ENGINEERING BIO-TERROR AGENTS: LESSONS FROM THE OFFENSIVE U.S. AND RUSSIAN BIOLOGICAL WEAPONS PROGRAMS

HEARING

BEFORE THE

SUBCOMMITTEE ON PREVENTION OF NUCLEAR AND BIOLOGICAL ATTACK

OF THE

COMMITTEE ON HOMELAND SECURITY HOUSE OF REPRESENTATIVES

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ENGINEERING BIO–TERROR AGENTS: LESSONS FROM THE OFFENSIVE U.S. AND RUSSIAN BIOLOGICAL WEAPONS PROGRAMS

Wednesday, July 13, 2005

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON PREVENTION OF
NUCLEAR AND BIOLOGICAL ATTACK,
COMMITTEE ON HOMELAND SECURITY,
Washington, DC.

The subcommittee met, pursuant to call, at 10:00 a.m., in Room B–318, Rayburn House Office Building, Hon. John Linder [chairman of the subcommittee] presiding.

Present: Representatives Linder, Shays, Jindal, Cox (Ex Officio), Langevin, Markey, Dicks, Norton, Christensen, and Thompson (Ex Officio).

Mr. LINDER. The Committee on Homeland Security, Subcommittee on the Prevention of Nuclear and Biological Attack will come to order.

The subcommittee is meeting today to hear testimony on engineering bioterror agents, and the lessons from the Offensive United States and Russian Biological Programs.

I would like to begin this morning by reemphasizing to our witnesses and to my colleagues, the primary mission of this subcommittee is the prevention of catastrophic terrorist attacks. In fact, this subcommittee is the only body of 120 committees and subcommittees in the U.S. House of Representatives that focuses exclusively on preventing two of the most catastrophic threats posed by terrorists against our Nation, nuclear and biological attack.

Our hearing this morning is the beginning of a series of hearings that will address the biological threat, and will lay the groundwork for assessing the role and responsibility of the Department of Homeland Security in preventing a bioterrorist event from occurring in this country.

The mission of the Homeland Security Department, first and foremost, is to prevent terror attacks from even occurring. The secondary mission is to protect the citizenry by hardening our Nation's infrastructure against potential terrorist attacks. Third, the Department must ensure that we are prepared to respond when, inevitably, terrorists devise a means of attack against which we have not guarded ourselves.

Prevention, however, must remain our top priority. This country cannot afford to falter to the third mission of response whereby we

find ourselves picking up the pieces after terrorists have succeeded; at that point it is simply too late.

In April 2004, President Bush issued his biodefense directive in the form of HSPD–10. Essential to this first-ever mentioned national biodefense strategy are four pillars, of which the first is threat awareness. This pillar firmly grounded in the notion that through the building of a strong intelligent capability to identify and characterize the biothreat, as well as understanding of our new scientific trends may be exploited by terrorists to develop biological weapons is paramount to our success. It is this aspect of the biological threat that we hope our experts will be able to address today, namely, the capability of nonstate actors to engineer organisms that can be used as a bioweapon.

The key to prevention is the analysis of threats, and this analysis is critical in determining where we should invest our resources. This government must be able to distinguish between any number of terrorist threats where there is a nuclear weapon or dirty bomb, and must be able to identify where terrorists are attempting to spread smallpox, or worse yet, a bioengineered agent that is designed to circumvent any known vaccine. And we should know whether they are simply looking to blow up an office building.

Undoubtedly, these are hard choices to make, but they are required of this government. And we must use both risk and consequence as a means of determining where best to spend our money and resources.

I am hopeful that our experts today will help get us on the right path. Since September of 2001, Federal-wide investment in biological defense measures has estimated more than $20 billion. Congress must now work to ensure this substantial investment is properly focused, make clear progress toward eliminating the most serious biological threats. And the witnesses should bring some perspective to the overall threat by providing the members of this subcommittee with insight into the current abilities of terrorists to develop, acquire and deploy a biological weapon.

I now recognize the ranking member of the subcommittee, Mr. Langevin, for an opening statement.

PREPARED OPENING STATEMENT OF THE HON. JOHN LINDER

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Mr. LANGEVIN. Thank you, Mr. Chairman. I would like to take the time to welcome our witnesses here today, and I look forward to the testimony.

This hearing mirrors one we had a couple of weeks ago on the ability of terrorists to build and detonate a nuclear weapon. We talked about the materials needed and the technical expertise required to carry out an attack. What we heard in this case was that, while building a nuclear weapon is not terribly difficult, success hangs on the procurement of fissile material. The basic conclusion, no nuclear material, no nuclear terrorism, provided my colleagues and I on the committee with a clear sense of the urgent need to secure known quantities of weapons-grade plutonium and highly-enriched uranium. I am glad to see that we are proceeding in a similar spirit to look at the threat of biological terrorism.

From what I have seen and read, there is a lot of competing information out there about the seriousness of the threat. I look forward to hearing from our panel of distinguished experts on this topic in the hopes that when we leave this hearing, we will have a concrete idea about the threat we are facing and its possible consequences.

I have read through the testimony, and I get the sense that the answer is not going to be a comforting one to the members of this subcommittee nor to the American public. The situation we are facing seems to be one in which the increased efficacy of the technology used in bioengineering has actually lowered the bar such that nonexperts now have the ability to build such weapons in home laboratories. The situation seems somewhat similar to the use of computers 10 years ago; you needed an expert to do a lot of tricks, to send or receive audio and video files across the Internet. And today, the technology does most of the work for you, and anyone can perform these kinds of tasks.

Unlike the case of nuclear weapons, where we saw that the overwhelmingly effective tactic to prevent construction of a nuclear weapon is to ensure that all the fissionable material is secured, we don't have that luxury in the case of bioweapons.

The proliferation of bioagents is vast, and there are hundreds of pathogens to choose from. The Centers For Disease Control has identified approximately 60 pathogens that they consider dangerous, and for which they suggest that the government secure its stockpile and countermeasures. And a good deal of the equipment needed to develop these weapons is readily available. Supplies such as DNA, growth media and other solutions can be simply ordered through the mail. The next step after creating the pathogen is putting it into a form which can be used as a weapon, and delivering the weapon to the target.

What I would like to accomplish today is to get a very clear sense of which points in the process are the sticking points, because it is presumably there where we will be best able to intervene to prevent such a weapon from being built.

What would be most helpful to me this morning is to have a clear, unvarnished and realistic picture in my mind of the threat and the possible consequences that we are dealing with in each of the possible bioweapons.

I look forward to hearing from our witnesses. And I thank you, Mr. Chairman, I yield back.

Mr. LINDER. The Chairman now recognizes the gentleman from California, the Chairman of the full committee, for any comments he might have.

Mr. COX. Thank you, Mr. Chairman. This is a very, very important hearing because it helps us focus on one of the fundamental challenges that policy makers at the Federal, State and local level are facing, the need to balance our investment against conventional terrorist attacks, such as truck bombs or IEDs, with the necessary investment that we must make to prevent and protect against potentially catastrophic threats such as biological terrorism.

The terrorist bombings in London last week were tragic, and they raised the question, while London was relatively well prepared to deal with the aftermath of a conventional series of bombings, would the same be true if there had been an anthrax attack last week in the London underground. Let's imagine the scenario. There are 3 million people who ride the Tube every day. When they leave the Tube, they go to work, or if they are visitors they tour London or, perhaps, catch an international flight. It is only 1 or 2 or 3 days later that people would start to get sick. They might then present themselves to an emergency room or to their doctor's office with respiratory illness symptoms.

There are no quick diagnostic tests for anthrax, but maybe an astute clinician would order a blood culture test for anthrax. We might never learn that this attack originated in the London underground. Prompt treatment prior to symptoms for any victim would be extremely unlikely. The number of deaths would easily be in the thousands. And this would be the result of a relatively low level biological attack in the same venue as the attack that occurred in London last week. A more carefully planned attack, with perhaps genetically-engineered bioweapons in the future could kill millions.

The biothreat is particularly worrisome because we know so little about terrorist capabilities and intentions. We also know that a bioattack could and would result in catastrophic loss of life. The Department of Homeland Security, therefore, must have experienced analysts to assess the threat on a continuing basis, and the Department must play a leading role in coordinating the development of antidotes and countermeasures to the most virulent agents we face today, and will certainly face increasingly in the future.

But as one of our witnesses has noted, countermeasures are fixed defenses. Those defenses can easily be overcome because of the rapid pace of technological development. Some experts believe that the hurdle for terrorist organizations to translate microorganisms into bioweapons is relatively high, others believe that this is a thin line of ignorance that could easily be crossed. Not only is technology rapidly evaluating and being transferred to the private domain, but also experts and scientists are spread all over the world. Dr. Alibek, who sits before us today, as a product and leader of the Soviet Biodefense program, is one of thousands of experts from the Soviet program that have the necessary knowledge and training to modify and weaponize biological agents. We must take into account individuals with this special knowledge as part of our antibioterrorism efforts.

The science and technology revolution in which we are now involved offers unprecedented hope if we are smart enough to exploit the opportunities before us; that is true both for biodefense and for improving our overall quality of life. At the same time, there is a dark side to the astounding progress of science and technology. The rapid pace of the technological development is the greatest single reason that bioterrorists must be taken more seriously than ever before.

I look forward to questioning our experts today, and to hearing their views on the unconventional threat posed by terrorist engineering of bioagents. I hope this testimony will also offer us insight into how best to reduce this threat and prevent against acts of catastrophic bioterrorism aimed at the United States.

Mr. Chairman, I want to thank you very much for convening this important hearing.

Mr. LINDER. Thank you, Mr. Chairman. Other members of the committee are reminded that opening statements may be submitted for the record.

We are pleased to have before us today a distinguished panel on this important topic. Let me remind the witnesses that their written statements will be made part of the entire record, and we would ask you to try to keep your comments to 5 minutes if you can.

Our experts are Dr. Kenneth Alibek, distinguished professor at George Mason University. Dr. Alibek holds the position of president and chief scientist of Advanced Biosystems. Dr. Alibek also served as First Deputy Chief in the civilian branch of the Soviet Union's Offensive Biological Weapons Program.

Dr. Roger Brent, President and Research Director of the Molecular Science Institute. Since middle 1990s he has advised various agencies in the United States and abroad on functional genomics, computation of biology and bioengineering.

Dr. Michael Callahan is the Director of Biodefense and Mass Casualty Care, CIMIT/Massachusetts General Hospital, Infectious Disease Division. He currently heads the working group on biological weapon threat assessment through the Department of Homeland Security. Welcome all. We thank you all for being here.

Mr. LINDER. Dr. Alibek, you may begin.

STATEMENT OF DR. KENNETH ALIBEK, EXECUTIVE DIRECTOR, CENTER FOR BIODEFENSE, GEORGE MASON UNIVERSITY

Dr. ALIBEK. Thank you very much.

Mr. Chairman, and the members of the committee, thank you very much for the opportunity to speak to such a distinguished group. I really appreciate this opportunity because I consider biological terrorism as one of the main, let me say, threats for the world and for the United States.

I am not going to read my testimony, I would like to put just some emphasis on what I consider is the biggest problems we are challenging now. First of all, in my view, biological terrorism is a kind of unique type of terrorism. What we need to keep in mind, biological terrorism is completely different from terrorism using explosives; it is a continuous type of terrorism. For example, if we remember our experience from 2001, when we experienced anthrax attack, probably everybody noticed that it didn't continue for a day, it continued for weeks, it continued for months. And every single day we are trying to understand who will be next, what is going to happen next, and how much money we need to spend, and what kind of economic damage we are going to suffer as a result of this very small attack.

And what we need to remember in this case, the amount of anthrax developed by somebody and sent by contaminated or let me say tainted mail was very, very little, very small, about 5 to 7 grams. It is a reasonable amount. And we see the level as similar in this case, it was 5 to 7 grams of anthrax, and the huge amount of money spent just to mitigate the threat of this attack. That is why, in my opinion, biological terrorism is a threat we face and will be facing for a long period of time.

When we talk about the Soviet Union's experience, the experience is quite extensive, quite extensive for many components. The Soviet Union had a very sophisticated, very powerful program. I am not talking about Russia; I don't know, and I do believe that Russia is not posing any significant threat to the United States, it is absolutely obvious. But when we talk about from the standpoint of expertise, knowledge, capabilities, the Soviet Union was able to develop one of the most—the most sophisticated offense biological program in the world. This program includes many different directions, to develop different types of biological weapons based on bacterial agents, viral agents, toxin agents and some other pathogens.

Significant research was focused on the development of industrial processes, what we refer to as biological weapons. New prototype biological weapons were under development based on new genetically-engineered pathogens. And one of the biggest problems was, of course, to develop new pathogens, genetically-engineered pathogens. And this work started actually sometime in the beginning of the 1970s. For a long period of time, the Soviet Union was strug-

gling trying to find appropriate ways to develop engineered pathogens. It was one time of, I would say, unsuccessful work. I don't want to say that people today would face the same problems because we are talking about the 1970s, 1970s is more than 30 years ago. Now science is completely different. We have got much higher level of sophistication in this field.

But at the beginning of 1980s, new biological weapons engineering pathogens appeared, they existed. And even talking about engineered pathogens, we need to keep in mind three major directions that scientists exploited in the field of developing genetically engineered pathogens, material pathogens. It is a simple genetic engineer manipulation which can result in new pathogens and new weapons which would be resistant to existing antibiotics, or at least some of the existing antibiotics. This knowledge exists; this knowledge is, let me say, widely published; and there is no significant problem to developing genetically-engineered pathogens.

There is another issue we need to keep in mind, it is the issue of how to manufacture these pathogens in large amounts, it is a completely difference situation. They can be manufactured.

Another direction, it is called immune subverting, or immune system subverting pathogens. There are several approaches that have been already developed, and this type of pathogens, they exist. There are some publications you would do a very thorough analysis. We confirmed there are publications already in open literature showing what kind of approaches can be used to overcome the natural immune response, or the immune response induced by vaccines, or some other immune system response. This knowledge is available now.

One of the most, let me say, unknown areas is the area of developing pathogens with newly induced virulent sectors. A kind of traditional pathogen could result in—manipulations could result in new pathogens having some new virulence factors. There are a couple of examples. We have got a publication which explains how some genes function in our nervous system could be inserted in the form of foreign gene, in the form of plasmic, in some material, or viral pathogens. And when the disease is developing, it produces completely new effect, in addition to existing symptoms. In this case, severity of disease is higher.

Now there are some other examples, and I give these examples in my statement. But what I would like to say in this case, of course what we need to keep in mind, I don't want to say that we are going to see a kind of low level terrorist groups they would be able to develop these types of biological weapons. But I would like to say is that knowledge is available to many countries, and there are some countries we suspect in working in the field of developing biological weapons. They do have such an ability, and they are able to develop these type of pathogens.

Just take a look at Iran. Of course we don't discuss this country in great detail, but if you do this in detail and you see what kind of universities and what groups are working in the field of microbiology, you would be amazed what kind of level of sophistication this country has in the field of medical biology engineering. As previously stated, that knowledge is already there. We know they are developing this, they have been published.

When we talk about terrorist groups which don't have state-sponsored programs, or they are not supported by states, they wouldn't have such an opportunity for a period of time. But when you talk about state-sponsored groups, the knowledge is there, and we need to keep that in mind.

Yes, today probably it is still early to talk about genetically-engineered biological weapons; tomorrow it could be a reality. Thank you.

Mr. LINDER. Thank you, Dr. Alibek.

[The statement of Dr. Alibek follows:]

PREPARED STATEMENT OF KEN ALIBEK

Mr. Chairman and members of the Committee, thank you for the opportunity to discuss with you the threats presented by biological weapons and biological terrorism. Addressing the issues of engineered biological agents and biological weapons is essential to increasing the understanding of how real the threat is and to determining whether or not it is likely that the United States will have to protect itself from engineered biological weapons in the near future.

In the former Soviet Union, the work to select new strains of virulent pathogens began in the 1970s. As the scientific leader of Biopreparat, the civilian branch of the Soviet Union's offensive biological weapons program, I was responsible for these projects from scientific and financial standpoints. There were a significant number of projects focused on developing various types of new BW, including the ones that involved genetically engineered pathogens. The projects with codenames like "METOL", "FACTOR", "BONFIRE", and "PODLESHIK". These names meant nothing and as I was told they were randomly selected and created by a computer. The work being performed in these programs, however, lead to a grim new reality in weapons development. Among the Soviet Union's areas of interest were new genetically engineered pathogens including antibiotic resistant strains of anthrax, plague, and tularemia; multi-drug resistant glanders and melioidosis; immune-subverting tularemia pathogen, and tularemia and plague pathogens with new virulence factors inserted into them. Of course I am not able to remember the specific details of each project even though I was responsible for all these projects. I had a large number of assistants or as we called them, project creators, who helped me work with principal investigators and institute directors and deputy directors. By 1990, there were approximately 30 project curators coordinating more than 300 projects, some of which involved the development of novel engineered pathogens and weapons, working for me.

One must only look at the Soviet Union's BW program to see that it is possible to develop genetically engineered pathogens. There is no doubt that the probability of developing sophisticated engineered pathogens is more feasible nowadays. It is very difficult to predict what the primary focus would be of a scientific group working on the development of such pathogens. For example, they could focus on the development of antibiotic-resistant pathogens, immune-subverting pathogens, or on pathogens with "added" virulence factors.

