Statement of

The Honorable Joseph Lieberman

United States Senator
Connecticut
October 6, 2004

Creating a BioDefense Industry:
BioShield II

Testimony by Senator Joseph Lieberman
Before the Senate Judiciary and Senate HELP Committees
October 6, 2004

Chairman Hatch, I am pleased to be here today continuing to work with you on these critical bioterrorism preparedness issues. You understand the urgency and complexity of these matters. There is no Member of the Senate who matches your expertise on biomedical research and development issues, intellectual property and liability protections, tax incentives for entrepreneurs, and FDA regulatory and bioethics issues. You have a powerhouse staff. I could not have a better, more influential and respected partner for the bills that we've introduced. Your leadership - exemplified by this hearing - is impressive and welcome.

Chairman Gregg, your leadership in enacting Project BioShield was exceptional. You demonstrated a real command of the complex issues we face in engaging the biopharma company as part of our national defense infrastructure. You have a powerhouse staff as well.

Senator Kennedy, you have been a leader on public health issues for many decades. The many prominent biotech companies in Massachusetts view you as champion who understands their issues. Your staff has always been considered to be one of the best on the Hill.

Senator Leahy, you and your staff were targets of the October anthrax attack. Fortunately, the letter was intercepted before it reached your office, making this a personal issue for you and your staff. You understand the threat posed by these pathogens.

Working together, there is nothing the four of us can't accomplish in terms of bioterrorism preparedness. Enacting BioShield II should be our next step.
10/15 - Bioterrorism's 9/11
None of us on the Hill - especially those of us with offices in the Hart Building - will forget October 15, the date of the anthrax attack on Senator Daschle's office. This date is the bioterrorism equivalent of September 11. We also need to remember October 5, the third anniversary of the 2001 anthrax death of Bob Stevens, a photo editor at American Media in Boca Raton, Florida, and November 17, the third anniversary of the discovery of a similar anthrax laced letter mailed to Senator Leahy. Similar anthrax attacks during these weeks were directed at NBC, ABC, CBS and other news organizations. All told five people died and thousands who might have been exposed were put on Cipro, including many of us and many of our staff.

This attack on civilians with weapons grade anthrax was unprovoked. And unlike the case with the 9/11 attacks, we still don't know who mailed the anthrax letters. As with the 9/11 attacks, we were totally unprepared for the anthrax-laced letters. We are responding forcefully to the 9/11 attacks - the commission that Senator McCain and I proposed has issued a superb report and the Government Affairs Committee, where I serve as the Ranking Democrat, is hard at work translating its recommendations into legislation. Unfortunately our response to the 10/15 anthrax attack has not been as forceful.

Unlike our response to 9/11, we have not seemed to consider the 10/15 attack to be the equivalent of a declaration of war. While we have taken a few constructive steps to strengthen our Bioterror defenses, we remain painfully vulnerable to another Bioterror attack, or a chemical or radiological attack.

Timeliness of Hearings

The issue in this hearing could not be more timely: Have we done enough in enacting BioShield to ensure that we will secure the development of the medical countermeasures we need in the event of an attack, what metrics are we applying to determine whether BioShield is sufficient, and, in the event that BioShield does not accomplish enough, what policy options exist for strengthening our effort with BioShield II.

It is not too early to ask these questions; this is urgent and long-term research. It often takes ten or more years to bring a new therapeutic to market and some of the research - particularly on new antivirals - may take many more than ten years. Stocks of bioweapons developed by the former Soviet Union might fall into the hands of terrorists. We know that terrorist groups are intensely interested in acquiring Bioterror weapons and they will have no compunctions about using them.

We can't wait several years to determine if BioShield is sufficient. We need to set clear metrics of its impact and take decisive action to move to enact BioShield II if that proves to be necessary.

