But I do think you could test it in humans.

Mr. TIERNEY. So in that perhaps it didn't do any harm, but we wouldn't know for sure it was going to work?

Ms. RYAN. Well, you'd have a good surrogate.

Mr. TIERNEY. No certainty but a probability.

Mr. RYAN. Dr. Fauci talked about take. I'm talking about a blood test that gave you a measure of the antibody response.

Mr. SUDOVAR. I was going to pick up on that same thing. I think Dr. Fauci described it this morning. What you can do, in our particular technology, non-human primates, because their red blood cells are virtually identical to ours, they circulate and dispense with bacteria, toxins and viruses similarly to how humans do, are an excellent surrogate measure for what will happen in humans. So it's the greatest certainty we can get without exposing humans to anthrax and then trying to fix is.

I think the other thing is, I believe, it's part of the regulations that the FDA has advanced in final stage for comment, but has not yet promulgated, they've indicated the desire for us, on a post-marketing surveillance basis, should there be exposure for some reason or another to anthrax, that we be required to go in, assess and evaluate the utility, really, of the safety and efficacy of our compounds as they're put into use. But I think the key here, as was just suggested, is that we certainly will know that they're safe compounds or what the shortcomings are if they're not. We'll also know, I think, with a high degree of certainty, particularly using it on human primates in my technology, they're highly predictive of human behavior.

Ms. RYAN. I'm just reminded that the annual flu shot is tested the way I was suggesting. In principle, we know what's in a flu shot and we know that it's safe and has been effective. But the exact mix each year does not go through full blown human clinical trials. It simply is tested the way I'm suggesting.

Mr. TIERNEY. Thank you.

Getting back to you, Mr. Sudovar, and the questions my colleague was raising, you indicated that you think your industry needs research and development money from the Federal Government. You think they need long term Government contracts. You think they need liability protection, support from security measures and FDA support in expediting all the research process. At that point, what risk would any of your venture capitalists actually incur? [Laughter.]

Mr. SUDOVAR. Well, there's a risk of pricing issues, such as the ones that were talked about this morning. I think there's significant risk in whether or not the technology works at all. We have dedicated, I want to make it clear for the record, and for the group here, that we have not taken a single dollar of Government funding, and this technology is quite a ways along. And that has been with a great deal of risk.

Mr. TIERNEY. I guess I don't doubt that. I'm just saying, when I look at all of that, I'm thinking, if the Government is going to do all of that for any industry or any company or whatever, ought not there be more of a partnership aspect going here than just somebody that ponies up the money and provides for protection against the liability?

Or on the other hand, maybe this ought to be the type of an entity that is Government operated by commercially owned, so maybe if the Government comes in and then just contracts out some of the work, you make your profit by performing the task, as opposed to having this endless stream of potential profits that might lead us in different directions. But you make a fair profit on it.

The Government, on the other hand, gets some return for its investment and as can be anticipated, you might find out that somebody does suffer damages from something, and when they can look, and the Government has generally been in a position to help them out, it's not been something the Government has turned their backs on. So there's going to be liability incurred somewhere, probably by the Government if everybody else is immunized from it.

Mr. SUDOVAR. I think the issue is one of availability of funds to us. I think we probably could take this offline, I'm not sure that it's appropriate to discuss here, the whole issue of our patent system and so on. We rely heavily on intellectual property as the basis and foundation for business in this country. I think to begin to tamper with that brings us down a dangerous road that I certainly don't care to go down. I think other members of my industry would support me in that contention.

Mr. TIERNEY. My time is up. I'll get back with you.

Mr. SHAYS. When we do the next round, we'll do a 10 minute each member. Putting the three panels together means that we don't focus as much sometimes on the same issue.

I'm just going to use some of my time to say, I happen to be very grateful that we have a system that encourages the private sector to get in, to develop a product. Some of the products that we now want to have generic drugs for, we wouldn't even have had those products to copy and have the generic had we not had people investing.