Ironically, even though I knew many of Biopreparat's projects during my time as part of the scientific leadership, I learned the details of some of these projects after I moved to the United States and read articles published by my former colleagues between 1992 and 2000. Interestingly, after 2000-2001 the number of publications in the fields related to biological weapons dropped significantly, then virtually disappeared. Before the disappearance of these types of articles, one could get a significant amount of information about the level genetic engineering research and what could be achieved in the field of biological weapons development. For example, two articles I read described very sophisticated work that focused on the creation of new, genetically engineered pathogens by inserting the human gene, beta endorphin, into *F. tularensis* and a smallpox performed using on non-virulent microorganisms, but anyone with an understanding of microbiology and molecular biology would understand how easily these changes could be transferred to pathogenic strains of the same microorganisms.

In the first of these publications a group of scientists studied how an attenuated strain of *F. tularensis* would produce beta endorphin in experimental animals and examined the changes it could induce in them. Immediately after I started reading the article I realized that the main purpose of this work was to create a genetically engineered pathogen that would produce additional pathogenic effects in humans. I found it interesting how they awkwardly tried to explain the necessity of the work.

The article started with a more or less logical explanation of how the beta endorphin could be a good replacement for morphine and other narcotic painkillers and could be used for the management of pain in people with debilitating diseases. It was logical from the point that the beta endorphin, which is produced by brain cells, is a more powerful painkiller than the existing morphine-like drugs. Another benefit of beta endorphin is that it doesn't cause addiction and could be used for a long period of time without causing any significant harm to the patient. The authors also explained that there were obstacles to this approach. For example, beta endorphin is a peptide, meaning it is subject to enzymatic cleavage by various proteases produced by our body and thus wouldn't have a prolonged effect. For this reason, the authors explained, it was necessary to find a way to keep this substance in the body for as long as possible to ensure a prolonged pain killing effect.

Up to this point, the work was logical but as I continued to read, the logic became hazy, then disappeared altogether. The authors suggested that the best way to keep the beta endorphin in the body for a long period of time was to insert a gene of this substance into a vaccine strain of *F. tularensis,* which wouldn't harm the patient, but while it multiplies it would produce the beta endorphin long period of time. I couldn't understand why they would use even a vaccine strain of a pathogen capable of multiplying in our body. Even using a vaccine strain would mean establishing an infection in the patient and so it made no sense to me why anyone would consider inducing an infection in a person to treat them. Additionally, the authors' explanation of using a pathogen to increase the length of time the endorphin was produced was illogical because the pathogen wouldn't stay in the body for a long time. As soon as the immune system developed specific antibodies against this microbe it would be eliminated from the body and the production of beta-endorphin would stop.

A third problem with the logic of this approach was that this type of treatment could be used just once. As soon as the body developed specific antibodies to the microbe future infusions of this "therapeutic preparation" would be ineffective as the microbe wouldn't be able to multiply in the body.

I thought that I might be missing something and continued to read the article. At the end of the article was a fascinating and revealing account of the results they had obtained. The authors explained that a few days after injecting the experimental animals with modified F. tularensis the animals developed severe muscle rigidity and became catatonic. The real reason for this research was obvious and counter to the humane reasons the authors had given at the beginning of the article.

The second article described the effects of beta endorphin when it was inserted in the Vaccinia virus, which can be used as a model for genetic manipulations of the smallpox virus, *Variola major.* The results were close to the same.

This work was funded by the former Soviet Union and I do not mean to imply that Russia is currently involved in this work. These examples are meant only to show what can be achieved in the field of creating genetically engineered pathogens.

In order to clearly understand what is achievable, let me give you a number of other examples that demonstrate the prevalence and level of sophistication of what is going on in the field of modulating pathogenic microorganisms. I am not saying the work described in these articles has a dual purpose and is being used to develop BW. What I want to say is that there exist many different methods and approaches to developing modified pathogens and that biotechnological advancements provide a large number of new examples each year. The modulation of pathogenic microorganism is not science fiction.

These are some examples:

Article One

Biomed Sci. 1991. All-Union Research Institute of Molecular Biology, Novosibirsk region.

Viral chimeric protein including a determinant of myelin basic protein is capable of inducing allergic encephalomyelitis in guinea pigs.

Shchelkunov SN, Stavitskii SB, Batenko LI, Gashnikov PV, Shchelkunova GA, Kostyrev OA, Sandakhchiev LS.

- A hybrid vaccinia virus expressing a chimeric protein consisting of thymidine kinase and the encephalitogenic determinant, S1, from guinea pig myelin basic protein was constructed. Infection of guinea pigs with the virus resulted in the development of allergic encephalomyelitis.

Article Two

Vopr Virusol. 2000 Nov-Dec;45(6):38–41.

[Immunogenicity of a recombinant strain of vaccinia virus, expressing a Venezuelan equine encephalomyelitis virus structural protein gene in peroral immunization]

Sviatchenko VA, Kiselev NN, Ryzhikov AB, Bulychev LE, Mikriukova TP, Netesov SV.

• Immunogenicity of recombinant vaccinia virus strain (VR26) expressing Venezuelan equine encephalomyelitis (VEE) virus structural protein genes was studied by oral immunization. Sera of animals immunized with VR26 contained antibodies specific to VEE virus, among which antibodies with virus-neutralizing activity were present. Evaluation of the protective efficiency of oral immunization with VR26 demonstrated a high level of animal protection from lethal doses of VEE virus. Rabbits immunized orally were highly resistant (protection index 142.9) to intranasal infection, which is of priority importance for antiVEE vaccine. Comparative analysis of the results of scarification and oral immunization with VR26 indicates that the type of immune response depends on the method of immunization. These results demonstrate good prospects of oral vaccination with recombinant VR26 strain for immunoprophylaxis of VEE.

Article Three

Proc Natl Acad Sci U S A. 1983 Sep;80(17):5364–8.

Construction of live vaccines by using genetically engineered poxviruses: biological activity of recombinant vaccinia virus expressing influenza virus hemagglutinin.

Panicali D, Davis SW, Weinberg RL, Paoletti E.

Recombinant vaccinia viruses containing the cloned hemagglutinin (HA) gene from influenza virus were constructed. The biological activity of these poxvirus vectors was demonstrated both in vitro and in vivo. Expression of HA in cells infected with recombinant vaccinia was detected by using specific anti-HA antiserum and 125I-labeled protein A, showing that HA synthesized under the regulation of vaccinia virus was antigenic. Immunization of rabbits with these recombinant poxviruses resulted in the production of antibodies reactive with authentic influenza HA as detected by radioimmunoassay, by inhibition of HA erythrocyte agglutination, and by neutralization of influenza virus infectivity. The production of antibodies directed against influenza HA suggested that the HA gene expressed in vaccinia is immunogenic. These data indicate the potential of genetically engineered poxviruses for use as generic live vaccine vehicles that have both human and veterinary applications.

Article Four

FEBS Lett. 1993 Mar 15;319(1–2):80–3.

Genes of variola and vaccinia viruses necessary to overcome the host protective mechanisms.

Shchelkunov SN, Blinov VM, Sandakhchiev LS.

Institute of Molecular Biology NPO Vector, Koltsovo, Novosibirsk region, Russian Federation.

Analysis of variola virus nucleotide sequence revealed proteins belonging to several families which provide the virus with the possibility of overcoming the barriers of specific and non-specific host defence against viral infection. The complement-binding proteins, lymphokine-binding proteins, and serine protease inhibitors can be assigned to this type, as can the proteins providing the orthopoxviruses with resistance to interferon. The revealed differences between the genes (proteins) of variola and vaccinia viruses under study are discussed.

Article Five

Vopr Virusol. 1997 May-Jun;42(3):115–20.

[Immunobiological properties of vp24 protein of Ebola virus expressed by recombinant vaccinia virus]

[Article in Russian]

Chepurnov AA, Ternovoi VA, Dadaeva AA, Dmitriev IP, Sizikova LP, Volchkov VE, Kudoiarova NM, Rudzevich TN, Netesov SV.

Immunological and biochemical parameters were studied in guinea pigs immunized with recombinant vaccinia virus containing full-sized gene of Ebola virus vp24 protein and then infected with virulent strain of Ebola virus. The majority of the studied parameters changed similarly in guinea pigs immunized with recombinant vaccinia virus and control guinea pigs inoculated with vaccinia virus both before and after challenge with Ebola virus. However, in animals immunized with recombinant vaccinia virus producing vp24 some biochemical parameters, the mean life span after challenge with Ebola virus, the level of antibodies to the virus, and the phagocytic activity of neutrophils indicated the development of immunological processes

other than in controls, namely, the development of immune response to vp24. Although these processes did not eventually lead to the survival of animals, they prolonged the mean life span and resulted in the production of anti-Ebola antibodies, though the level thereof was low. These data demonstrate that recombinant vaccines against Ebola fever are a promising trend of research

Article Six

Mol Gen Mikrobiol Virusol. 1997(3):24-7.

• Recombinant vaccinia virus expressing Japanese encephalitis virus protein E]

Cheshenko NV, Petrov VS, Protopopova EV, Netesova NA, Konovalova SN, Belavin PA, Loktev VB, Malygin EG.

Recombinant vaccinia virus expressing protein E of Japanese encephalitis virus has been constructed. Polyclonal antibodies to JE virus reacted with recombinant protein E in immunoblotting. Immunochemical analysis of the recombinant protein E with monoclonal antibodies showed that both group specific and receptor domains of the protein were intact.

Article Sevent

J Virol. 2001 Feb;75(3):1205–10.

Expression of mouse interleukin-4 by a recombinant ectromelia virus suppresses cytolytic lymphocyte responses and overcomes genetic resistance to mousepox.

Jackson RJ, Ramsay AJ, Christensen CD, Beaton S, Hall DF, Ramshaw IA.

Pest Animal Control Cooperative Research Centre, CSIRO Sustainable Ecosystems, Canberra, Australia. R.Jackson@cse.csiro.au

• Genetic resistance to clinical mousepox (ectromelia virus) varies among inbred laboratory mice and is characterized by an effective natural killer (NK) response and the early onset of a strong CD8(+) cytotoxic T-lymphocyte (CTL) response in resistant mice. We have investigated the influence of virus-expressed mouse interleukin-4 (IL–4) on the cell-mediated response during infection. It was observed that expression of IL–4 by a thymidine kinase-positive ectromelia virus suppressed cytolytic responses of NK and CTL and the expression of gamma interferon by the latter. Genetically resistant mice infected with the IL–4-expressing virus developed symptoms of acute mousepox accompanied by high mortality, similar to the disease seen when genetically sensitive mice are infected with the virulent Moscow strain. Strikingly, infection of recently immunized genetically resistant mice with the virus expressing IL–4 also resulted in significant mortality due to fulminant mousepox. These data therefore suggest that virus-encoded IL–4 not only suppresses primary antiviral cell-mediated immune responses but also can inhibit the expression of immune memory responses.

Dear members of the committee.

These examples show the level of sophistication that already has been achieved in the areas of creating genetically engineered pathogenic microorganisms. Unfortunately, these or similar, techniques are already available to countries suspected of being interested in developing biological weapons or that are working on dual-use technologies. However, we need to be cautious before stating that terrorist groups are able to develop sophisticated genetically engineered pathogens. Groups that are not state sponsored do not have the level of scientific sophistication needed to develop such pathogens at this point of time. Of course, that does not mean they will not develop this sophistication in the future or that they would not be able to obtain such strains. Though the threat of terrorist groups developing genetically engineered pathogens may not be immediate, it is important to recognize that it could be a threat in the future. We must diligently monitor the situation and be on the look out for possible changes in the field that could increase the availability of this technology to terrorist groups so that we can be best prepared for possible bioterrorism attacks involving genetically engineered pathogens.

Mr. LINDER. Dr. Brent.

STATEMENT OF DR. ROGER BRENT, DIRECTOR AND PRESIDENT, MOLECULAR SCIENCES INSTITUTE

Dr. BRENT. Well, I am grateful to Chairman Cox, Chairman Linder and Ranking Member Langevin for being asked to testify here.

I am from Hattiesburg, Mississippi originally. I graduated from the University of Southern Mississippi in math and computers. I

went to graduate school in Cambridge, Mass to learn molecular biology, and stayed at Harvard for the next 25 years.

In the 1990s, I helped start Molecular Sciences Institute, it is a nonprofit publicly-supported genomic research lab in Berkley, California. Now a lot of the work we do involves developing technologies, for example, making little machines inside cells so the cells can tell you what is going on inside them. I am kind of a technology guy in biology. If you want to get from point A to point B in a laboratory, I can tell you ways to do that, I can probably come up with some new ones. I, and a bunch of other people since 1987, wrote one of the main manuals or cookbooks on how to do this, four volumes now, Current Protocols in Molecular biology; thousands of pages; 20 years in the public domain; 10,000 and more subscribers worldwide. 600 bucks will get you a year subscription continual updated to the cookbooks. Those are reasons that I am here today.

By 1996 revelations from Iraq after the first Gulf War, combined with stories coming out of the former Soviet Union from scary people like Dr. Alibek here, combined with information about Al-Qa'ida, have begun to terrify the U.S. government about renewed danger from classical biological weapons and the increasing dangers from new ones.

Beginning in 1997, I was tasked to advise the Defense Department, along with some other technically-inclined biologists—there is only a handful—as to how to strengthen the Nation's defenses against biological attack, and I have continued to do so. After 2001, September 11, this got much less advocational.

But in this work I regularly received in-depth briefings on the U.S. and former USSR programs, trends and offensive and defensive capabilities, the public health system and the response system, the detection systems. And I have been forced to think about the big picture and about the strategic issues. I would like to make a few brief points about the threat and the defense against it.

The most important enabler is there is a decentralized Moore's Law-type revolution and biological understanding that has been going on for more than half a century. Recombinant DNA is more than 30 years old. Revolutionary changes, each year there is an increase in human capability. Revolution changes have revolutionary consequences. And much of the 21st century will reflect these changes breaking surface into human affairs. And mainly it is for the good, it will help enable personalized medicines, longer and healthier lives for Americans, clean energy to reduce our dependence on Middle Eastern oil, the list goes on. Real cures for the diseases that ravage the developing world. But there is a negative consequence. There are now tens of thousands of people who could engineer drug resistant anthrax, maybe hundreds of thousands. There are tens of thousands of people who could remake a virus like SARS, or augment existing organisms to make them more deadly, and their numbers will only grow. If you imagine a contagious disease spread by people who make the disease who just cough on people, you could kill millions without the Cold War steps of weaponization.

Because this threat has changed from the days of the Cold War germ war program, our defense posture needs to change. Although it is a good thing we now have enough smallpox vaccine and that

we are working on a more modern anthrax vaccine, it is important to remember that stockpiles of vaccines and drugs are fixed defenses against known threats. In that regard, they are a Maginot Line because adversaries, if they know of these defenses, can and will outflank them. In the end, fixed defensive countermeasures can be no more effective to the defense of the United States that the Maginot Lines was to the defense of France in 1940.

So it is a hard problem. But the U.S. leads this revolution and it benefits from the consequences. The biology establishment in the U.S.—university, industry, non-profit—is the best the world has ever seen, and it can help protect against the threat if it is constructively engaged.

Building a defense is a problem of real gravity and complexity; it will require R&D and policy efforts sustained over decades, which will mean that it will need to enjoy sustained consensus bipartisan support, as was true for Government support for science and technology during the Cold War. So it is a hard problem. But successful effort will pay back many fold in better health and increased economic activity. And if we can get the right policy, we can help ensure that the U.S. can capture the benefit of the investment in terms of new industries and economic growth. Thank you.

Mr. LINDER. Thank you, Dr. Brent.

[The statement of Dr. Brent follows:]

PREPARED STATEMENT OF DR. ROGER BRENT

Chairman Cox, Ranking Member Thompson, Subcommittee Chairman Linder, Subcommittee Ranking Member Langevin, distinguished Members, it's an honor to appear before you to address issues related to engineered biological weapons, lessons from the US and Russian Cold War programs, and the consequences that modern developments in biology have for development of engineered biological weapons.

I'm from Hattiesburg, Mississippi, where I graduated from University of Southern Mississippi in computers and math. I went to graduate school in Cambridge, Mass., to learn molecular biology, and stayed at Harvard for 25 years. In 1997 I helped start Molecular Sciences Institute, a nonprofit public genomic research lab in Berkeley California. My faculty appointment is at UC San Francisco. The science we do is fundamental, but has broad applications to biology, medicine, and industry, for example to help biotech and pharmaceutical companies find drugs.

A lot of my work involves developing technologies, for example making little machines inside cells to tell you what is going on inside, and I'm kind of technology guy, You want to get something done in the lab, I can tell you good ways to do it and with luck think up and get working some new ones as well. Related, since 1987 I help write one of the main lab manuals, really kind of like a giant cookbook and or recipe book, Current Protocols in Molecular biology, that tells you how to work with get from point A to point B working with bacteria and viruses and DNA and cells. $600 bucks gets you a year's subscription, continually updated, almost 20 years in the public domain, 10,000+ subscribers worldwide.