Many of us believe that BioShield is a step in the right direction, but we don't believe that BioShield is sufficient. If we listen carefully, we will hear that the biopharma industry -- which is hiding on this issue -- is saying that BioShield is not enough. So we already have strong warning signs that more needs to be done. And Senator Hatch and I - and hopefully Senator Gregg and Kennedy - will shortly be introducing BioShield II, a bill to set the terms of the debate just as our earlier bill served as the source for BioShield. This hearing starts the process for considering these additional legislative measures.

Nature of the Bioterror Threat

There is no terror threat greater than that of Bioterror. With an attack with a plane, a chemical attack or a radiological dispersion device (a dirty bomb), the loss of life can be catastrophic, but the perimeter of the attack is fixed. With an infectious disease, the perimeter of an attack might grow exponentially as the infection spreads. It is possible to kill thousands with a bomb, chemical or radiation, but it is possible to kill millions with a Bioterror pathogen.

In the 2001 anthrax attack, the terrorist wrote a note in the letter to Senator Daschle that said, "09-11-01. You can not stop us. We have this anthrax. You die now. Are you afraid? Death to America. Death to Israel. Allah is great." If this note had not been included in the letter, and if the intern who opened the letter hadn't been suspicious, it is possible that some Senators and many Capitol Hill staff from our offices -- perhaps hundreds -- might have died. We would only have discovered the attack in hospital emergency rooms, where Cipro might have proven to be ineffective. Cipro works as a prophylaxis only when it catches anthrax early, before the toxins are released into the bloodstream, which can happen within 24 hours of an infection. Our current anthrax vaccine is administered in six shots over 18 months.

The 9/11 Commission report states that al Qaeda "was making advances in its ability to product anthrax prior to Sept. 11" and cited former CIA Director George Tenet as warning that an anthrax attack is "one of the most immediate threats the U.S. is likely to face." Russia developed dozens of strains of anthrax and the security at these former bioweapons laboratories is suspect. It is estimated that a mason jar of anthrax spores sprayed over an urban area could infect 400,000 residents, and if undetected until they started showing up in emergency rooms, kill half of them. It is also estimated that one hundred anthrax laced letters could cross contaminate thirty million letters and infect 10,000 people with anthrax. Imagine what would happen if our mail system - which processed over 200 billion pieces of mail last year - were closed for a few months. What we need, and don't yet have, is a therapeutic that disarms the anthrax toxins at a late stage of the disease -- which is the aim of a pending RFP at the Department of Health and Human Services (see below).

We saw the potential for morbidity and mortality, and massive economic disruption, with SARS. When SARS was rampant, Beijing, Hong Kong and Shanghai closed down. Quarantines were imposed and China authorized the death penalty on anyone who willfully spread the disease. During the epidemic, there were reports that the SARS virus was mutating to become more virulent. In China's countryside, fear of SARS has led to some villages setting up roadblocks to keep away people from Beijing and at least four riots against quarantine centers have been reported in recent days. Thousands were quarantined in China. In the end SARS spread to thirty countries on five continents, sickening nearly 9,000 and killing 850. SARS is a zoonotic disease that apparently can jump back and forth between animals and man, which makes it much more difficult to eradicate it. We may not have seen the last of it.

We can also remember the devastating impact of the 1918 Spanish flu pandemic that killed more than died in the first World War, about 30-40 million people (equivalent to 100 million today). In the month of October, 1918, 200,000 Americans died of the disease, 43,000 soldiers died, and 28% of our population was infected. The flu's lethality rate was only 2.5%; the lethality rate of the most common form of smallpox, variola major, is 30% and for hemorrhagic smallpox it approaches 100%. The lethality rate for SARS was about 15%. If the 1918 flu pandemic killed the equivalent of 100 million people, think of how many smallpox or SARS -- both of which could be weaponized by terrorists -- could kill.