So for instance, when I went out to California, there's a company that's invested close to $800 million to $900 million to develop a drug for Alzheimer's. And they don't know if it's going to work. And then they lose all of it. So there's got to be somehow a happy compromise in our system to enable us to accomplish what you all want to do, but still get that inventiveness, that ingenuity out there that creates these drugs that have been very helpful in our country.

I get the sense from GAO that the bottom line of your point is, that good manufacturing practice compliance is essential to the production of good vaccines. You want the good production practices, and then you're going to end up with a better vaccine. And you said that post-marketing surveillance is critical for bio-defense vaccines as well.

When I heard you, I basically, I'm listening to a company that arbitrarily changed its fermenters and its filter. That strikes me as being, my trying to build a house before I had the permits, and then being pretty unhappy when they say I can't have the house. Is this a common practice for a company to do? Is the culture different based on different kinds of—I get the feeling, for instance, in vaccines, maybe this isn't considered unusual. Is it?

Ms. KINGSBURY. When we were going about this work, we had hoped to be able to find out, find some actual information about

that. I think Dr. Melling might be able to comment a little bit about that.

Mr. SHAYS. Let's have him do that.

Ms. KINGSBURY. But maybe not. There are proprietary issues in our going to talk to how other companies deal with the FDA that kind of didn't allow us to go down that path. We are going to be looking at any regulatory entity that there is a regulation on the books that something be reported to FDA, and it's not reported to FDA, and FDA doesn't have the processes in place to notice that it wasn't reported strikes me as a not very rigorous process.

Mr. SHAYS. And it doesn't breed confidence in the system. I mean, you have a sole source producer, unfortunately, BioPort is an example of the kind of combination you wonder about. It's gotten so much Federal dollars, and I look at it and say, good grief, I don't want that to be my model.

But in the end, they arbitrarily changed the fermenting system and the filtering system. And they did not report it. And there is an assumption that somehow they were improving the process. But they were changing the process that they had gotten licensed for. Isn't that correct?

Dr. WINEGER. If I might, I'd like to interject there. And perhaps it's a matter of definition. The original fermenter that was in place at the Michigan Department of Public Health when the vaccine was licensed was indeed a glass-lined fermenter made by a company called Fodler. In about the 1990 timeframe, when I was working with the Army and we wanted to find ways to accelerate the amount of vaccine that the corporation could produce, the obvious choice was to put in additional production lines, if you will.

Fodler was no longer in business, and no longer made fermenters. The first choice would have been to buy an additional fermenter exactly like the one they had, to thereby minimize the changes. That was not possible. So they did a lot of rigorous investigation to get one the same size and shape, because fermenters come as tall skinny ones and short fat ones and different kinds of bacteria like to grow in different ways and all those types of things.

So we, the Department of Defense, worked with Michigan Department of Public Health to purchase, install and validate the fermenters in 1990. I believe, and correct me if I'm wrong here, the original paperwork to the FDA on the change of those fresh fermenters was filed in a timely fashion, and it took the FDA 3 years to approve those fermenters.

Mr. SHAYS. So in that case they were notified of the fermenter—the filters?

Ms. KINGSBURY. The filters they were not, right. The filters are different.

Mr. SHAYS. Would anybody on your staff care to add anything?

Mr. MELLING. I think that, of course we're looking 10 years back in time here. Maybe if we can take a positive lesson from this, which is, these are a group of products, biodefense vaccines, that have been orphans of the storm for probably going on 30 or more years, which is I think why we're sitting here today with really only one vaccine currently being manufactured that is licensed, a range of other requirements.

And Congressman, I think you asked the question earlier, what could be done to encourage more people to participate in what is a worthwhile and essential activity. I think it comes down to, this is an area actually that needs to be appreciated. I, like Dr. Johnson-Wineger, she and I have known each other for 30 some years. We have again seen occasionally the orphan come out into the sunlight. It happened during the Gulf war when there was a vaccine potential biological weapons issue. And then it all went away again.