Which is why I'm here today. By '95–'96 revalations from Iraq after the first Gulf war, combined with stories from scary people like Dr. Alibek here, and a flow of information about Al-Quade had begun to terrify the US government about the danger from classical bioweapons and the increasing dangers of new ones. Beginning in 1997, I was tapped to to advise the Defense Department as to how to strengthen the nation's defenses against biological attack. As such, I continually receive in-depth briefings on the U.S. and former Soviet Union programs, trends in offensive and defensive capabilities, and the public health system and been forced to think about the big picture and the strategic issues.

I'd like to make a few points about the threat and the defense against it.

(1) There is a decentralized, Moore's law type, revolution in biological understanding and capability going n worldwide for more than half a century. In some cases, biotechnology is advancing faster than computer technology. For example, the density of components on computer chips continues to double every 18 months—while certain abilities to read and write DNA double more like every 12 months.

Just as with computers, revolutionary changes sustained over time have revolutionary consequences, and much of the first part of this century will reflect these changes breaking surface to impact human affairs. The US leads this revolution and benefits from its consequences, and it is likely that the ability to manipulate DNA will be as important to the economy of the 21st century as the ability to manipulate electrons and bits was to economy of the 20th century. The consequences of this revolution will help enable personalized medicines, longer, healthier lives for all Americans, clean energy that reduces our dependence on Middle East oil, and cures for the diseases that ravage the developing world such as AIDS, TB and malaria as well as an improvement its food supply

(2) Unfortunately, the negative kinds of activities that this revolution in knowledge and capability constitute a sea change compared to the abilities that powered the US and USSR offensive biological warfare programs during the Cold War. Even through the early 1990s, a great deal of the activity in programs such as the one Dr. Alibek helped direct could be categorized as "microbiological process engineering", how to "weaponize" germs and viruses, coat them with agents that protected them from the environment, to make the disease causing particles rugged and controllable.

(3) By contrast, there are tens of thousands of people worldwide who can now engineer drug resistant bacteria, and thousands with the ability to remake a virus like SARS, or perform other engineering tasks too numerous to mention. Their numbers will only grow, so I would not be surprised if, by 2010, there were more than 100,000 people worldwide who had the knowledge and access to the lab equipment they would need to use to make, say, anthrax resistant to Ciproflaxin. Since the breadth of dissemination of this technical knowledge base will only increase, if you assume that some of these people may be motivated to undertake these tasks, then you have to look at the next decades are a time of great and increasing risk. If you further assume that some individuals or groups may be motivated to use relatively crude deployment methods, at the limit including infecting themselves and spreading the disease by human transmission, then you have to figure that the increase in the risk is higher still. These projects could be carried out by individuals or small groups of people; there would be no need to recreate the Cold War programs of the nation states.

(4) And its important to note that the potential mortality is enormous. When one uses the words terrorism or bioterrorism, they sometimes connotes local events, such as the horror in London. But remember that it would be possible to mount a coordinated attack spread by aerosol—dust or fog from sprayers—or by infecting members of a group with a contagious disease who initiate a multifocal ourbreak of a contagious disease transmitted human to human.

An attack with a contagious disease that circumvented existing defenses would not be confined to a single location but would be national and international in scope. An attack that killed 1% of the US or world human population would be a strategic disaster, a catastrophe only rivaled by the 20th century spectre of nuclear war. I believe it is the proper province of government to protect against such catastrophe.

(5) Although its a good thing we have enough smallpox vaccine, and that we are working on a more modern anthrax vaccine, it's important to remember that stockpiles of vaccines and drugs are fixed defenses against known threats. There is a name for fixed defenses that can easily be outflanked. They are called "Maginot Lines". Because adversaries can and will outflank these defenses, in the end, by themselves, stockpiled defenses against specific threats will be no more effective to the defense of the US than the Maginot line was to the defense of France in 1940.

(6) It is therefore important to move the US defense posture from one mainly based on fixed defenses against known or knowable threats to one that is complemented by flexible detection of new threats and agile responses to them. Effecting this change is a solvable problem but it is a complex one. Doing it right will require changes in strategy, policy, and institutions, and generation of a S&T base and an industrial structure that can provide the technical means to enable the shift.

(7) Numerous elements of the defense effort, both policy, "soft power" elements, as well as technical elements, are naturally international in scope and will require broad international participation and support.

(8) The US biology community, university, nonprofit, industry, is the best the world has ever seen. If it can be constructively engaged, it is entirely capable of protecting against the current challenges. But engaging this community and constructing this defense is a problem of such gravity and complexity that it will require R&D and policy efforts sustained over decades.

(9) One consequence of the complexity of the problem that the defense effort needs to enjoy sustained, consensus, bipartisan support, both from the government, which will need to pay for it, and from the scientists, engineers and industrialists who will

help execute it. We built and maintained such consensuses during the Cold War and they enabled us to get the job done.

(10) Successful effort will pay back manyfold in increased security, better health and increased economic activity, and attention to right policy will help ensure that the US can capture the benefit of its investment in terms of new industries and economic growth.

I am attaching an article expanding on these topics that has been circulating in samizdat form in policy circles for almost two years. A version of it will be published in Tara O'Toole's biodefense journal later this year.

Mr. LINDER. Dr. Callahan.

STATEMENT OF DR. MICHAEL V. CALLAHAN, DIRECTOR, BIODEFENSE & MASS CASUALTY CARE, CIMIT/MASSACHUSETTS GENERAL

Dr. CALLAHAN. Thank you, Mr. Chairman, committee members.

Like my predecessors, I can forego much of the testimony with regard to the gravity of the threat, and focus with more precision on some of the evolutions of the convening of technology intent in the nooks and crannies of the planet where these features and these factors co-exist.

I will speak specifically with regard to three applications. My first is, as a clinical infectious disease doctor who works in the developing countries of the world in management of the diseases caused by these agents, specifically lassa fever, hemorrhoragic fever, Marlburg, Ebola, epidemics from the past, cutaneous anthrax in northern Nigeria and other places. These are listed in the testimony.

My second contribution will shore up a lot of what

Dr. ALIBEK HAS SAID. I work extensively in the former Soviet Union; I spend 30 percent of my time there. I spend that exclusively at the bench top with former weapon scientists in 14 institutes tempering priorities to the Department of State's biological bioindustry initiative.

A key point here that I would like to stress is that this program, unlike any of the others, has used the biodefense market and the biotechnology market of western nations to create a market pull, to bring these former weapon scientists to participate in part of the solution. And for this reason we have had excellent access to these institutes. These former weapons scientists, many of them aging, and many of them with their children here in the United States receiving higher education, call upon us across international cell lines to tell us that there has been a laboratory accident, to tell us they have a sick loved one in a Russian or former Soviet Union hospital. So as a physician, we attend to them.

As advocates and collaborators, we try to help them in their education. And our statistics are quite good. Out of 177 currently engaged programs spanning 14 institutes, I will tell you that the timeline for radical medical countermeasures to the agents of bioterrorism number 11 percent. 11 percent of our total portfolio in the Harvard system, and using the best of our academic and biotechnology resources here in the United States, has new answers coming out of the former Soviet Union program. It is that which they prepared, they also mitigated against. They had to consider blow back. They will perceive that there was an offensive use capability by other nations that were targeting them as well.

So they have been thinking about unknown threat agents being lodged at them for some time, and this is a paradigm shift in the way they have developed their own science.

The third and last application, which I will minimize for the purposes of this testimony, is that the Department of Homeland Security is embarking on a huge effort to bring subject matter expertise and intelligence community members together to chart a path. We are having great difficulties with this because of arbitration and because of some of the conflicts, and the fact that, quite frankly, our expertise is not read in.

I would like to contrast, as we go along the remaining time, with the sharp distinctions with nuclear weapons. The chairman and several others have already talked about these, but I would like to crystallize these for you because it is quite policy relevant.

First and foremost, you need to understand that there are seven critical ingredients to the manufacture of biological weapons. I would like to go through them with just a couple comments in each and try to help to develop good questioning off of those.

The first of these ingredients is access to agents. There is a lot of attention being spent at the locks or freezers in the former Soviet Union, this is important. It is what the Defense Threat Reduction Agency's priority goal is, and BII and Department of State is doing that as well; it is not necessary, though. I work in all of these countries and see these diseases as a routine evolution of human ecology, and I have several of the supporting materials that are in your folder that will talk about that in some detail.

We have over 200 laboratories in Subsaharan Africa from where we have documented anthrax and plague from humans. And these are laboratories which have the capability to isolate, to purify and to amplify to these agents from all the background infectious organisms. I will also note that many of these labs are occurring in fundamental Islamic communities or are far outside the scrutiny of western nations. They are, quite literally, at the end of the path.

Number two is that, in addition to the agents which are easy to get and found in every country of concern to the United States, is that there is a critical choke point, an actionable choke point with regard to the reagents. There are several reagents that are very helpful at amplifying these agents from their background. Several reagents. It might be an antibody, it might be a plasma that could be used for the construct of a genetic organism, or with the advent evolving technologies, it might be a small scale fermenter, an ager roller bottle system, or an agent which helps to produce a high, dry powder which has high loft efficiency. Reagents is a critical actionable place to focus on.

Expertise. Here I return our attention back to the former Soviet Union program because it epitomizes this to some degree. Expertise migrates much better than the technologies do. And the experts from all the programs, and quite frankly, in ill-intentioned, nefarious-minded, moderately-trained microbiologists out of the European program cold return to these western nations and reconvene all the necessary ingredients of this technology and infrastructure to do covert manufacture. I will note also that the reason why this is so holoendemic in developing countries in the world is because the veterinary communities produce their own pharmaceuticals lo-

cally. They need anthrax to make an anthrax vaccine that is used in northern Nigeria to treat the local economy, which is on the hoof. So there is an economic force driving the technologies of these developing and small-scale weapons as well.

Technology also contributes in a meaningful way to the reconvening—remodeling really—of old-style, traditional biological weapons, such as those that were found in the U.S. program prior to its dissolution in the early 1970s. You can take an old agent, an anthrax spore preparation, and you can modernize it, and this increases its magnitude and its ponderal impact, its impact upon the human populations. This is depicted in my third handout, which talks about, at one magnitude, reduction in the number of spores that you need based on the incorporation of modern immunologic principles and the use of a single new technology which became available in 2002.

Beyond expertise and technology, I will end quickly with some of the small points. One is budget. In our laboratory modeling exercises of small-scale biological weapons, we can produce 14 million lethal doses of anthrax as a model agent for a reagent cost of 36 pounds British Sterling. That is the reagent cost, that is not salaries. And this is done. It is not a theoretical laboratory modeling exercise, it has been done with the surrogates. It was mapped very carefully. It has an Excel spreadsheet that goes with it, and a list of reagents and inventories.

It is also important to note that the people who participated in that exercise used all open source information, they used the U.S. Patent Office and they used out of print microbiology textbooks. It is a scary incredible thing, and it is not just theoretical, it has already been capitalized both in laboratory modeling and in actual experience. I refer you back to the intelligence community's information on the American anthrax attack in 2001, which we won't discuss here.

So after the budget, finishing up, production capability. I will just remind you—and this reflects the first point about the holoendemic nature of these laboratories is that you need a covert production capability. With the modern technologies, these laboratories are downsized. The laboratory model that was used to produce that anthrax biological weapon was 200 square feet, had a capital infrastructure cost of about $220,000, and the graduate students were not salaried, so there were some cost benefits in there as well.

What is so often overlooked in our homeland security threat analysis programs is that skilled research capital, even terrorist capital, needs to be preserved. So another choke point is to focus critically on the protection of terrorists while they are producing these agents. While biological containment, the laboratory equipment that you have that protects your workers from being infected can be improvised not at the highest level that is needed for aerosolized agents that are highly dangerous pathogens.

So here we look for the hypervaccined individual, and we look for things such as consistent antibiotic immuno suppression, which has been used in other programs as well.

My summation is short because it is made easy by colleagues here. The traditional weapons exist; they are very possible, they

are very plausible, they have been modelled extensively by our European partners. The agents, the technologies are all preexisting. And one of the tragic benefits is that as we develop benefits in modern health care and modern technology, which serve us well, they have a dark side, they have a down side. And it is these same technologies which have dramatically increased the efficacy and the efficiency of killing of these threat agents.

I will stop there, and I look forward to your questions.

[The statement of Dr. Callahan follows:]

PREPARED STATEMENT OF DR. MICHAEL V. CALLAHAN

Mr. Chairman, distinguished Members, it is an honor to appear before you to present information on the threat of traditional and next-generation biological weapons. My perspective is derived from experiences as a tropical medicine physician who studies and treats the diseases caused by these agents, from experiences working with former biological weapon scientists in Russia, and threat assessment activities on behalf of the Department of Homeland Security's National Bioterrorism Analysis and Countermeasures Center (NBACC).

I am a staff physician in the Division of Infectious Diseases at Massachusetts General Hospital in Boston, Massachusetts, and the Director of Biological Threat Defense at the Center for Integration of Medicine and Innovative Technology (CIMIT). CIMIT is a multi-institution, non-profit research organization funded by the U.S. Government to identify near-term solutions for critical military and civilian medical problems. Since January 2002, I have also worked with the U.S. Department of State, in particular with the Bio-Industry Initiative (BII), a program which uses the U.S. biotechnology market and academic collaborations to redirect former Soviet biological weapons scientists to peaceful, sustainable medical research. Prior to this position I was on faculty at the Center for International Health at Boston University where I served as clinical investigator for tropical medicine research projects in sub-Saharan Africa. I currently maintain tropical disease research activities in five developing countries, which is pertinent to the discussion below. Since the October 2001 anthrax attack, I have worked with biological terrorism working groups from the National Academy of Science, the Department of Defense, and the Department of Homeland Security. My focus areas are risk analysis of small scale biological weapon production, and consequence management following mass-casualty infections and poisonings.

This subcommittee has asked that I provide some perspective on the threat of engineered biological weapons. As there is considerable debate about several aspects of biological weapons, I have attempted to support this testimony with photographs from the field and from laboratory modeling activities. I will emphasize here that I am not an expert on the former U.S. biological weapons program that was disbanded in 1971. I also understand that Dr. Alibek will provide testimony on the Soviet biological weapons program under Biopreparat. My reference to the FSU (Former Soviet Union) program will therefore, be restricted to information gained from ongoing research collaborations with ex-biological weapons scientists from 10 Russian institutes. It should be emphasized that my experiences helping BII to develop drug and vaccine commercialization opportunities for former weapons scientists have resulted in access to several institutions previously closed to westerners (Figure 1). Further transparency is gained, perhaps ironically, by relationships forged from my medical care of former weapons scientists and their family members, and on occasion, emergency medical consultation to infections resulting from laboratory accidents. Finally, it is probably relevant that my experiences conducting clinical research in remote African and Asian locales have sensitized me to some of the challenges a terrorist lab would encounter when attempting to make a biological weapon in an austere environment (Figure 2).

What is our current understanding of engineered biological weapons?

Most experts agree that biological weapons are the original weapons of mass destruction. Throughout history, the overwhelming majority of biological weapons were used in a crude form. For example the first recorded use of biological agents was in 1346 when the Tartars catapulted plague-ridden corpses into the city of Kafka. In more recent history, a branch of the Japanese army, Unit 731, reportedly dropped plague-infected fleas in ceramic bomblets over cities in China in WWII, which likely accounts for unusual changes in the epidemiology of this disease in several regions. Prior to the genomic revolution of the last two decades, laboratories

in several countries worked with variable success to stabilize infectious microorganisms and toxins so that they could be stored and deployed with greater efficiency and predictability. The advent of molecular biology, advances in our understanding of infectious diseases and immune regulation, and advances in micro-particle engineering and micro-encapsulation have all resulted in technologies that can be used to either advance the properties of biological weapons or as countermeasures to protect against them.

Past military interest in biological weapons was driven by the realization that a comparatively small investment is required to make a tactical weapon capable of killing a large number of enemies. In rare cases, military weapons programs considered biological weapons as part of strategic campaigns. The interest in using biological toxins and infectious microorganisms as weapons was also driven by characteristics of the agents themselves. For example, in contrast with other munitions such as nuclear, chemical and conventional high explosives, only biological weapons are self-replicating. Moreover, these agents can be scaled-up from seed stock to a full stockpile on short notice and with considerably less engineering, manufacturing, capital investment and production signature than would be produced by nuclear or chemical weapons. A related characteristic is that biological weapons can be covertly transported as either minute quantities or in a form that leaves no signature, thus allowing the agents to cross international borders and be produced behind enemy lines. Military strategists also noted that only biological weapons could be successfully deployed without detection, a desirable characteristic if attribution is to be avoided. By the time clinical symptoms would appear, those that deployed the weapon would be many hours or days distant. Most ominously, and in stark contrast to chemical and nuclear weapons, contagious biological weapons such as killer influenza and smallpox, have the unique capacity to cause casualties far beyond the immediate impact zone.

Biological Weapons and Terrorism

Many of the characteristics that make biological weapons attractive to past military programs also make them desirable to the terrorist. Fortunately, the convening of biological weapon capability and terrorist intent has not as yet resulted in a mass-casualty incident. Unfortunately, several disquieting observations of the October 2001 anthrax attack using the U.S. mail system merit emphasis. First, the attack illustrated that advanced expertise had readily been exploited by a bioterrorist; the preparation in the Daschle letter contained extraordinarily high concentrations of purified endospores. Second, the spore preparation was coated with an incipient which helped retard electrostatic attraction, thus increasing aerosolization of the agent. Third, the choice of the near-ubiquitous Ames strain, combined with the absence of forensic details in either the agent or the letters, indicate that the terrorist is scientifically informed, wary of detection and *extremely* dangerous.