Public health authorities are concerned about the incidence of avian influenza in humans. There is now concrete evidence that this virus can be transmitted human-to-human. When humans contract the pathogen from birds, the death rates are very high; a majority die. Since January

2004, a total of 23 confirmed human cases of avian influenza A (H5N1) virus infections have been reported in Vietnam with 19 deaths and 12 cases in Thailand with 9 deaths. These cases were associated with widespread H5N1 poultry outbreaks that occurred at commercial and small backyard poultry farms. Since December 2003, nine countries have reported H5N1 outbreaks among poultry. More than 100 million chickens have been culled in an effort to stop the outbreak. The virus now appears to be able to infect mammalian hosts, including pigs and cats, an unusual prowess for an avian virus. This raises concern as pigs are also hosts of human flu viruses and this could yield a hybrid avian flu strain that can be passed human-to-human. The avian flu virus apparently is now carried by migratory birds so it may be very difficult to eradicate the virus. We have no vaccine for the disease and the one therapeutic -- Tamiflu -- is only effective if given very early after the onset of symptoms. It is feared that the virus might evolve resistance to Tamiflu. Public health officials believe that in theory the avian flu could cause a "pandemic killing millions of people worldwide, and possibly hundreds of millions." Whether H5N1 could be used as a Bioterror weapon against agriculture or humans is not known.

In 1947 there was an outbreak of smallpox in New York City. Eventually two of the twelve who were infected died. But the smallpox vaccination campaign was massive -- 500,000 New Yorkers received smallpox vaccinations the first day and eventually 6.35 million were vaccinated in less than a month, 85% of the city's population. . President Truman was vaccinated prior to a trip to New York City.

If we suffered another smallpox outbreak, it is not likely that a vaccination campaign would go so smoothly. It is now estimated that if the current smallpox vaccine were deployed in the United States 350 to 500 individuals might die from complications. The current vaccine is not recommended for patients who have eczema or are immunosuppressed, HIV-positive or are pregnant. Even worse, based on a 1971 accidental release of smallpox from a Soviet bioweapons laboratory, some speculate that the Soviets successfully weaponized a rare and especially lethal form of smallpox, hemorrhagic smallpox (with near 100% lethality).

Mother Nature's pathogens are dangerous - smallpox, anthrax, plague, tularemia, glanders, typhus, Q fever, Venezuelan equine encephalitis, brucellosis, botulinum toxin, dengue fever, Lassa fever, Russian spring-summer encephalitis, Marburg, Ebola, Bolivian hemorrhagic fever, Argentinean hemorrhagic fever and fifty other pathogens could kill thousands or even millions. But on the horizon are more exotic and deadly pathogens.

We have reports that the Soviet Union developed genetically modified pathogens such as a hybrid plague producing diphtheria toxin. This manipulation increased virulence and made the plague microbe more resistant to vaccine. Other possibilities include a Venezuelan Equine Encephalomyelitis-plague hybrid is a combination of the virus and the bacteria; we have no idea what symptoms such a pathogen would manifest or how we might diagnose or treat it. Other hybrid pathogens might be developed, including a Venezuelan Equine Encephalomyelitis-Ebola hybrid.

We have reports that the Soviet Union developed a powdered form of Marburg (a hemorrhagic fever where every cell and organ of the victim bleeds). Symptoms of Marburg include kidney failure, recurrent hepatitis, inflammation of the spinal cord, bone marrow, eyes, testes, and parotid gland, hemorrhaging into the skin, mucous membranes, internal organs, stomach, and intestines, swelling of the spleen, lymph nodes, kidneys, pancreas, and brain, convulsions, coma

and amnesia.
Genetically modified pathogens are another possibility. In 2001 the Journal of Virology reported that Australian scientists seeking to create a contraceptive for mice used recombinant DNA technology to introduce Interleukin 4 into mousepox and found that it created an especially virulent virus. In the words of the scientists, "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." This public research suggests that introducing IL-4 can create an Andromeda stain of a virus, information of potential use to terrorist sociopaths. In addition, published studies describe how to create a recombinant vaccina virus to induce allergic encephalomyelitis in rabbits (and potentially - highly lethal smallpox virus capable of causing paralyses in humans) and how to synthesize the polio virus in a biochemical laboratory .