This has happened from time to time. And as you've heard today, it's very clear that vaccine development is a long term issue. You don't develop a vaccine in 6 months, 1 year, or 2 years. So what is needed is adequate funding. It's continuity of support, and I think it's a message, which I think now is going out, that this is indeed intellectually challenging, scientifically worthwhile, and in fact, something that is a humanitarian cause. I think those are the things that will attract people to work in this field.

But again, over this long period, I know when I was in the U.K. and here, from time to time it was extremely difficult to even keep a minimum program running. People didn't reach——

Mr. SHAYS. Jack, I need to cut you off here. Let me just say to the Members, we're going to 10 minutes. Bernie, if you——

Mr. SANDERS. Not now.

Mr. SHAYS. I'm going to just have a few more questions, then.

Is vaccine production viewed differently by the FDA as other types of drugs? You're nodding your head, could you respond? You were trying to give us the message that somehow it could be, that somehow the requirements could be different. I need to understand why.

Ms. RYAN. The requirements are really onerous. You're absolutely right about phase one, phase two, and phase three.

Mr. SHAYS. But they were designed to protect people. You wanted to have a small group of people first and know it wouldn't harm you, and you want to begin to know if it is effective, and then you expand the group and you expand it. So when you say onerous, I thought they were there for a reason.

Ms. RYAN. That is why they're there, but I think things have become somewhat subverted. One of the programs we have is for a rotavirus vaccine for inoculating babies against rotavirus diarrhea. It's partnered with Glaxxo SmithKline. The phase three trials involve 50,000 infants, and may go as high as 100,000. Merck has a similar trial that's now 60,000 infants, may also go to 100,000.

Mr. SHAYS. Are you suggesting a third phase is including more than——

Ms. RYAN. But the reason, and I understand why it happened. But understanding it doesn't sort of make it right. A previous rotavirus vaccine was withdrawn, because there was a very, very rare side effect. And so the agency has now become extremely conservative and is asking for longer, larger trials, which on the face of it, is exactly the right response.

But in fact, the same number of children are being exposed, and the risk of finding those very, very rare side effects is no better in the trial than it would be in post-marketing surveillance. And were it not for the fact that——

Mr. SHAYS. We understand. Just so I'm clear.

Ms. RYAN [continuing]. I have a partner like Glaxxo, I couldn't do it.

Mr. SHAYS. I understand. Let me just interrupt you. So you're suggesting that the post-marketing, in a sense, be almost the trial, the third phase?

Ms. RYAN. Well, that it go out there into the real population, so it's not just being tested in academic hospitals, the real exposure and the real incidence of very rare side effects would be monitored. And if they are dangerous, it can be withdrawn.

Mr. SHAYS. Do you all agree that post-marketing is an important element? I should be fair to you, Dr. Wineger, it leads me to the question, that's where I think the military has its biggest breakdown. It seems to me, once they've got it approved, or once they've got a tacit acknowledgement they can use a pharmaceutical product, there is no post-marketing, there is no sense of how it's impacting our troops. I guess I want to know, do you both believe that post-marketing is important?

Ms. RYAN. I believe it is. And I think that vaccines really should be tested the way drugs are. And some of these enormous trials mean that only the large pharmaceutical companies can develop them.

Mr. SHAYS. You just said something that I'm going to expose my ignorance. The way drugs are, in other words, you're suggesting you don't need this larger market, larger testing if it's not vaccines?

Ms. RYAN. A large phase three clinical trial for a drug is 3,000 to 5,000 patients. Some of these vaccine trials, where every second child in Finland is being part of a vaccine trial doesn't really make sense to me.