I use this well-publicized case to demonstrate that from the *perspective of the terrorist,* biological weapons are likely to be the optimal choice for inducing terror. As a practical point, the terrorist is likely to be attracted to any means which causes maximal disruption, terror and loss of confidence while using the minimal amount of skilled personnel, specialized resources and financial investment. For example, the skills required for bioweapon manufacture may be derived from manufacturing practices that use similar technologies such as the fermentative and agricultural sciences, vaccine manufacture, potable water treatment and environmental microbiology. In this regard, bioweapons offer specific advantages for covert manufacture by the terrorist:

1. The agent may be produced using equipment designed for other peaceful purposes (so called 'dual use').
2. Production requires minimal space and time, a characteristic that is increasing with modern technology.
3. Unlike any other weapon, infectious microorganisms are self-perpetuating, and therefore may be propagated among the terrorist groups or cells.
4. Several agents can cause casualties beyond those originally infected.
5. When human assets need to be preserved, these weapons allow the perpetrator to escape detection.

From the perspective of the threat analyst, there are 7 overlapping conditions that need to be present for a terrorist group to produce an effective biological weapon. Failure to meet any of the following conditions can thwart an attempt at weapons production. These conditions are consolidated from consensus opinion of different U.S. Government working groups, by CIMIT's modeling activities and from field experiences working with over one hundred laboratories in Southeast Asia and sub-Saharan Africa (reference Figure 1: a clinical infectious disease laboratory in rural northern Nigeria. The laboratory technician and I are holding up red blood cell agar

plates containing the non-hemolytic *Bacillus anthracis* which was isolated from the skin lesion on a local goat herdsman. In this region, estimates of 15–40 cases of cutaneous anthrax are observed annually): the seven conditions for biological weapon production are:

1. *Access to agent:* this condition requires that the terrorist has the ability to isolate or procure the microorganism or biological toxin. Note that many threat agents are endemic in Neotropical regions of the globe, *including all countries of concern to the U.S.* Naturally-occurring infections resulting from these microorganisms are routinely encountered in domestic animals, *as is the local expertise required to recognize these infections.* Procurement can involve coercion, misrepresentation of intent, or illegal purchase from a former weapons program or strain collection.
2. *Reagents:* this condition includes availability of factors required for successful biological isolation and amplification. Examples include specialized or improvised culture media, sporulation-inducers, and incipients to stabilize the agent or to improve purity.
3. *Expertise:* technical know-how can be derived from other disciplines. In modeling studies stated knowledge gaps to weapons manufacture may be overcome using internet based literature and patent reviews, use of out of print texts, and identification of solutions from parallel scientific or manufacturing disciplines.
4. *Support technology:* this category includes laboratory assets such as roller bottles, agar trays, fermentors, lyophilizers, egg incubators, cold storage capability, animal testing capability and biochemical test kits. The recent commercialization of an unnamed technology has dramatically simplified the challenges to manufacture of one bioweapon by allowing a less refined preparation to be used.
5. *Budget:* in both resource rich and austere economies, the financial cost of procurement, laboratory consumables, animals and maintenance of laboratory operations is significant. In modeling studies, the anticipated budget required to complete all manufacture tasks posed a greater challenge to a minimally resourced terrorist group than did other tasks.
6. *Covert production:* modeling for small scale anthrax suggests that a small appropriately-equipped laboratory with a footprint of 250 ft2 would meet the production needs of a small scale spore weapon. Although many agents can be purified and engineered in simple microbiology laboratories (which are found worldwide), large scale production, coating and stabilization would require a purpose-designated facility.
7. *Laboratory Safety:* skilled technicians require protection, however the procurement of specialized safety equipment is closely monitored. For this reason safety capability may be improvised, or lab workers may be hyper-vaccinated and maintained on antimicrobial prophylaxis to permit lower levels of containment to be used.

What can the Former Soviet Union Weapons Program teach us about Engineered biological weapons and bioterrorism?

Recent terrorist attacks in Russia have prompted government actions to protect against terrorism. However, an ethnically diverse population, poor border controls, regional corruption, and the continued conflict in Chechnya have all produced conditions that could still result in a biological weapons attack by terrorists. According to one Russian government official, "In no other place do the microbes, the expertise, the infrastructure co-exist in such close proximity with terrorist groups and chaotic times" (name omitted). In the last 2 yrs the concern about terrorism has prompted new levels of disclosure and cooperation between the Russian Federation and the United States. In the last 2 years there have been 4 conferences in Moscow and St Petersburg where prevention and response to bioterrorism was a major topic. These conferences are important for a second reason in that they provide a forum whereby the FSU scientists present previously unknown countermeasures or vaccine strategies which were used to protect production workers or government personnel from the USSR agents. Some recently described technologies, such as non-specific immune enhancers (immune modulators) have little precedence in Western biodefense and are exciting new additions to the BII's Advanced Vaccine and Drug Development program.

Traditional weapons programs

Traditional biological weapon manufacture is best illustrated by the former U.S., British and Soviet era production methods. In the Soviet era program, simple methodologies such as microbial fermentation were conducted on a grander scale. In two former production institutes (Stepnogorsk and Berdsk) fermentors used to produce weapon strains were many thousands of liters in volume, over two stories in height and under continuous stringent environmental control.

In these programs the kill efficiencies of the weapons were increased by maximizing the number of viable microorganisms in the final munition rather than focusing on engineering of the organisms (which came later). SRCAM scientists recount that in the case of anthrax, attention was focused on increasing fermentation and spore production efficiency, and spore recovery using a number of methods such as foam flotation. Other expertise was directed at improved methods of milling to produce progressively smaller clusters of spores, a condition for successful delivery and sequestration in the terminal alveoli of the lung. By report, there were occasional production misadventures where fermentation runs were contaminated by other bacteria or anti-bacterial phages which destroyed the entire production run.

In the years since the end of the Russian program, our scientific understanding of microbial metabolism and the improved efficiency of automated small scale fermentors have increased the amount of vegetative bacteria that can be produced with minimal resources. Parallel sciences, such as biological insecticides which use bacterial spores afor peaceful purposes, have provided clues to maximize yield in a small laboratory. Perhaps most disturbing is the growing availability of small scale, autonomous operating fermentation systems which reduce the need for skilled technicians and a complex support infrastructure (e.g. Bioflo IV Fermentor, New Brunswick, Inc). These systems are becoming more common in agricultural regions of Africa.

When considered as a whole, traditional weapons technologies with alterations rather than genetic engineering are the most likely to be employed by a moderately resourced, moderately skilled terrorist group. There are many open sources and skilled personnel who can provide guidance to help assemble the critical components necessary for weapons development. Potentially, a former weapons scientist from Stepnogorsk could travel to country in the Middle East and reconvene a weapons capability from available veterinary, agricultural and clinical microbiology resources. For Middle Eastern countries, the easiest solution would be to isolate a virulent epizoonotic pathogen from a local infected animal. These scientists need not bring anything with them but their expertise.

To summarize, efforts to prevent traditional biological weapon production should include efforts to prevent migration of skilled personnel to hostile groups. Additional measures for prevention of weapons development include tight scrutiny of international collaborations and tracking the importation of small scale bacterial growth systems and close human and animal surveillance efforts to detect infections resulting from deficits in the safety of a weapons laboratory.

Next-generation Biological Weapons

Next-generation biological weapons are those that benefit from new technologies, those made from previously unknown infectious agents or biological toxins, and those where a traditional agent is dramatically altered by the addition of a high-tech capability. One concept that is central to discussions of enhanced virulence biological weapons is that the same open source methodologies that advance our ability to improve upon human health may also be commandeered for nefarious purposes. A second point is that traditional biological weapons such as those produced in military weapons programs can be *modernized* to achieve new levels of lethality. The following case is used to illustrate this point.

In the former U.S. weapons program, estimates were made about the number of anthrax spores required for an LD50 (dose required to kill 50% of a population) and LD90 (dose required to kill 90% of a population). Extrapolations from these estimates indicate that between 8,000-10,000 spores would be required for infection. These estimates are likely accurate for the anthrax strains used in the pre-1971 program. Unfortunately, in recent years there have been dramatic advances in the modeling of airflow in the human lung which in turn has driven the field of aerosolized drug and vaccine delivery. In the last 8 years, particle physicists and pulmonary scientists have worked together to improve the efficiency with which drugs reach the alveoli of the lung, which is also the preferred target for the aerosolized anthrax spore. A parallel advancement has occurred in the field of immunology where new organic coatings have been invented which dramatically increase the uptake of particles by the specialized cells in the alveoli. Unfortunately these cells are also responsible for providing the anthrax bacillus with a protected beachhead for replication. The result is that two unrelated technologies, a method for generating small drug and vaccine aerosols, and the development of a specialized coating, are responsible for dramatically reducing the number of spores required to produce a successful infection. (Figure 3 depicts the methods used to produce a coated anti-floculated spore as well as the calculated reduction in spore concentration required for infecting 80,000 people in a large city. Select steps and information omitted for this testimony)

Genetic engineering has also played a role in altering the capability of biological weapons. Toward the end of the Soviet biological weapons program an effort had been made to make several agents resistant to antibiotics. Much of this work was done using techniques considered inefficient by today's standards. Biological weapon analysts with expertise in molecular biology believe that drug resistant biological weapons are a moderate probability event that could have disastrous consequences. The reasons for this are based in the current health care impact of antibiotic-resistant microorganisms, which are arising as a consequence of indiscriminate antibiotic use. What is not clear is how likely it is that a biological weapons scientist could make a threat agent that is both highly resistant *and* highly virulent. Such balanced capability would require that the organism be continuously tested against animals to maintain virulence. Thus in this case, the requirements needed to engineer-in genes for antibiotic resistance might also require an attendant investment to insure that the agent remained highly pathogenic.

Next generation biological weapons may also be engineered using *negative selection* techniques. In this case antigens to which the patient's immune response is directed are removed from the biological weapon. In worse case scenarios, the terrorist might eliminate the antigen on a bacteria, virus or toxin that was used as the basis for a government vaccine. If the patient was exposed to one of these antigen-negative biological weapons, they would be immunologically naïve resulting in more severe infection and/or death. These types of agents are known as *vaccine-evading* biological weapons. Unfortunately, the concept that such agents could be developed is dramatically illustrated by the need for new vaccines to protect against circulating strains of influenza A/H3N2.

Next-generation biological weapons also include the engineering-in of properties that influence the ability of the body to mount an immune response. In recent years, there have been several publications which have demonstrated this concept to biodefense scientists and potentially, to any terrorist with internet access. One of the most disquieting publication in 2002 described a method for defeating vaccine-protected animals by inserting a gene which down-regulated the immune system resulting in overwhelming infection and depth (reference provided upon request). Another publication which will appear in an international journal this September describes a methodology which single-handedly solves two separate challenges facing a biological terrorist: how to move virulence genes from one agent to another, and how to store a biological weapon without depending on freezers and liquid nitrogen (reference provided upon request).

One of the most ominous of engineering feats that could be used by biological weapon scientists is to induce host tropism into the agent, whereby the agent is altered to favor infection of a specific human genotype. This seemingly far-fetched concept is already demonstrated by certain tropical parasite infections that cause more significant infections and sequelae in certain ethnic groups.

The efforts of the biological terrorist to produce a new threat agent can also be assisted by natural events. This scenario is best illustrated by current experience with avian influenza in Southeast Asia. Since 1998, the pathogenicity of this bird virus has increased as has its ability to infect the upper respiratory systems of pigs and humans. The result is that infected patients are exposed to a novel, highly pathogenic respiratory virus to which their immune system is completely naive. The danger of this event is exacerbated by the fact that influenza, unlike anthrax, can be transmitted from person to person.

I will summarize this written testimony by reaffirming the concept that the dark science of biological weapon design and manufacture parallels that of the health sciences and the cross mixed disciplines of modern technology. Potential advances in biological weapon lethality will in part be the byproduct of peaceful scientific progress. So, until the time when there are no more terrorists, the U.S. Government and the American people will depend on the scientific leaders of their field to identify any potential dark side aspect to every achievement

Again, I appreciate the opportunity to present this information before the Committee. I shall be happy to answer your questions and to provide additional documentation supporting the material presented.

Figure 1: (LEFT) Smallpox collection at VECTOR's building 6B, Kotsovo, Russia.Vector and the CDC are the only 2 centers publicly acknowledged as having smallpox (RIGHT) BL4 Russian P3 containment in Building 1

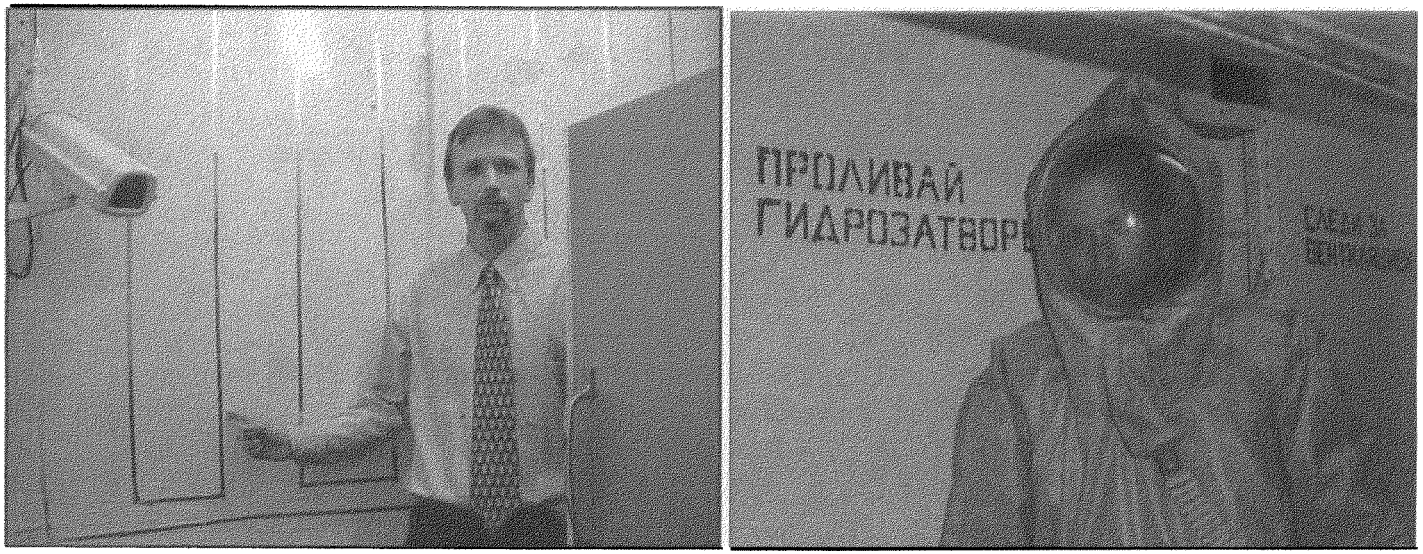
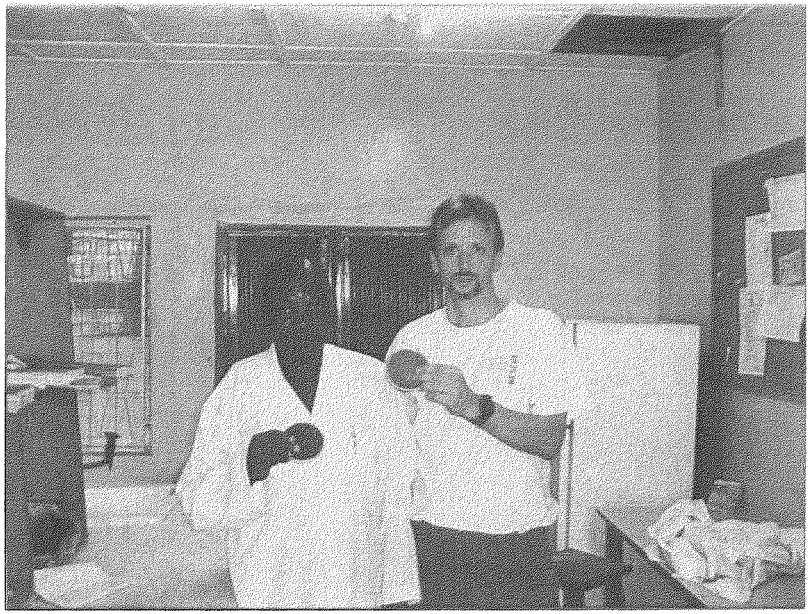
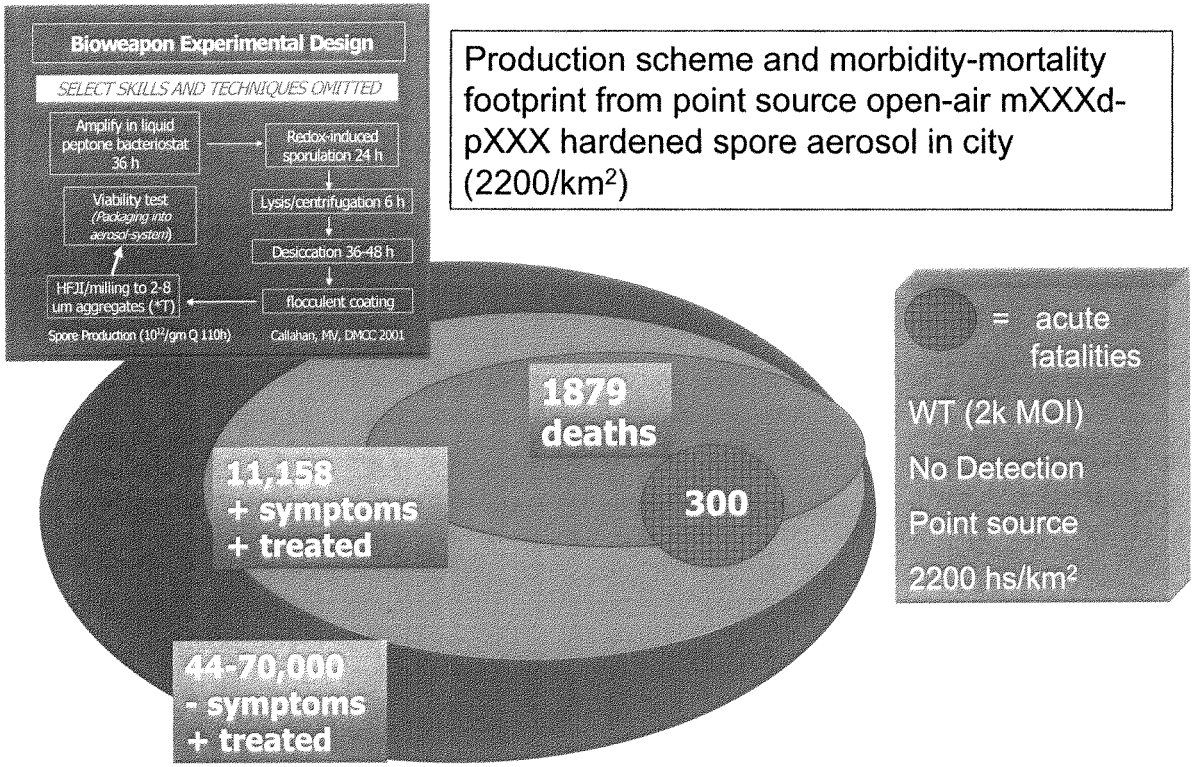


Figure 2: Anthrax bacillus growing on improvised red blood cell agar. The pathogen was recovered from the skin lesion of a rural goat rancher. Clinical microbiology laboratory in Kaduna Region, Nigeria





Callahan et al.
NBACC Jan 2004

Figure 3

Mr. LINDER. Thank you very much. I want to thank all of you for your reassuring testimony.