Other possible pathogens - some of which the Soviet worked on - include antibiotic resistant pathogens. The Soviets apparently developed a strain of plague resistant to ten different antibiotics, and a strain of anthrax resistant to seven different antibiotics. Some claim the Soviets developed a strain of anthrax resistant to the current U.S. anthrax vaccine. A part of this research in a hamster model was published in Vaccine, so this information is available to terrorists.

Other exotic pathogens might include autoimmune peptides, antibiotic induced toxins, and bioregulators and biomodulators. An autoimmune peptide might stimulate an autoimmune attack against the myelin that sheaths the target's nerve cells. Antibiotic induced toxins are hybrid bacteria-viruses where antibiotics administered to treat the bacterial infection stimulate the virus to release a deadly toxin; the greater the doses of antibiotics, the more toxins are released. Bioregulators and biomodulators are synthetic chemical that bond to and disrupt receptors that govern critical functions of the target, including nerve, retinal, liver, kidney, heart, or muscle cells to cause paralysis, blindness, schizophrenia, coma, or memory loss.

Some of these might be available now from the 60 bioterror research laboratories maintained by the Soviet Union. Eventually, terrorists might be able to set up full-blown biotechnology laboratories. Rogue states could do so and they might then transfer bioweapons to terrorists or lose control of them. Over the long term, as the power of modern biotechnology grows, the Bioterror threat will grow and increasingly virulent and exotic weapons might become threats. In November 2003 the CIA's Office of Transnational Issues published "Our Darker Bioweapons Future," which stated that the effect of bioengineered weapons "could be worse than any disease known to man." The rapid evolution of biotechnology makes monitoring development of bioweapons extremely difficult. Some of these weapons might enable the development of "a class of new, more virulent biological agents engineered to attack distinct biochemical pathways and elicit specific effects, claimed panel members. The same science that may cure some of our worst diseases could be used to create the world's most frightening weapons." It specifically mentioned the possibility of "binary BW agents that only become effective when two components are combined (a particularly insidious example would be a mild pathogen that when combined with its antidote becomes virulent)"; "designer" BW agents created to be antibiotic resistant or to evade an immune response; weaponized gene therapy vectors that effect permanent change in the victim's genetic makeup; or a "stealth" virus, which could lie dormant inside the victim for an extended period before being triggered.

Illustrating the speed with which biotechnology is advancing to create new bioterrorism threats is a recent announcement by Craig Venter and his Institute for Biological Energy Alternatives that in fourteen days they had synthetically created working copies of the known existing bacteriophage virus Phi X174. Other researchers had previously synthesised the poliovirus, which is slightly bigger, employing enzymes usually found in cells. But this effort took years to achieve and produced viruses with defects in their code. So the timescale has shifted from years to weeks to make a virus. There are other bigger viruses that would require more time to assemble. Venter asserts that his team could make a bacteria with about 60 times larger genome from scratch within about a year of starting. Does this mean that the debate about whether to destroy smallpox virus stocks is pointless because any virus or bacteria whose DNA sequence is published is eventually going to be easily creatable by labs all around the world?
These pathogens might be deployed by terrorists, sociopaths or rogue states that have no compunctions about killing massive numbers of "infidels" or enemies in the West. They would be experience great joy in sowing widespread panic, injury and death in America. Osama Bin Laden's spokesman, Sulaiman Abu Ghaith, bragged that al Qaeda has "the right to kill 4 million Americans" in response to deaths he claims the west has inflicted on Muslims. We are facing sociopaths with no compunction about using whatever weapons of mass destruction they can develop or secure. They would see the potential to unleash a weapon in North America and trust that our borders would be closed so that it would only rage here and not spread to the Muslim world.

Economic Consequences of an Attack

The Brookings Institution estimated that a Bioterror attack would cause one million casualties and inflict $750 billion in economic damage. An earlier Office of Technology Assessment found that there might be three million casualties. If there are this many casualties, what can we expect in the way of public panic and flight? A 2004 poll finds that "most Americans would not cooperate as officials would expect them to during a terrorism incident." Only 2/5 said that they'd "follow instructions to go to a public vaccination site in a smallpox outbreak" and only 3/5 would "stay in a building other than their own home..." A vivid vision of what an attack might look like is found in Albert Camus' The Plague, with its incinerators and quarantine camps. We can review the history of the Black Death, which killed up to one of half of Europe's population between 1348 and 1349.