Mr. SHAYS. Any other comments? Dr. Wineger, do you want to just comment about the post—our committee has basically had too much experience with, I'll speak for myself, I feel that the Department of Defense lacks credibility in this particular area. Once they've got approval, it's all steam ahead. And there isn't proper recordkeeping, there isn't proper post-marketing analysis of what's happened. How can we in this committee have the confidence that's going to change?

Ms. WINEGER. Well, first of all, I'd like to differentiate, if I could, between the responsibilities of the manufacturer and the responsibilities of, in this case, the user. I believe that the comments that were provided earlier were directed toward the responsibility of a manufacturer to conduct post-marketing surveillance.

Mr. SHAYS. I think that's different. BioPort is so close to being part of the Defense company. It's gotten its money, it's been basically pushed by the DOD, it's been overseen by the DOD, it's been funded by the DOD. So I just kind of feel you're both the same.

Ms. WINEGER. Well, I would agree that the anthrax vaccine immunization program that the Department of Defense has adopted is a different situation than most others. But I would remind you that the Department of Defense purchases and uses many other vaccines and many other drugs. We do not have any type of responsibility for post-marketing surveillance of those products. So if indeed you want to characterize the manufacturer, BioPort, and the Department's anthrax vaccine program as unique and different

from all others, then I'd be happy to provide some comments on that.

My point was that it is not traditionally the consumer, the user's responsibility to do that post-marketing survey.

Mr. SHAYS. The problem is, though, when a company has to analyze what's happened to DOD employees, they don't have their records. It's almost disingenuous to even suggest that there can be that followup, because the records that are kept by the military are confidential, they don't have access to them. And in many cases, the records are so poorly kept. You're not suggesting the manufacturers be out in the battlefield, and in your hospitals. Maybe we should. Is that what it's going to take?

Ms. WINEGER. What I'm suggesting is that there are a number of mechanisms in place for individual reporting and for monitoring the side effects of the vaccine. While the recordkeeping may not be perfect, certainly in a battlefield situation, indeed, many of the immunizations are given in U.S. locations. As far as I'm aware, there's no prohibition from the manufacturer or the FDA or any other body from coming in and inspecting those records.

Mr. SHAYS. The problem is, though, and I won't belabor it, is that during the Gulf war, we don't know, of the military personnel who claim Gulf war illnesses, there was no recordkeeping of when they were given the drugs, when they were given vaccines, when they were given shots, the cocktail effect and so on. I don't want to open up with Bernie on this one. [Laughter.]

But the bottom line is, there are some big challenges here.

Ms. WINEGER. I appreciate that.

Mr. SHAYS. I would love to just ask if, particularly those who had worked on the study with you, if there's any question we should have asked you that you want to respond to, any comment you would like to make as well.

Ms. HEINRICH. I was just going to comment that it's very hard to do really good post-marketing surveillance. FDA is very much in favor of post-marketing surveillance in many instances, and in some have asked for this and have tried to require it. But it's very, very difficult to do after the actual approval has been made on a particular drug or vaccine.

In terms of your good manufacturing practices and differences between vaccines and drugs, those manufacturing practices are very consistent. The other thing that I wanted to add is that anthrax isn't the only vaccine that has suffered from problems with their good manufacturing practices. Last year when we had the vaccine shortage for flu, it was because there were at least two producers that were having difficulty with their manufacturing practices. So it's something that the FDA and all of us involved in oversight, I think, have to be rigorous about.

Mr. SHAYS. Anyone else?

I'll tell you my concern in closing. My concern is that we're going to have two standards. We're going to have one standard for civilians and the vaccines they receive, we're going to have another standard for the military. I'm just concerned that the population is different, the testing may end up being different. And I'm hopeful that we're going to reanalyze this and make sure there's one standard. We need to speed up the process, but make sure that it's ulti-

mately going to achieve its objective of providing safe products that also are very effective.

Does any other Member want to say anything?

Thank you very much, and we will adjourn this hearing.

[Whereupon, at 2:15 p.m., the subcommittee was adjourned, to reconvene at the call of the Chair.]

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