This is quite alarming stuff, and I think we are just beginning with it. I have said to many people this is a subcommittee to prevent nuclear and biological attack, and nuclear is really easy compared to biological.

I will recognize myself for 5 minutes to begin the questioning.

Dr. Alibek, did they ever weaponize the biology in the former Soviet Union? Was the biological weapons, were they weaponized or were they just—

Dr. ALIBEK. The Soviet Union weaponized a big number of biological weapons and had industrial facilities to manufacture biological weapons.

Mr. DICKS. Could you pull your mike up?

Dr. ALIBEK. The Soviet Union weaponized a big number of biological agents, and had some biological weapons stockpiled, and had big production capacity to manufacture many stocks of biological weapons, specifically anthrax, plague, tularemia, glanders, melioidosis, bacterial biological weapons. Viral biological weapons, the smallpox, Venezuelan equine encephalomyeltis, new types of biological weapons based on Ebola, a GTU hemorrhagic fever.

In this case, let me put it this way, this new paradigm actually appeared when the Soviet Union started manufacturing some old antibiotic-resistant biological weapons, antibody-resistant anthrax, antibody-resistant plague, antibody-resistant—in the 1980s, there was a big number of attempts to develop immune-subverting biological weapons, and so on and so forth.

Mr. LINDER. That answer is yes.

Dr. Callahan, are we getting good access to the labs in the former Soviet Union?

Dr. CALLAHAN. Yes. And what is also critical to know is that Dr. Alibek is referring to the production capability, which is really 4 to 6 institutions, the Croftburg, Stavuguart, and several of the others. But the Russians choose those programs—and Ken can talk about this in great detail—based on the return on the investment, on the capital investment, some large fermentation capability involving multi-story, tens of thousands of liter fermenters were used. The Russians also had a B plan, though. Those were the very expensive high efficiency agents that sat on bench tops, and these—the pace to improve the efficiency of these agents remained in single scientific labs. And this is one of our critical focus areas is going after the former Soviet Union B plans. Short answer, yes, there is multiple levels of weaponization, there were multiple levels of technical development, and all have benefited from the evolution of technology and their migration across international borders.

Mr. LINDER. Dr. Brent, are we wasting $20 billion?

Dr. BRENT. Good question, sir. I don't think in a democratic society, it is possible not to make defenses against known threats, smallpox and anthrax; I don't necessarily think those are bad things, in fact, I don't think those are bad things at all. I do think a defense posture based exclusively on stockpiling responses to known threats at a time when what is going to come at you is impossible to predict, is not going to work in the end.

So what proportion of our resources we spend on flexible detection and agility versus the known threat is a key political question.

Mr. LINDER. We are going to face flu every year, and every year it is going to be a different version and need a different antidote. If a SARS outbreak occurred, something like that, could somebody with a modicum talent in this business genetically alter that virus and make it more virulent, spread faster and make it more difficult to treat?

Dr. BRENT. The short answer is yes, sir. At least—you have clear paths to taking a virus like SARS and making it more deadly, you don't know that the thing you end up with would be as contagious as the thing you began with, but it might. So maybe a nation state doesn't take that bet, but maybe a terrorist group says what the heck.

Mr. LINDER. But the blow back would concern them just as much.

Dr. BRENT. Might.

Dr. CALLAHAN. I also need to add in here, working the Avian Influenza Syndrome and surveillance program throughout Asia, we are critically concerned about Avian Flu. I understand Sue Simonson has talked to you. We used the tippy top of the international flu community to help understand how to mitigate against this threat. It is a catastrophe. And one of the biggest evidence of this is that the influenza R&D for weaponization is occurring in small chicken farms throughout southeast Asia; you can't forget that. Second point is that the co-infection between a normal circulating strain are current H3N2 and an H5N1 is statistically extremely probable. And what we see with the evolution of influenza in Southeast Asia, be it southern China, Hong Kong, the Himalayan region, and we go and see these patients and work with these collaborators, we are finding it slightly different from each other. That is bad news. That means it is not a single point transition, but it is a virus trying to find its way. And this is a very important point and is a live fire exercise for biological defense of this country.

Mr. LINDER. Thank you. My time is—the Chair will now recognize Mr. Langevin for 5 minutes.

Mr. LANGEVIN. Thank you, Mr. Chairman. And thank you, gentlemen, for your testimony again.

I would like to start, if I could, going back to Dr. Callahan, you mentioned choke points during your testimony, and I mentioned it in my opening statement, which are actionable. One you mentioned was vaccination of the terrorist weapon-builders. Can you expand on that and other choke points, and steps that we could take to identify—how we can identify these individuals?

Dr. CALLAHAN. The sad misfortune is that vaccination technology is as old as dinner, I mean, it is literally two centuries old, and for that reason the technologies to vaccinate and protect an underresourced biological weapons scientist working in a remote lab are preexisting.

I will note, though, that vaccines have a certain amount of efficacy. Our current vaccines are woefully inadequate, with the exception of potentially the smallpox dry vac. Without exception, our currently deployed stockpiles of vaccines are less effective. We use

these vaccines as clinical infectious disease doctors protecting our people that go into harm's way. We are not very interested in their long-term efficacy because, quite frankly, there is going to be the need for other care.

So choke points on vaccines are a difficult issue. One of the ones that has shown up, though, in the laboratory modeling though has not been control of the agents, has not been tracking the vaccines, it has been tracking a critical recently emerged technology. In this year alone, in the first 4 months of 2005, there are 19 papers that have been produced which provide heavy, excellent answers for the challenges facing a biological weapon scientist working in the Khandalar cave. They usually allow them to forego cold chain refrigeration to store their agent. That way they could acquire genome in one place and put it into an agent to be used for dissemination.

So certain technologies are a critical choke point. And Dr. Brent can probably comment more on that, as can those that are tracking technologies and migration around the planet, so I will stop there.

Mr. LINDER. Dr. Brent, did you want to comment?

Dr. BRENT. I would like to, if I could. You wish there were more choke points, or that those points felt more narrow than they do. Again, there is probably hundreds of thousands of people with the expertise in the world and the access to laboratory equipment to make anthrax resistant to the main drug, Ciproflaxin, it is not hard. So the reagents, you know, the equipment and reagents, they are sold to worldwide market. The vendors of technologies and synthetic DNAs are all over the world, they are in basements in Shanghai selling to the U.S. market. They are bombarding you by your e-mail on the Internet with special deals and cut price offers.

I am not convinced that there are very good choke points, particularly when you move from this paradigm of a Cold War Germ War program with weaponization and so on, to this specter of an individual or a dedicated group of individuals who is willing to infect themselves and infect other people. Then one of the choke points becomes the ability to work with viruses or synthetic DNA. There may be tens of thousands of people with such expertise in the world, half of them in the U.S., half not.

Mr. LANGEVIN. Dr. Brent—and the other two can comment—you seem to indicate in your testimony that fixed response capabilities are really inadequate, stockpiling certain antidotes may only have a very limited value. Can you expand on that? And what are we to do if there really is a minimal limited value?

Dr. BRENT. Well, okay. This is a delicate and important point. For example, I mean, a Ciproflaxin stockpile, if I am a terrorist, I will immediately make sure that my anthrax is Ciproflaxin resistant; so that is just a flag, outflank me. So that is among the easiest manipulations to perform.

The amount of the resources you spend on such fixed defenses versus the amount you spend trying to devise a more flexible detection system and a more flexible response system is one of the key questions, but there are almost— Dr. Callahan can correct me—60 pathogens on the so-called select agent list. We don't want us to be spending a couple billion dollars on each of these agents on the

select agent list, working down the category, we would bankrupt the country and we wouldn't make ourselves more safe.

Mr. LANGEVIN. Dr. Alibek.

Mr. ALIBEK. Just a couple of words to add to his discussion.

Not all genetically-engineered pathogens would require completely new therapeutic measures. For example, if you talk about anthrax-resistant Ciproflaxin, we have got some other antibiotics which can handle this infection, for example, Doxycycline. Doxycycline, they are good antibiotics to treat anthrax. For example, we have new technologies now, for example, we develop antibodies, specific antibodies for anthrax treatment. The antibodies don't care whether this pathogen is antibiotic resistant. And we have such a huge number of examples. In some cases, let me say some genetic manipulations will create a completely new pathogen and our defense wouldn't work against this pathogen.

But in some cases our existing defense, they are still capable to deal with these pathogens. So the only issue in this case, we need to understand what kind of technologies can bring a completely new paradigm against these type of pathogens. We need to develop new defense against war pathogens; we shouldn't do anything because our existent war is being developed, medical measures are capable to protect against these pathogens.

Mr. LINDER. The time of the gentleman has expired. We might have another round.

The Chair now recognizes Chairman Cox for 5 minutes.

Mr. COX. Thank you.

We have before us three witnesses, each of whom deserves about a half hour time to himself, and I am sorry we have the 5-minute rule here. I am just going to dive in with a solitary question that is unrelated to what I really want to pursue, but it is just something, Dr. Brent, that you said in your testimony that I hadn't really considered before.

Are you suggesting the possibility, or are you contemplating the possibility of suicide coughers? You know, we have got people, as we saw with 9/11, who were content to fly airplanes into buildings, I suppose there isn't any reason to think that such people wouldn't mind infecting themselves and then just spreading themselves about as the agents.

And what you suggest, therefore, is that the Cold War model, or really the model of all prior history in warfare, is out the window; we shouldn't be looking necessarily for weaponization, the terrorists themselves become the weapons. Is that what you are suggesting?

Dr. BRENT. That is correct, sir. That is not to say that if a nation state had a lot of money and could employ many hundreds of people to make a program, they might not want to weaponize their agents and make them more controllable. And perhaps, anthrax is easily disseminated but it is not that infectious, but a terrorist group might want to use a contagious disease, or a disaffected individual. Already the technology exists to resynthesize small viral genomes. And an important thing to do in the 21st century is to, beyond the terrorist, make sure the hacker doesn't appear, the person who makes something and just wants to—

Mr. COX. And that is really the point I want to get back to with you and Dr. Callahan. But first a question for Dr. Alibek. When the Soviet Union was at large, the Soviet Union produced genetically-altered super plague, and also antibiotic-resistant anthrax. By the cease fire of the Gulf War in 1991, when we discovered that Iraq had weaponized anthrax, were they using the same kind of antibiotic-resistant anthrax that the Soviet Union had developed?

Dr. ALIBEK. No. The Soviet Union, the major anthrax biological weapon developed and manufactured in the Soviet Union, it was so-called natural anthrax. It didn't have—because this technology was quite old, first technology was developed sometime in the 1950s for industrial production, another technology was developed in the 1980s. It is a new type of biological weapon. But it was a biological weapon for military deployment, not for terrorist deployment.

New research on antibiotic-resistant anthrax started sometimes in the 1970s, and it resulted in new types of antibiotic-resistant anthrax sometime in the second part of the 1980s. And this new type of anthrax was tested and was ready to be accepted by the Minister of Defense for military deployment.

Mr. COX. But to your knowledge, this has been contained within the Soviet Union, and now Russia.

Dr. ALIBEK. Yes. This is what I would like to see in this case. The Soviet Union never had desire to share this technology with anybody else. Officially there was no, let me say, exchange between the Soviet Union and any other country. The program was highly secretive, and nobody wanted to share any information whatsoever.

Mr. COX. Well, that really takes us then to Dr. Brent's point about the garage hackers. If is it true that biotech is right now on the cusp of an explosion and it is like computers in 1965, and it is very primitive right now compared to what it is going to become 10 years, 20 years, 30 years from now and there is going to be a great democratization in opportunity to produce things that up until now have been very sophisticated, it poses very serious problems for those of us planning defenses.

I think, Dr. Callahan, you have been very helpful to the committee in providing what I would refer to as the seven habits of highly effective bioterrorists. The seven characteristics that you describe as sine qua non of terrorist groups that might want to produce bioweapons, to what extent would this phenomenon of the garage hacker, if you will, if it is real, defeat our ability to rely on these seven characteristics? I mean, would it really require the kind of budget, for example—which is one of your seven factors that presently it does—would we be able to drill down on these preconditions to prevent terrorism, or do we need to rethink it.

Dr. CALLAHAN. Yes. Those are focus areas for interdiction, both for the intelligence community and for those that are monitoring migration technologies and agents. Using the garage hacker as a term, I need to stress that the technologies are now being downsized to the point where the laboratories operate autonomously. Before the scientific community and the biotechnology community was dependent on critical pieces of hardware in other institutions, gene chip machines, PCR machines, trial fermenters, and these sort of kept these programs very integrated for biodefense, or

the normal construction of our understanding of clinical infectious diseases. The problem now is that there is an incredible community which is producing technologies, an entrepreneurial community which is producing technologies for civilian peaceful use that involved the propagation of infectious agents and their byproducts that marry medicine and vaccines, biological insecticides, fermentation sciences, endermatic control systems, and basically countermeasure flocculents and environmental mediation systems all use critical elements that are downsized. Literally our 30 liter process fermenter weighs 130 pounds, it is easy to transport with two people.

So these systems are throughout Africa. We see them all the time, they are a normal part of agricultural pesticide generating systems.

There is a key point that I need to also instill on this, it is that the biological technology revolution, if you compare it to your analogy of the computer revolution, it is not 1965, we are in the late 1980s and the speed is picking up. We are consistently spending a lot of our attention looking at the open source published literature, and it is outpacing the Department of Homeland Security's ability to do threat assessment. We can't read fast enough nor cross-train enough for the infectious disease or molecular biologists at the pace necessary to determine what is the threat.

So we are just picking up the big stuff, and we are probably about a year behind. We have received several red alerts this month alone for publications that will show up next month.

And you mentioned, also, this interesting point about the suicide biological weaponeer. What is missing in our calculus, with the exception of the intelligence community's contribution, is terrorist intent and what they are willing to do. And think of our situation, when we were responsible for controlling the public health security of the homeland during 2003 SARS epidemic, and we have an international airline en route from Hong Kong and we get an alert that there are two SARS contacts on board. So what do we do? If we have that alert, it is a normal public health problem, it is going to inconvenience every passenger on that jet while we do contact tracing, but imagine if the intent is different and there is no alert. Imagine how that changes the response among civilian groups. This has been modeled, not by the Americans, but by the Europeans, looking at the American economy and the impact on our financial centers. And for the reasons that are obvious in an open source forum, we can't go into the specifics, but it is intent.

So an e-mail to The New York Times saying, hey, I have already been there and done my coughing versus somebody that you catch on the plane, these are very different responses to basically the same biological threat, the preexisting live fire and natural experience, someone with SARS coming to the U.S. that we pick up at the borders, versus someone that doesn't want you to know.

Mr. LINDER. Dr. Brent.