Imagine what would happen if the attack involves a pathogen for which we have no diagnostic, vaccine or therapeutic. If we resorted to quarantines, what would the rules of engagement be for the police and military forces we deploy to enforce it? Would it be possible to establish an effective quarantine if there is mass panic and flight? Would our hospitals be overwhelmed by the "worried well"? Would public health workers continue to serve or also flee? If our hospitals are contaminated, where would Americans receive medical care for non-terror related emergencies?

What would happen if a Bioterror, chemical or radiological attack closed Atlanta's Hartsfield International Airport - which handled nearly eighty million passengers last year? Or what would happen if we put a hold on the one hundred and twenty million international airline arrivals and departures we see each year? What would happen if we were forced to close our borders with

Mexico and Canada - with 500 million crossings last year? What would happen if we restrained the 2.79 trillion automobile passenger miles driven in the U.S., one billion of which exceeded 100 miles?

What would happen if a terror attack rendered certain types of business activity uninsurable? What will happen if large swaths of residential real estate - none of which is currently insured for acts of terror - were contaminated and rendered worthless with anthrax spores?

Near Total Lack of Medicines

We are vulnerable to a Bioterror attack in many ways, but one of the most troubling is that we have essentially none of the diagnostics, therapeutics and vaccines we need to treat those who might be exposed or infected. If we don't have these medicines, we are likely to see quarantines and panic, which will amplify the damage and disruption. My office is on the 7th floor of the Hart Building, immediately above Senator Daschle's office. We were told if we immediately started a course of treatment with Cipro we would not die, so there was no panic. Think what would have happened if the government had said, "We don't know what this is, it's deadly, we have no way to tell who has been exposed, and we have no medicines to give you."

In the summer of 2000 the Defense Science Board found that we had only one of the fifty-seven diagnostics, drugs and vaccines we most need to respond to a Bioterror attack (we had a therapeutic for chlamydia psittaci, a bacteria). It projected that we'd have twenty of the fifty-seven within five years and thirty-four within twenty years. But today we have only two of the fifty-seven countermeasures (we now have a diagnostic for anthrax).

At this rate of developing these medical countermeasures, we won't have twenty of them available until 2076 and we won't have thirty-four until 2132. This list does not include antibiotic resistant pathogens, hybrid pathogens, genetically modified pathogens, and a host of other exotic Bioterror pathogens.

Little Sense of Urgency

The Congress and Administration have not responded to the anthrax attack with an appropriate sense of urgency, especially with regard to the development of medicines. We have not responded with a crash industrial development program as we did when we developed radar during the Second World War or as we are now undoubtedly undertaking to detect roadside bombs. Reluctantly, I would characterize our national response as lackadaisical.

December 4 is the third anniversary of my introduction of legislation to provide incentives for the development of medical countermeasures - including diagnostics, therapeutics and vaccines -- for Bioterror pathogens (S. 1764). Chairman Hatch, October 17 is the second anniversary of our introducing our first bill together on this subject (S. 3148) and we introduced our current bill on March 19 of last year (S. 666). Twenty months ago President Bush proposed Project BioShield, a bill based on one of the twelve titles in our bills, and it was finally enacted into law on July 21. If we enact one of the titles of our bill every two years, it'll take 22 more years to complete our legislative work.

The critical issue for this hearing is whether Project BioShield, Public Law, Public Law 108-276, is sufficient or whether we need to supplement it with BioShield II, a bill that you and I intend to introduce this Fall. BioShield is only one title of our proposal - the title that provides that the

government will define the size and terms of the market for a Bioterror countermeasure in advance before a biopharma companies puts its own capital at risk. This is a necessary first step; companies won't risk their capital to develop a product unless they can assess the possible rate of return (product sales) on their investment.
Enacting BioShield is a step in the right direction. If we were to enact only one idea first, this is the right first step. We will now see how the Department of Health and Human Services implements this law. We will see what R&D priorities it sets, whether it projects a market for these products sufficiently large to engage the better biopharma companies in this research, and whether it sets contract terms that company Chief Financial Officers find acceptable.