Dr. BRENT. I couldn't agree more. But to back off a bit, maybe there is other ways to approach the issue. So, for example, let's not think in terms of the technology. Your hacker, if it is a kind of slightly antisocial male teenager, may be deterred by a mandatory life imprisonment. If you let something out and it hurts people, it

won't be funny, you won't get a slap on the wrist, you will go to jail for the rest of your life, and people would spit at you on the street when you are released, should you ever be released. So it is, you know, so we can begin to think what deterrents would look like for the different kinds of attackers. Deterrence is probably the hardest for members of the dedicated terrorist organization.

Mr. LINDER. Thank you. The time has expired.

The Chair recognizes the gentleman from Washington State for 5 minutes.

Mr. DICKS. Let me ask a question, and any of you can take a shot at this. Yesterday we had a hearing in another subcommittee on what we are doing in our BioShield program, and one of the things that was disturbing was that the Department of Homeland Security has only done four material threat assessments on—you talked about 60 possibilities here, only four of them have been done, and one of them on radiological hasn't been transferred over to the Department—or hasn't been accepted by Health and Human Services. So it seems as if we are not doing a very effective job of looking at vaccines or various countermeasures, whether they—how effective they would be is a question that has been raised here this morning.

But have you looked at this, is this an area of grave concern, the slowness in which Homeland Security is reacting and doing these threat assessments.

Dr. ALIBEK. Thank you. It is very important in my opinion, a very interesting question. I have been watching what was going on in the field of biodefense for the last four or five days after we heard the anthrax attack, and I noticed that many things have been done correctly, but at the same time, I see big holes in our preparedness for biodefense.

And BioShield program was a very good program, good program, let me say, by its intent; but you know, when we came, let me say, to the evolution of this problem, we started noticing that we still have huge numbers of issues that are unresolved. And our problem actually exists on two levels. First level is just to understand the reality of one another type of threat. First to understand what kind of threat we should consider as most and least of threats at this point in time, for example, just in terms of types of the pathogens and types of biological weapons.

Second, what would be the most probable way of deploying biological agents? We need to know there are very many different ways to deploy biological agents.

Third, what kind of consequences would you expect from each type of threat? We should not use something like, say, in the case of anthrax attack, we are going to suffer having 1 million casualties. Of course, it doesn't work this way. We still, in a kind of nonscientific field, are saying just try in some cases to reduce the understanding of threat, in some cases to increase and make it kind of catastrophic.

The situation is completely different. We haven't even started doing much to understand the differences. Let me give you a simple example, because in the field of military biotechnology and military biological weapons and biological weapons defense, we always analyzed the possible number of casualties based on a specific age

and range of people—young adults, people between the 18 and 50 years old, in this case because everything was based on the use of biological weapons against troops. But now we have got a completely different paradigm.

We have got a situation where we are going to have a big number of children infected with biological agents; we are going to have a big number of elderly people. This is the most vulnerable population, and the level of threat posed by biological weapons to these people is much more grave than when we talk about young adult populations.

Just take a look at a simple example. A lady could die in Connecticut. She was 94 years old. It was obvious the infectious dose for this lady was much, much lower. She didn't require 10,000 to 20,000 spores to get infected. This is one of the examples, and we have dozens of areas we haven't started to explore.

Mr. DICKS. So you are concerned we are not reacting and coming up with various strategies?

Dr. ALIBEK. In my opinion, what is going on at this point of time, we haven't identified all types of threats, we haven't identified all types of specific research we need to conduct; and, of course, based on this, we don't have appropriate treatment for all possible threats we are going to face.

Mr. DICKS. Dr. Brent.

Dr. BRENT. Mr. Dicks, if I could, I think whatever good there is—and there is probably some good in enumerating possible threats and then detailing detailed responses to those—what good that has is coming to the end of its shelf life, if it hasn't already.

So we should not call these things strategies, either; we should call them tactics. An individual defense against an individual thing is a tactic. So I would not think it is a good use of time, personally, for the Department of Homeland Security to list 100 threats.

Mr. DICKS. But they can't spend any money out of the biological fund, out of the bioweapons fund, until they have done a material threat assessment.

Dr. BRENT. Understood, sir.

Mr. DICKS. So the HHS says, I am sorry, we can't fund you, Mr. Pharmaceutical Company or small firm, to develop a countermeasure, because the Department of Homeland Security has not done its material threat assessment.

I don't think Congress intended to hold up everything to come up with some comprehensive document, and they have only touched on four areas out of 60 possibilities that you have discussed here today.

Doctor, do you have anything you want to add?

Dr. CALLAHAN. I am intimately involved with the material threat assessments and can tell you about their benefits and their lessons. The key point here though is, if you step back and look at it the way our former enemy looks at it, each of these strategies is easy to defeat. We have vaccine-evading biological weapons. We have detector-evading biological munitions. These systems are currently

Mr. DICKS. So do we do nothing?

Dr. CALLAHAN. Negative. What happens is, there needs to be a paradigm shift with our approach to the problem.

Dr. Alibek actually has worked and has expertise in nonspecific immunomodulators, the way you enhance immune response in a way that will bolster nonspecific immunity.

It is absolutely critical to understand that you might not get anthrax, you might get something that is anthrax-like. It has the guts and the payload of the anthrax bacillus put inside another spore. It will defeat our public health surveillance capability because it won't grow on the right plates in our reference labs. It will defeat the clinical diagnostic criteria because it may not show up correctly in the hospital labs, and it will present, clinically, differences so that you don't get necrotic skin lesions in the injuries.

So, again, we need to sort of step back and think of an integrated approach that involves all elements of our scientific discipline, spanning molecular biology, but certainly more terrorist intent and understanding the force and futures that modulate the strategic thinking to make these offensive agents.

They are agents of terrorism. They want to get away with the crime, and they also want to be culpable and say, look what we did to you.

Mr. DICKS. But is anybody doing that actually?

Dr. CALLAHAN. Think of the subject matter that must have been convened by Homeland Security through DHHS in part. What happened is that we used an anthrax expert. We used a botulism expert. We used a tularemia expert. These people are mono-bug people. They have been working all their life with one agent and their ability to think like a terrorist in a Kandahar cave cannot be replicated by a well-resourced scientist in some major academic or biotechnology institution.

We need to step back and produce a realistic premise for the force and features which influence these technologies in bringing them together for bad use. So we really need an integrated plan. The detectors need to not detect a single antigen on an anthrax spore, they need to detect difference in change, rapid amplitude escalations we need for the unknown. And quite frankly, this has a tremendous return for our public health preparedness for avian influenza and the as yet unknown infectious diseases that give me job security for next year. Nature is working for me.

Mr. LINDER. Your time has expired.

The gentleman from Connecticut is recognized for 5 minutes.

Mr. SHAYS. Thank you.

One of the points I think you make, Dr. Callahan, is that one of the advantages you all have in biological warfare is you get everyday practice from Mother Nature; and unlike our defense for other types of threats, what we do for Mother Nature, we can then transfer in terms of what we ultimately do for someone who is manipulating the process.

It points out, I will just make this observation, the most important thing we can do in this country is to have a capability to detect so we can prevent an attack. Consequence management, it is huge when it comes to biological warfare; it not as important, frankly, when it comes to even the horrific bombing that happened in London. But it points out the need to have the PATRIOT Act, the ability to get into these cells, the ability to know what they are thinking before they do it.

Just an observation I want to put on the table.

Dr. Alibek, I have been to some of your stomping grounds in Russia, and it is pretty frightening still to see biological agents that are in refrigerators with string and wax. And it is not to prevent someone from opening that refrigerator; it is just to know when they did it.

Speaking about Mother Nature, and I want to know if this is true, I was told, as the permafrost melts, that there are biological agents that have been basically in a frozen state for years that may come to threaten us again.

Is that hype or is that a possibility, particularly as it relates to animals?

Dr. ALIBEK. Unfortunately, I participated in the first discussion we started in 1989 in terms of the possibility of finding the smallpox virus in permafrost. Unfortunately for us, what I would like to say is, one of the reasons why one of the scientific entities in the Soviet Union started the discussion was because of the possible threat that the United States would start accusing that facility in working with smallpox when the smallpox work was prohibited. The reason to create this story about permafrost and the possibility to find a viable virus was based on a desire to cover the actual work with the smallpox virus.

Then it became—I have no idea at what point it became kind of a scientific entity and many scientific groups started visiting some locations. But I was a part of a very small meeting in 1989 with individuals involving the Deputy Minister of Health of Russia, the director of microbiology work and myself when I was—

Mr. SHAYS. Give me the bottom line here.

Dr. ALIBEK. The general idea was, we need to find some explanation to cover our work with the smallpox virus.

Mr. SHAYS. One of the great organizations in the world, in my judgment, is the World Health Organization. They go anywhere. They have limited resources. I am just interested in knowing, do you feel that we could be using the World Health Organization better than we are using it today?

Let me just start with you, Dr. Brent.

The question is, can we be using the World Health Organization better than we are today?

Dr. BRENT. Certainly, sir. These things like the Centers for Disease Control and WHO, which is a little bit more of a paper-shuffling place, but not totally, these are like the fire department; we need every one of them we can get and we owe them our support.

I would personally like to see a greatly beefed-up World Health Organization. The Centers for Disease Control has something called the EIS, the Epidemic Investigation Service, which is one of the most prestigious postings a young person who is interested in public health can have.

The director of the WHO has called for a world EIS which would attract the best young people in the world. I think any support we can give them is money that is extremely well spent.

Mr. SHAYS. When I went to Geneva a few years ago, and we said we wanted to have a meeting with the World Health Organization about biological warfare, the director basically said, well, they don't

really get into that. This was a number of years ago. We said, well, we are coming anyway.

We started to meet with people that he didn't even, frankly, know—this is a former director, didn't even know were involved in this effort. I thought that was rather curious.

Let me just go to Dr. Callahan and I will come to you.

Dr. CALLAHAN. Things have changed at the WHO. They recognize their importance as an integrated group to be able to do offensive use biological threat mitigation because their representative countries include areas that are not often traveled by Americans specifically.

Let me take you, as a practical example, to the benefits of the WHO versus agencies of the United States Government. During the SARS epidemic the CDC was deployed also to Hong Kong and to the Quandong Province in South China. I was on the WHO attachment, and I went to all the closed areas, and there were no other Americans permitted to go there.

So this is a critical point, that in order to have—you need to be card carrying and integrated into the international agencies in order to be not deemed as, you know, a country of their concern. So the WHOs can be very critical, unless you have some excellent new talent in the WHO from the current administration who can continue to further this issue.

Dr. ALIBEK. Just a couple of words. I have visited many countries, talked to many government officials, talked to many experts in the field of biological weapons defense in many countries, and what I noticed in many cases they try to acquire as much as possible information from the United States defensive program. They analyze our publications, they analyze what we do, they analyze our CDC efforts and so on and so forth.

At this point in time, in my opinion, the international community is not involved appropriately in being a part of a kind of international biodefense effort. In my opinion, it is time to start a bigger international program, and maybe the WHO would be a good place to start the program.

Mr. SHAYS. If I can respond to the chairman, Mr. Chairman, this might be one of the reports that we get out to encourage this. I would recommend to this committee we go visit the World Health Organization.

Mr. LINDER. We expect to do that. Thank you.

The Chair recognizes the gentleman from Massachusetts for 5 minutes.

Mr. MARKEY. Thank you, Mr. Chairman.

Dr. Alibek, back in the fall of 2001, Mr. Shays and I had you in to testify to our nonproliferation task force on these issues, and you recommended if there was ever any anthrax attack, that the best prevention was to ion the mail, to make sure all mail was ioned.

The next day, this complex was evacuated because of an anthrax attack and all of our mail is now irradiated. But you gave us a warning with 24 hours' notice that hit us.

Now, Michal Freedhoff on my staff, she was actually in one of the rooms that was hit in the Longworth Building, and she wound up on Cipro for 2 months. But we very much appreciate your warning.

My question to you would be, what else should we be worried about? Give us a scenario that we might be concerned about, attacking the Capitol or attacking some other facility in the United States.

Dr. ALIBEK. First of all, thank you very much for remembering what I suggested.

But it had a kind of downside, because immediately after I said this, CDC started blasting me, saying, never ion the mail, because it is going to result in the acceleration of anthrax spores. And I was kind of shocked because it was absolutely obvious that people who were concerned, they could do this, because it was absolutely obvious that spores could be killed quite easily.

In my opinion, the lady who died in Connecticut, if she had had a chance to ion this mail, covering it with some piece of fabric, the probability was for her to be alive.

Mr. MARKEY. Who attacked you at that time?

Dr. ALIBEK. CDC.

Mr. MARKEY. And what was their misperception?

Dr. ALIBEK. It is always, when you put on the scale, two things. For example, okay, you ion mail and have got a lower probability to get infected, and you don't do this in the high probability. You have to choose.

Mr. MARKEY. Give us a warning today. Give us something.

Dr. ALIBEK. First of all, what I would like to say, of course, I don't want to be a kind of alarmist, but I strongly believe it is not a matter of if, it is a matter of when, when we are going to see the second attack. If you ask me what is the probability of using different pathogens in terms of the attack, in my opinion, anthrax will be again the weapon of choice.

What kind of deployment? There are different scenarios. In this case, one of the probable cases—again, maybe anthrax—but the number of places to be mailed could be quite large.

In this case, our preparedness should be based on several principles: first, fast identification, fast diagnosis, fast treatment of people and providing antibiotics as fast as possible.

What is absolutely essential, just organize a visual monitoring system. Any person who is appearing with more or less obvious symptoms or suspected symptoms of anthrax should be treated immediately. It should not be discussion whether or not it is anthrax.

In this case, one more thing: In my opinion, we need to pay attention to what DARPA is doing in the field of anthrax protection. In my opinion, DARPA is the most sophisticated entity at this point of time, and it knows what kind of research and what kind of development needs to be done in this field to protect against anthrax.

If we are able to commercialize everything that is being paid and funded by DARPA, within in the next 2 or 3 years we are going to have three or four very good therapeutic measures, new vaccines, highly effective, fast-working vaccines. Second, antibiotics, existing and improved antibiotics for anthrax, we have very good approaches on specific antibodies to treat which could be used compared to antibiotic treatments and several other approaches.

Mr. MARKEY. Let me go quickly to Dr. Brent, only because time is limited.

Dr. BRENT. I would like to echo Dr. Alibek's point that DARPA maybe is the most effective government agency right now able to prosecute kind of the applied research that is sometimes necessary. I would say, however, that if I am an adversary and I see there are four or five good anthrax countermeasures, I will not attack you with anthrax. So I don't know how useful it is to scenariolize.

Mr. MARKEY. Dr. Callahan, do you think that we have adequate security around biohazard storage facilities in the United States?

Dr. CALLAHAN. Yes, I think they have dramatically improved in recent years, but they are easily circumvented by the novel engineering of a new agent. And getting a new anthrax strain out of Texas, South Dakota or Maine, we can have a few in about 10 days.

Mr. MARKEY. I thank each of you very much for your important work in this area. Thank you.

Mr. LINDER. The Chair recognizes the gentleman from Louisiana for 5 minutes.

Mr. JINDAL. Thank you, Mr. Chairman.

In an earlier comment, I heard the panel, and just now, talk about these novel bioengineered agents that could be used in an attack that might circumvent our detection equipment, our treatment, our vaccines.

My first question is, how easy would it be for a terrorist group—an individual agent as opposed to a state-sponsored group, how easy would it be for them to manufacture such an agent that would easily circumvent our defenses and our vaccines? Is that something that a terrorist group acting alone can do today, or is the technology diffuse enough that they could easily do this today?

Dr. BRENT. I am afraid it is, sir. There are tens of thousands of DNA synthesizers worldwide, and the kind of capital costs for a lab that you would use to, let's say, resynthesize a virus and get live virus out, it is probably a couple of million dollars, if that, $1 million worth of capital equipment. There are probably more than 1,000 research groups, more than 10,000 people with the kind of generalist training to do that.

So is there any intersection between the people who know how to do it and the people who might want to do it? I can't answer that. Is it likely there will be such an intersection in the future? I believe there will be.

Mr. JINDAL. Given that—and I know the ultimate answer is obviously we would want to do all these things and we want to have an integrated approach, but given that answer, how would you allocate scarce resources? As you have to choose between hardening targets; as you have to choose between boosting generic, as you talked about, nonspecific immunity; as you think about developing new vaccines; as you think about new detection centers, how do you set priorities?

Dr. BRENT. Sir, if I can, flexible detection. We know we have been hit, this is what hit us. Agile response.

Components of agile response now that could be gotten going quickly include things like being able to make prophylactic antibodies against a new agent. They may involve new phase therapies. There are ways to make vaccines quickly. There are ways to speed up drug discovery.

There is a great amount of creativity within the biological community in the U.S. which is kind of up for that. So that would be the mantra.

Mr. JINDAL. I am sorry. Yes?

Dr. ALIBEK. In my opinion, when we think about a bio threat, in addition to vaccine development, it is going to be a long shot to develop vaccines. We need to start working very hard in the field of developing immunomodulating preparations to modulate our immunity response. Because this is the way to create, let me say, a kind of broad spectrum of preparations capable for self-administration. This is first.

Second, we need to begin to focus on our—in many cases, for viral and bacterial infections, for late-stage and therapeutic modalities and preparations, because, for example, you would talk about anthrax. The early stages of anthrax we can treat. As soon as the disease has come to the late stage, we have serious problems and these diseases are becoming incurable. We need to be put attention to this.

In my opinion, what is absolutely essential, there are some new signs emerging now, that especially, probably, Dr. Brent could support. Recently they started developing a new science; the name of the science is bioinformatics. Bioinformatics actually allows us to develop, let me say, completely new principles for vaccines and, specifically, antibodies. This principle we call reverse vaccinology principle, meaning that we don't need any pathogen, we don't need to dissect the pathogen. What we can do is bioanalysis of genome and pathogenics of the pathogen; we can define specific targets. And actually, just recent data, emerging data, shows that actually it is maybe science fiction now, but it is a way to develop multipathogen vaccines and multipathogen antibodies.

This is what I am saying for the first time in this audience, because this is just first ideas, and these ideas are feasible; and maybe if we start exploring these directions, in 3 to 5 years we will be able to bring first vaccines that will be effective against three to five different pathogens, for example, anthrax and plague.

Mr. JINDAL. One final question. I am sorry to interrupt you, but our time is limited.

Are there other countries, is there any other country out there that you see that is further along than we are in terms of equipping their public health sector, their emergency rooms? Is there anybody out there that is doing this better than we are today?

Dr. ALIBEK. No. No. The United States is the most sophisticated country in this field.

Mr. DICKS. But is it adequate?

Dr. ALIBEK. It is the most sophisticated in the world. But when we talk about how much we can achieve, of course, we have a significant gap yet.

Dr. BRENT. Mr. Jindal, if I can go back to the flexible detection and response, let me say that is what you want to get going now, but at the same time you put in things like understanding how to gin up the human immune system. That is probably a 20-year kind of goal-directed research program to get to that.

So you start doing both now, build your detector network, build your agile response, do what you can to conceptualize that system,

but put the money into something that will pay off more properly in decades.

Mr. JINDAL. Thank you, Mr. Chairman.

Mr. LINDER. The Chair recognizes Dr. Christensen for 5 minutes.

Mrs. CHRISTENSEN. Thank you, Mr. Chairman.

Just for the record, Mr. Alibek, when you responded to the gentleman from Massachusetts on what instructions you might give, I note that the instructions were around normal public health responses, something that we are stressing. I don't feel that we are adequately prepared in this country, and it is a point that many of us make over and over again.

Let me ask a question about a bill that we had introduced last year and were planning to reintroduce again called Rapid Cures. I have always been concerned as we went through BioShield hearings last year that we were talking about preparing for agents and we had no clue as to what the biological agent might be, what form it might come in, whether it would respond to any of the things that we were spending all this money to create the countermeasures for. The Rapid Cures Act would help us to shorten the time if an agent came that we had not previously identified to developing a cure, a vaccine, and so forth.

Would you suggest that in addition to research that would boost the general immunity and provide some general protection, that we pursue a course of trying to develop the time to develop countermeasures? Anyone can answer that.

Dr. ALIBEK. You touched a very important topic. In my opinion, you are absolutely right when we talk about the BioShield program. The program actually is based on old traditional approaches, how we deal with these infectious diseases. We are talking about diagnostics systems, vaccines and therapeutics.

What we need to do, in my opinion, first, we need to develop a new program, we need to analyze new and traditional novel approaches for protection development. We haven't started doing this work yet.

Second, in addition to when we talk about specific modulation of immunity response, we are hearing very positive things. Let me say we allow the immune system to build its own defense while the victim is still alive.

But what is important in this case, and this is one of the critical points, when we talk about many diseases, especially contagious diseases, we need to keep in mind two things. First, we need to save the life of the victim; second, to reduce the infectiousness, the contagiousness of this victim; and, third, we need to create immunity for the population.

In this case, let me say, in order to solve all three problems, we need to develop some new preparations, and some preparations already exist. A person is becoming less contagious. We reduce the severity of this infection. This issue is important for bioterrorism events and for emerging infections, like the common avian flu.

For example, we try to develop vaccines, but we don't pay attention to some other cultures. In many cases, we do two things: Either our victim survives or dies. In this case, if he or she survives this infection, it is much better than if this person dies. It is obvious.

In this case, when we talk about modulating in a community, it is not an issue of saving lives, it is an issue of, first, increasing the probability of survival; second, reducing the contagiousness of this person; and, third, creating a kind of immunity population. In this case, we would be able to prevent an epidemic.

In this case, this is just a short explanation that not all directions have we explored yet.

Dr. BRENT. Mrs. Christensen, not only is having anything that enables you to move more quickly from a new pathogen to a new drug a good thing, but I want to point out one consequence in addition to helping the defense.

Anything that streamlines drug discovery cuts the cost. The cost is significant, the drug company might say $800 million, I might say $400 million, but it is a lot of money. Cut the time drastically, cut the cost drastically, and that enables things like the Wellcome Trust, foundations like that; now they can spend $40 million for a drug and use it in the developing world.

So national security and some of the other properties in the world go hand-in-hand.

Dr. CALLAHAN. I would comment only that the natural experience of facing a threat agent that you don't understand, we haven't done very well. If we think back about SARS, that was using 2003 technology. It was using some of the most resource-rich laboratories around the planet. It took 19 days to actually isolate the specific genera of the organism, and that came from an electronmicrograph of a patient's lung.

By the time we returned to Hong Kong, there were 470 people on ventilators, and we were flying ventilators all around in Southeast Asia to try to shore up their health care capability, which, by the way, is a Western standard.

So, to your first point, to mitigate against these events, an unknown threat agent, we are going to do poorly based on what our current success record has been with avian influenza in the past, orthopox viruses in the past, particularly the recent cow pox from several years ago, and SARS being a crystal clear example of our capability when put on the line.

The second point is, DARPA has been mentioned, as has BII. These two extremes of resources have not been capitalized on in a major way. The reason why I will suggest to you that we need a closer attention here to support the Homeland Security effort is because BII in Russia is looking at countermeasures that haven't even been considered by the Western cognition, by the American sort of way of thinking. Classic antibiotics and vaccines for one bug, nonspecific immune enhancers and bolstering the immunity of a population have some principles in natural history and, of course, military history.

The last and final point is that DARPA is certainly one of the convening arms for these technologies and needs to be supported with subject matter expertise, it needs to be read in and integrated.

This just raises a critical concern because imagine being that biotechnology company that you are trying to entice with biodefense dollars, and yet your antigen, the thing in the bug that you are trying to block, needs to be classified because it is so easy to circumvent it if you are a terrorist. So that is not the way that science

and certainly not the way basic science infectious disease has operated.

So these are some of the dilemmas which are procedural, which are policy relevant and involve all the basic science community, which is intending to publish, as well as our intelligence and medical intelligence communities.

Thank you.

Mr. LINDER. The Chair recognizes the gentleman from Mississippi for 5 minutes.

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

I guess, as I listen to the testimony, I am real concerned as to whether or not the approach that we are taking as a country and as a committee is the proper approach.

We heard testimony yesterday on BioShield, and I am wondering, first, are we approaching BioShield in a manner that the scientific community supports, or are we just putting money out there and people are chasing the money? I hope you understand what I am saying.

I will take any answer.

Dr. CALLAHAN. Clearly, these are large appropriations and large allocations, and they entice a lot of competitive grants. The trouble is that the best of the experts are oftentimes individual scientists in small laboratories and they are largely disengaged from the system.

The second point is, there is a huge resource in the biotechnology-for-profit sector. The best of the minds get bought away from the academic centers. As opposed to the DHS effort, it capitalizes heavily on the national labs, usually driven by the need for security clearances and to put big fences around things. The trouble is that those shops tend to be single shops and they try to keep everybody else out.

If we are truly mission driven and we are truly trying to get the best of the talent at the table, we need to step back a little bit to a great review using the best of our review capabilities out of NIAID, CDC, DARPA specifically, and USAMRID, to find these agents that can really help us with this.

Dr. BRENT. Just that BioShield may be necessary, but not sufficient, or at least some parts of it might not be. It is not a bad thing that there is now enough smallpox vaccine to vaccinate everybody in the United States. But it is limited after that.

Then I am going to just cite what Dr. Callahan said. We need to engage. There is all the talent here to make the defense work, but it needs to be engaged perhaps by complementary mechanisms.

Dr. ALIBEK. Unfortunately, I don't want to be over-critical. In 1998 or 1999 when I testified first on the Hill, I said if we don't develop in the beginning our concept of biodefense and agree to develop a good threat assessment in terms of bioterrorism, we are going to suffer and we will never have any appropriate defense. This suggestion, of course, my testimony could be found in the archives.

Now, 7 years later, we are still there. I am not saying we were not able to develop a better biodefense. Yes, we did. But we still suffer because, in many cases, what I notice—and it looks like this is what you actually asked—in many cases, when some solicitation

appears, a huge number of companies start applying for these solicitations, in many cases having no knowledge in the field.

What they do in this case, they hire some consultants, they put a good list of people who would work for this work. They get funding from the government. Then they throw away these consultants and start doing this work. In this case, we shouldn't expect any kind of good results from this type of approach.

In this case, in my opinion, a national register, for example, of the most effective biodefense entities, we need to establish it, and we need to establish some kind of entity to determine what we need first for the country.

Mr. THOMPSON. I am going to get back to you, Dr. Brent.

One of the things, Mr. Chairman, I think at some point we are going to have to look at whether or not we are moving along in the right direction. We are spending an awful lot of money. But if we are spending money on a Model T instead of the latest and best science, we are just spending money.

Mr. LINDER. If the gentleman would yield for a moment, it gets back to the point that I keep repeating, that there are a finite number of terrorists and an infinite number of ways to hurt us, and we ought to be looking for people instead of things.

The other point I want to make is, we heard testimony yesterday that HHS gave a sole-source contract for a vaccine to a company that had never produced the vaccine. I just think that that is not a sound business practice. Here we are a year from having the vaccine brought to us, and we sole-sourced it. We didn't put it on the market. We went out and bought a temporary supply of vaccine from another company.

I am just concerned that with all this money out with BioShield and people responding sometimes to RFPs, but sometimes just sole-sourcing of the product, that we are still not doing what is in the best interests of this country.

Dr. Brent?

Dr. BRENT. Sir, I would be inclined to cut people a little slack on the procurement. There are only six companies or so that even have standing in the vaccine business now, and they are scrambling. So my inclination would be to cut some slack on things like sole-source procurement, but to recognize that the procurement model is not alone going to get us through.

We need technical development programs tantamount to kind of radar and ICBMs during the Cold War. You can't just go out and shop for that; you have to begin to think how to configure the right defense complex.

Mr. THOMPSON. So you sole-source it to somebody who hasn't done it?

Dr. BRENT. In the first year maybe you cut them a little slack.

Mr. DICKS. If the gentleman would yield for a second, are you suggesting that we should do R&D, or do like the Defense Department does, spend some money on research and development before we go out and try to buy the finished product?

Dr. CALLAHAN. The critical issue, I think, is to test the system for its responsiveness. It is research fleet-afoot. We can do that again with natural experiments. We are doing it with avian influenza at this time by producing an integrated surveillance, iron-

ically, in using former Russian biological weapons scientists who are capturing avian flu as it migrates south.

The second point is looking at the case studies from SARS and West Nile virus. We are doing really badly, and these are diseases that, in hindsight, are actually fairly easy to subtype. These are practice experiments, they are live-fire exercises, they demand capital investment; and everybody is working hard, because they know the threat is real. It is not a scenario, like TOPOFF or another event. It is a real event; people are dying and are on ventilators.

Dr. ALIBEK. I talked to both companies, BioPort and VaxGen. Both of them, let me say, present the same vaccine, actually, based on different technologies. When I talked to representatives of these companies, they tried to convince that their vaccine is the best one, but when you analyze it, of course—let me put it this way.

I haven't seen anything with the VaxGen vaccine which would make this vaccine more appropriate than the existing vaccine. In this case, of course, it is not my business; it is the business of DHHS. But, for me, it is very difficult to comprehend why we are trying to buy a vaccine from a company which hasn't proven—which doesn't have a proven record yet, instead of, let me say, promoting the existing vaccine.

I am not supportive of this company, Emerging BioSolutions, or BioPort. I know they have got problems. But when we put them on the same scale, two different vaccines, I see no big difference.

What needs to be done, in my opinion, of course, we try to spend about $1 billion to buy this vaccine. Why, for example, we don't support at this point of time—when we don't have a new vaccine, we support this production, but at the same time we develop new regulations, new requirements for new vaccines, second generation vaccines, which would be working much better than existing vaccines.

In my opinion, this is the way to go, because when you have two different vaccines—which actually are the same, in my opinion, of course—it makes no sense to me.

Mr. LINDER. The gentleman's time has expired.

Ms. Norton is recognized for 5 minutes.

Ms. NORTON. Thank you, Mr. Chairman. I apologize that another hearing kept me away from hearing all of the testimony. I understand that before I came in there was some mention of something that is of special interest to me, that perhaps the most likely biometrics attack would be an anthrax attack, an attack of the kind we have already had, the one kind of attack we know something about.

The one place that is protected to any degree, of course, is the Capitol and the Federal agencies in the event of an anthrax attack. Whether anthrax or some other substance, I think the public is far more focused on what would happen if there were an attack in a closed system like a subway or a bus, the kind we have just had in London.

I just reintroduced a bill for ordinary security protection in public transportation systems and rail. That is just the ordinary stuff, cameras and so forth. But I think there is far more concern about some kind of bioweapons attack, which some might regard as easier to do, coordinated London-style.

I am wondering what you think the consequences of such a use, some kind of biological substance, would be in a subway system like here in the District of Columbia or in New York.

Also I am interested in what I understand was some mention of broad spectrum antibiotics. Whoever would be best informed on those subjects.

Dr. CALLAHAN. I think that you are hitting a critical point, which is that fairly moderate efficiency biological weapons gain efficiency when kept contained. They also, if we model HVAC systems for indoor air attack and HVAC systems such as serving this room, allow for remote delivery of an agent, allowing chances for folks to get away.

The third point, which is very much in evidence in the community here, is that buildings tend to house a lot of the same type of people, and if those are desirable targets, be it military personnel, government officials, school kids, whoever, you get a higher return. This is actually modern military strategy, it falls into the CARVER–SHOCK analysis.

So indoor air attack is absolutely critical. The detectors are woefully inadequate and the currently deployed ones all have device-defeat capability with currently existing technology. That is a fact.

Ms. NORTON. Well, if that happened, let us say, in a subway car, would you end up shutting down your entire subway system for a long time just to decontaminate it? What would be the consequences?

Dr. CALLAHAN. The area denial consequences are vast. The current projections right now, for example, if we have another SARS event on an airplane, because that happened in Southeast Asia, is, you don't decontaminate the plane, you scrap it.

With subway systems, the amount of effort that would be required to decontaminate those systems to allow for the return of public confidence in those systems is so extraordinary, you might call upon the cost of the Brentwood postal facility decon as an example for that.

Ms. NORTON. Yes.

Dr. BRENT. Ms. Norton, the reference to the anthrax attack may be fighting the last war. It may not be. I can't say that. But it implies an attack that is confined in space. It is an event. It happens at a given time. It infects a given place.

Not all the threats that are conceivable are of that kind. There can be just contagious disease, in which case the consequences are catastrophic and the task of defending against them is harder even than what you said.

Ms. NORTON. And I take it, we don't have any defense at the moment against such an attack in a closed system such as a bus or subway.

Dr. BRENT. Well, with SARS, no.

Dr. CALLAHAN. No, and the key point is the migration. Remember, these are not conventional high explosive events, neither are they really dirty bombs; but these materials, particularly if infectious, but also in the case of anthrax spores, they are going to migrate. So your contaminated zone, how big a yellow circle you draw around the District of Columbia, the city of Boston or New York, gets bigger and bigger over time. And if these are infected patients,

a contagious disease such as killer flu or another agent like that, then your problems have a tremendous magnitude.

Ms. NORTON. So I take it the problem of infection is even worse than the problem of death.

Dr. CALLAHAN. Oh, absolutely. It is how big a ring you need to treat. And also there are huge consequences to treatment. There are several people in this room who have been on Cipro for 2 months. That had a burden to them, and for clinical infectious disease, we are realizing it now.

Dr. ALIBEK. Just again a couple of words. I still believe—maybe not everybody is going to support this—anthrax at this point of time is the biggest challenge and the biggest threat for us. Why I am saying this? I know anthrax firsthand. I know it is a very stable pathogen. It can be manufactured easily. It produces very severe effects. It could cause contamination. All parameters, unfortunately, are saying that anthrax is still a big threat.

The issue is this, of course: Even if we discuss that if we develop good protection against anthrax, somebody would use something else, it is absolutely correct. But what we need to do, in my opinion, we need to focus on anthrax for many points.

Just imagine a situation, an anthrax attack in our subway system. In this case, even just—of course, it is very hard to say how many casualties we are going to have. It depends on many factors, the severity of the attack, the amount dispersed, how soon was the attack, how fast we organize treatment and so on and so forth.

But one of the biggest problems is going to be the full contamination of the entire Metro system. In this case, can we imagine this: Washington, D.C. with a nonfunctional Metro system. In this case, people wouldn't go visit the Metro system until we say the entire system is absolutely decontaminated.

In this case, in addition to all these challenges, we are going to face the challenge for weeks or for months to just do the decontamination work. We can imagine what kind of chaotic situation we are going to have in Washington, D.C.

That is why, in my opinion, when we talk about anthrax—I talked to the Department of Transportation, I discussed these issues with them. We need to develop—in my opinion, the problem we should be focusing on specifically on anthrax as the first pathogen we need to take off the table.