Unfortunately, we all heard a deafening silence from biopharma industry -- the target of this legislation -- as BioShield was being considered. The industry did essentially nothing to fix the Administration's draft - which the industry privately stated was laced with dysfunctional provisions. The industry did essentially nothing to pass BioShield. And the industry has said essentially nothing since BioShield was enacted.

It is clear to me that BioShield is not sufficient to secure development of the medical countermeasures we need, indeed, I believe it is woefully insufficient.

Basis for Industry Skepticism

The industry is skeptical that the government will be a reliable partner during the development of Bioterror countermeasures. The basis of its skepticism runs deep.

The industry points to the Cipro procurement as a case in point. In 1999, before the anthrax attack, Bayer, the developer of Cipro, was asked by FDA and CDC to secure a label indication for Cipro for anthrax. The government wanted to have one antibiotic available that was explicitly labeled for anthrax - it understands that patients might be reluctant to take a medicine for anthrax where it is not labeled for this indication. Bayer incurred the expenses to do this with no expectation of ever utilizing the product in this manner, and when the attack occurred, Cipro was the only therapeutic with a label indication for anthrax. Bayer handled this emergency with honor. It immediately donated huge stocks of Cipro, 2 million tablets to the Postal Service and 2 million tablets to the Federal government to be used to protect those who might have been exposed or infected. The government then sought to procure additional stocks of Cipro and demanded that Bayer sell it as one-fourth the market price. Threats were made by Members of Congress that if Bayer would not agree to this price the government might step in to challenge the patent for Cipro. Bayer readily agreed to the deep discount. We can assume that every other purchaser of Cipro then demanded this same price and that this cut Bayer's market return for Cipro. To add insult to injury, Bayer has had to defend itself from lawsuits by those who took Cipro in response to the attack even though it did what was asked, provided more than enough free product to treat all patients and greatly reduced it's stockpile pricing. Bayer also was deeply concerned with employee and plant security risks when it was publicly identified as the sole source of this counter-bioterrorism agent.

The industry view this incident as proving that with regard to bioterrorism research, no good deed will go unpunished. If a large pharmaceutical company can be manhandled this way, what

would happen to a small biotechnology company? The industry expects that if there is an attack, and the company has the indispensable medicine we need to respond to it, the government is likely to steal the product. The industry is deeply skeptical of the government already. It has very complex and often contentious relationships with other HHS agencies, including the Center for Medicare Services, the Food and Drug Administration, and the National Institute of Health. It has constant battles with state Medicaid agencies. This is not an industry that trusts government.

Some in Congress have proposed legislation that feed industry fears. In 1994 and 1995 legislation was introduced in the House (H.R.4370, introduced on May 10, 1994, and H.R.761, introduced on January 31, 1995) that provided the government with eminent domain power with regard to AIDS to confiscate "all potential curatives and all data...regarding their development," including the patents for such compounds. Similarly, in 1999 and 2001 legislation was introduced in the House (H.R.2927, introduced on September 23, 1999, and H.R.1708, introduced on May 3, 2001) that provided for the compulsory licensing of "any subject invention related to health" where the government finds it "necessary to alleviate health or safety needs" or the patented material is "priced higher than may be reasonably expected based on criteria developed by the Secretary of Commerce." Legislation has been introduced that would deny the benefits of the R&D tax credit for research by pharmaceutical companies where the products that arise from that research are sold at higher prices abroad than in the United States. See H.R.3665 introduced on February 15, 2000.