Mr. LINDER. The time of the gentlelady has expired.

Would you be willing to sit through a few more questions? I have a couple of questions.

Dr. Callahan, you talked about the 19 studies that have come out this year, talking about the migration and movement of these facilities. Would you expand on that?

Dr. CALLAHAN. Can you restate the question?

Mr. LINDER. You talked earlier about 19 studies you read this year about the movement of some of these labs and the migration of the expertise.

Dr. CALLAHAN. Yes, and the tragedy is how difficult it is to find a forum outside of Homeland Security and the Intelligence Community to share that information. The reports come in because they shore up the capability of remotely operating terrorists, specifically for small-scale laboratories.

Most of the reports have to do with the new methodology which has been proposed by a well-intentioned group which is thinking about another problem, the preservation of genomic material being a specific example. Then what happens is, they go ahead and put it out there, and because of the lack of review at the international level and the fact that many of these journals are international and Internet-based, that allows the information to get out there.

So there is no single group in the United States at this time that is doing formalized reviews, and this is an excellent space for the Homeland Security to convene expertise here. The closest is the National Bioterrorism Analysis and Countermeasures Center, which is a part of Homeland Security, based at Fort Detrick.

But that makes use of highly specific basic scientists. Unfortunately, the real space is the convening of all these disciplines to help determine the threat waiting, and those people are remarkably rare. We have to grow them, in fact.

Mr. LINDER. Did you want to comment on that?

Dr. BRENT. I concur.

Mr. LINDER. You also mentioned several times avian flu. Is there a way you think that terrorists could expand on that?

Dr. CALLAHAN. Yes. We find avian influenza disquieting in the extreme, and the reasons are basically that most of the work is already being done for the terrorists. The second point is that the number of countries that are demonstrating cases of avian influenza in humans are increasing by the month, effectively, as are the number of cases within each of those countries.

Several of those countries have become more difficult to work with in recent history because these are economically relevant diseases and can stress their economies greatly. I call your attention to the reports on 2003 SARS and its impact on the Government of China's economy.

But think also about DPRK. Avian influenza is found on both sides of DPRK, and we know it migrates on the wings of birds, so you can bet that North Korea has a critical threat to its protein stocks. Since one out of three chickens eaten on the planet is grown, raised and eaten in China, including in these countries, it is a big deal.

So what do we do about avian influenza? The first thing is, we don't know exactly what the final humanized version of avian influenza is going to be like. We do have important countermeasures from a chemotherapeutic standpoint. These are the new inhibitors, drugs that have been on the market for some period of time; and it would be technically more difficult—not impossible, but more difficult—to clone out or negatively select out the resistance of those features.

So investing in this new class of drug, broadening its capability and then, most critically, investing in a fast through-put vaccine capability to make this system, to make this use of a threat agent less viable, is an appropriate investment of resources; and it fits our routine public health needs as well as our needs in biodefense.

Mr. LINDER. Thank you.

Mr. Dicks?

Mr. DICKS. Thank you.

Just following up on that, Mr. Chairman, you said prepare a quick vaccine preparation capability. Is that what you are saying?

Dr. CALLAHAN. Yes.

Mr. DICKS. Talk about that a little bit. Some of these vaccines cost $800 million, or they are very expensive.

Dr. CALLAHAN. Yes. It is interesting that the production cost is actually much smaller. Remember, the majority of these vaccines have never been tested with exposure in humans.

Mr. LINDER. If the gentleman will yield, I think Dr. Brent said 400 is closer to it.

Dr. BRENT. That is for a small molecule drug, sir.

Mr. LINDER. But when the pharmaceutical firms tell us $800 million, they are also considering opportunity costs. If they spend $400 million for a drug, what could they have made if they had invested it elsewhere? Would they have doubled their cost?

Mr. Dicks. How much does it cost to have this kind of a capability? Do we have it now?

Dr. BRENT. The vaccine—not to bore you with the kind of decline of the vaccine industry in the U.S. over the past 40 years, but the number of companies has contracted. They are hunkered down by threats of product liability lawsuits; cost of development has gone up, et cetera, at the same time that the technical capabilities for making new vaccines have exploded.

Recombinant DNA taught us how to make flu vaccine that would be pretty good within a week or two of sequencing the latest flu strain. We don't have that production capability, we don't have the kind of precertified and good to go.

There are other more experimental things, like DNA vaccines. I personally believe that a prudent defense strategy in the United States would have several kinds of pretty good vaccine capabilities stacked up in addition to the ones—

Mr. DICKS. Should that be done at HHS? Where is it done?

Dr. BRENT. It should be done by creation of a government bio-industrial complex, and likely it should be orchestrated by the government, but done by the private sector, which is somewhat different from the pharmaceutical biotech private sector that exists.

Dr. CALLAHAN. And critically important to national health security is that that be American-owned. Our current vaccines are purchased overseas, and we know from working with our close European partners that vaccines purchased by the U.S. were not available for U.S. use when our own vaccines for the past H3N2 season became compromised with a contaminant.

In other words, we own vaccines manufactured in offshore locations that can be commandeered by the host countries to meet their own emergency public health needs. So that is a critical point.

Mr. DICKS. But who should take the lead on this? HHS?

Dr. CALLAHAN. HHS is absolutely the source for basic science expertise. I believe that the biotechnology sector is going to advance this, because their incentives are greater and they think very much outside of the box.

Mr. DICKS. The companies themselves?

Dr. CALLAHAN. The companies.

Mr. DICKS. They are going to need some incentive from the government to do this, right?

Dr. CALLAHAN. Indeed, the process for which that could be executed is not completely clear at this time.

Mr. DICKS. Since we have not done these material threat assessments and we have this money left in project BioShield, the $5.6 billion of which only a small part has been committed, should we start using that money? Would that be a possible source?

Dr. CALLAHAN. Creating models that mimic the threat for which a technology user and a technology response like a company can respond to are absolutely valid ways of testing the system, absolutely valid.

The last point I will just mention is computational. Dr. Alibek has talked about this. We can predict mutations that can arise in an agent. This involves computational science, which is a fairly recent intersect with biotechnology and molecular biology.

But we can take flu and understand the permutations in its genome that will happen over time and anticipate in advance our vaccines needs. It will not be in production, which commands huge investment in our resources, but it can be there as a prototype, as a seedling that is ready to go.

The last point is that the $800 million—which Dr. Brent and others can talk about; we all consult with biotechnology companies so we understand their perspective—is that, A, they are not getting good guidance; B, they find that the BAAs and the allocations and appropriations are not very linear for them and easy to decipher; and, C, they don't have the capability to test their system and to argue in the marketplace that they have the best deal for the government to choose. And the discussion of sole-source appropriations, I think, is pertinent here as well.

Mr. DICKS. Dr. Brent?

Dr. BRENT. Mr. Dicks, where the home for this thing is within the government almost doesn't matter so much to me from the outside. This will be with us for many decades. It is important that there be a centralized science and technology development apparatus which is able to orchestrate, a la the way that DARPA and the other agencies within the Defense Department do.

Mr. DICKS. Should that be at HHS, NIH, CDC? Where would you put it?

Dr. BRENT. I would put it either in DHS personally or in some new entity. There needs to be DARPA-like technology development.

Mr. DICKS. The reason DHS I think is suspect is because they have not handled this material threat assessment thing very effectively, and some people feel there is—Chertoff is going to come out today and say we need a doctor, somebody with medical and the kind of training you have, in the Department of Homeland Security, to provide a person who understands all of these kinds of issues and how this should work, which we don't have at this juncture.

Dr. BRENT. That is a start, sir.

Mr. DICKS. Well, thank you.

Dr. ALIBEK. Unfortunately, I must say this: What we haven't done yet, we haven't developed a good committee or group of very, I would say, respected people, knowledgeable in the field of biological weapons threat.

Unfortunately again, many people try to pretend that they know biological weapons threats. But in many cases we have, I would say, a number of people inside the United States who have first-hand knowledge of the field of biological weapon threat, and they understand what kind of agents could be the more threatening agents and what types of threats we need to handle.

In this case, you establish such a panel, working either for Congress or any kind of agency, and they will determine first, for example, the level of threat coming from different pathogens. We do have many, many projects of this type.

But when we see that kind of standard, not very comprehensive, not very sophisticated knowledge, if we want to start this work, we need to stop for a second, we need to do this work. It is not going to take much time, 3 months, 6 months, and it could be done.

Next, after we define the threat, we will start working with a bigger group of scientists and figure out what kind of technologies we have available to mitigate each type of threat, specific technologies, and what kind of prospective technologies we have at different stages of development to meet prospective threats.

As soon as we have got this done, in my opinion the picture is becoming absolutely clear. But at some point—we discussed this in 1998, in 2000, immediately after 2001–2002, and now it is 2005 and already 8 years, and we still aren't there.

Mr. Linder. Mr. Shays, do you wish to inquire further?

Mr. SHAYS. Thank you very much. This is a great panel. Frankly, this is a terrific committee. If you had said 6 years ago that we would be in the Ways and Means Committee Room talking about the issues that we are talking about, I look at these old pictures of former chairmen and I think this is a strange world we are in.

But the one thing that is fairly clear to me is, the technology is going to continue to advance, and I use that with quotes, so that less sophisticated operatives will be able to do horrific things.

One of the hearings that I had in my National Security Subcommittee before September 11 that blew me away was a noted doctor of a major medical magazine, and he ended the hearing by saying, "My biggest concern is that a small group of dedicated scientists will be able to create an altered biological agent that could wipe out humanity as we know it."

That is why I think, Mr. Chairman, the work that you are doing is essential. The likelihood of this happening is smaller than a conventional attack; the consequences, though, are horrific.

I want to know if I should dispose quickly of this issue. In 1972, the U.S. and more than 100 nations signed a Biological and Toxin Weapons Convention, which basically barred possession of deadly biological agents except for defense research. However, and this is the issue, no mechanism was set up to make sure people abided by it; and the city inspector I saw in Russia proved that no one was paying attention to it.

Do you think it is conceivable that we will be able to have a convention process that will enable us to look at biological sites and be somewhat assured that bad things are not happening, or do you think it is almost pointless because folks can be in garages and elsewhere?

Nodding heads will not be on the record here. I will start with you, Dr. Brent. What is the answer?

Dr. BRENT. I think that having conventions that track down technologies and look for particular things might well give a false sense of security, so I don't think you can do it like that.

I think there is a great deal of value to be had in not only criminalizing, but stigmatizing, maybe even hyper-stigmatizing, deliberate research in biological weapons in the U.S. and worldwide, the idea being to create a moral climate in which if somebody down the hall was doing something sinister and you were worried about it, you might drop a dime to your local enforcement agency.

So I think there is some value in conventions prohibiting things. I don't think there is going to be security in surveilling sites and stuff.

Mr. SHAYS. Thank you.

Dr. ALIBEK. I would absolutely agree in my opinion, because terrorist groups, they don't sign agreements. Of course, whatever we decide, they are not going to follow the rules of war.

Mr. SHAYS. They are not going to tell us where they are making it either.

Dr. ALIBEK. At the same time, what I would like to say, what we are missing now when we talk about a threat is coming, what kind of threat and so on and so forth, and what we can do about this, in my opinion there is one more important piece missing, and this piece is so essential in my opinion, if we don't pay strong attention to this issue, we are going to suffer again.

Dr. ALIBEK. Because what we don't have, for example, in the field of any kind of discipline—science, technology—we have got special, let me say, programs; universities which are teaching, let me say, special extras—

Mr. SHAYS. What is your bottom-line point? What is the point you want to make?

Dr. ALIBEK. What I want like to say, we need to establish a national educational program for biodefense extras in the field of nonproliferation, counterterrorism, investigation—

Mr. SHAYS. So your point is that in the United States we don't have enough qualified people going into this area?

Dr. ALIBEK. We don't have enough qualified people who would be able, let me say, to deal with the more, let me say, sophisticated threat.

Mr. SHAYS. Let me go to you, Dr. Callahan.

Dr. CALLAHAN. My only two points in response to that is, with regard to the treaties, we can use all of our other benefits and attributes of the United States, such as our health care, to get out there and to penetrate into the countries of concern. Using Russia as a specific example, is that we are in almost all the nooks and crannies of the open programs in the Ministry of Health, kept out only of the Ministry of Defense programs and a couple little shops out in the far east of Russia.

The key point is that those have been driven by strong incentives for sustainable value and economic development, quite frankly, because we bring Merck and Pfizer with us rather than the Department of Defense. We bring money and we bring autonomy, and we bring the ability for them to work in a private market.

It is that second group that you talked about, the Ted Kaczynski bioweaponeer, someone in the basement who is supported by novel technologies, who is going to be the more dramatic of the two and make a loud bang in a small place. That can happen behind national lines in university laboratories, and then there are smaller biotech shops. And that is where the intelligence community needs to intersect with the biodefense community to provide steering and guidance, because those communities remain largely disengaged because of the need for clearances and the need to keep your subject matter experts operating in open source. Some mechanisms to get a large number of people informed for informed research and development to mitigate against these threats is absolutely critical.

Mr. SHAYS. Thank you. Thank you, Mr. Chairman

Mr. LINDER. Does Mr. Thompson wish to inquire?

Mr. THOMPSON. Yes, Mr. Chairman. And let me say that I am absolutely appreciative of the three gentlemen and their testimony. It has been quite enlightening, and I do appreciate it.

One thing I would like to kind of get your individual thoughts on, everybody pretty much agrees anthrax is kind of number one on the list, or something like that—

Mr. SHAYS. No. You have got a shaking head here.

Mr. THOMPSON. Well, all right. Then give me number one and number two, and then I will ask for number three.

Mr. SHAYS. Yeah, I want to know that, too.

Mr. THOMPSON. So if it is not—

Dr. CALLAHAN. These are probability estimates. And we are all products of our experience in a formal weapons program, in molecular biology and technology, and in the remote developing countries where you see these diseases all the time.

I do actually put anthrax up there because of the technical challenges; you don't have to store it, it lives forever, and you don't have to feed it. It is also easy to get because it is found in almost every neotropical country that is available. So I do actually put anthrax up there. And there is also a great cache with it right now; it is easy to recognize in all of the cultures in the world, including terrorist cultures. And also it has huge public health importance in countries of concern because it kills a lot of meat stock. It is a huge pathogen in veterinarian populations. It happens in areas there.

After that, I am going to go to avian influenza. And this is another wild-type agent, meaning naturally occurring agent, which could be commandeered and used for ill purposes. And it is a great example where you will have tremendous impact in undermining of confidence, for which you do not have an effective disease, and for which you will have guaranteed contagion and transmission, so that would be number two.

Third would be the moderately engineered pathogens, those that are hardened to survive in sunlight and survive in low-halogen environments. They make them difficult to decon.

And after that, we are going to get into much more complicated agents, and then go back to those zoological pathogens, such as Glanders and those that will affect your agriculture reserves and meat stocks.

Dr. BRENT. I think Dr. Callahan just made the key point, which is that in my mind a potential adversary might go with what they

knew and felt comfortable with. So Dr. Callahan can run around the world picking clinical isolates out of disease outbreaks and prioritize things that way. Dr. Alibek worked in a successful Soviet program which had anthrax as one of its major weapons.

If I were, you know, doing things, I might do what I know. I might resynthesize SARS, put a toxin on it, infect myself, and cough on people. I don't know that it is worth while to prioritize the risk if every expert who imagines an attack imagines things through the prism of what they would find to be easy and devastating.

Dr. ALIBEK. What I would like to say, yes, when we talk about terrorist groups, in many cases they have no scientific ability or technological sophistication, for example, just to work on 5, 10, 15 different pathogens and to choose the best one just to deploy.

In this case, it is the issue of what they can have access to or what they can achieve and so on and so forth. But unfortunately, even if we proceed from this point, unfortunately anthrax is becoming first. And too, the ability, technological and so forth, anthrax is there. In this case, whether or not we like it, anthrax is the weapon of choice, and we need to get rid of anthrax. I am not saying that we shouldn't prepare for other agents. There is a huge network of agents and we need to have preparation, but in terms of probability, actual ability, anthrax is taking place number one.

Mr. THOMPSON. Thank you, Mr. Chairman.

Mr. LINDER. Thank you, gentlemen. This has been an eye-opening experience, and I expect we are going to do this again. It makes me wonder if we have blown the $20 billion I talked to you about, and if we should keep that money and be flexible and quick.

I have one question to each of you. What would you say if I told you a scientist from Sweden said that Iranian children emigrating with their parents from Iran to Sweden have all been vaccinated for smallpox; what would that mean to you?

Dr. ALIBEK. It is very hard to say. They are two different ways of explaining it. First, analyzing the Iranians, I have noticed they still believe that smallpox could come back. And they do some vaccinations of smallpox and some development and so on and so forth. That is why if, for example, when they vaccinate against smallpox, meaning that it could come back without having actual knowledge, or it could be a special agent, because if they have some information that Iran is working with smallpox virus.

Talking about Iran, I am finishing some analytical work, and hopefully I will deliver it quite soon to one of the government departments. I see that Iran is having a very big interest in military-type biotechnology and medical biology. In this case, I didn't see smallpox, but what I saw, actually, is quite disturbing. In this case, looks like there is some biological weapons activity in Iran.

Mr. LINDER. Thank you very much. This hearing is adjourned.

[Whereupon, at 12:10 p.m., the subcommittee was adjourned.]

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