The industry response to these threats to its patents must be seen in light of the events of March 14, 2000. On that day a White House spokesman apparently indicated that the government might move to challenge some biopharma industry patents for genes. The industry lost $40 billion in market capitalization in the panic that ensued on Wall Street. That was not only the beginning of a deep drought in biotech company financing, it was the beginning of the collapse of the entire NASDAQ market. A similar collapse and drought had occurred in 1993-1994 the Clinton Administration proposed that the prices of "breakthrough drugs would be reviewed by a special government panel.

The issue of price controls and patents was recently considered and rejected by NIH in response to a petition for the government to march-in on the patent of Abbott Laboratories for ritonavir (sold under the name of Norvir), an AIDS therapeutic. The petitioner, Essential Inventions, asked that the government cancel the license of this patent to Abbott, which it alleged was charging too much for Norvir. The petitioner had also been involved in the 1994-1995 NIH proceeding, where NIH reviewed the impact of its 1989 protocol to review whether "reasonable" prices were being charged by companies that had licenses with NIH. NIH found that this price review process was destroying the NIH technology transfer program - companies simply would not enter into agreements with NIH. As a result, NIH repealed the price review process. The new march-in petition raised essentially the same issues and if the petition had been granted, we could have expected that the NIH tech transfer process will be crippled - again, as it was from 1989-1995. In rejecting the petition, NIH did not state, however, that is has no right to march-in based on the price of a product, implying that it could or might assert such power in the future. This can only have a chilling impact on companies considering entering into biodefense procurement and research agreements.

Aside from fears about government actions, we could not have picked a worse time to ask the industry to undertake a whole new portfolio of research. The biotech NASDAQ index stood at 1380 and it now stands at about 725. The Amex biotech indexed peaked at 801 and it now stands at about 525. The Dow Jones pharmaceutical index peaked at 420 and it now stands at about 275. The biotech industry raised $32 billion in capital in 2000 and only $16 billion last year. In June of this year, 36% of the public biotech companies had stock trading at less than $5 per share. There were 67 biotech IPOs in 2000 and only 7 last year. The industry losses each year continue to run to $4 billion. The National Venture Capital Association reports that only 2% of venture money went into biodefense following the October anthrax attack.

Of the 506 drugs publicly disclosed to be under development by the 22 largest pharmaceutical companies, only 32 are for infectious disease and half of these are aimed at HIV/AIDS. In 1967 we had 67 vaccine companies and in 2002 we had 12. World wide sales vaccines is about $6 billion, but the world wide sales of Lipitor are $10 billion.

In addition, it is not clear whether the government is able or willing to provide the industry with the operating margins - profits - it sees for its other products. The operating margin for successful biopharma companies is 2.76 to 3.74 times as great as the operating margins for major defense contractors. This means that the defense contractor model will not work to engage biopharma companies in developing medical countermeasures for bioterror agents. Whether the successful bipharma companies are "too profitable" is a separate issue. The issue addressed here is the operating margin that successful biopharma companies seek and expect as they assess lines of research to undertake. If the operating margin for biodefense research is less, or substantially less than the operating margin for non-biodefense research, it is not likely that these companies will choose to undertake biodefense research. This research is a voluntary undertaking putting their capital at risk; there is no requirement that they do this when the prospects for profits are not competitive with that from other lines of research.

Mostly we are seeing the industry hiding, not commenting on the pending legislation, not participating in the legislative process, and making every effort not to seem to be unpatriotic or greedy. Companies do not say in public that they are disinterested. They will not say what package of incentives would be sufficient to persuade them to take up biodefense work. They fear a debate on patents. They feel besieged by the current drug import debate, pressure from CMS over drug prices, and the debate over generic biologics. While I understand these fears, we simply have to know what it would take in the way of incentives to establish a biodefense industry. If the incentives in BioShield or BioShield II are not sufficient, we need to know what incentives are sufficient. We need to know what reassurances would persuade the industry that what happened to Bayer will never happen again. And only the industry can give us a clear answer to these questions. We cannot have a dialogue on these urgent national questions without the government listening and the industry speaking.

Shifting Risk to the Industry

The goal of BioShield II is to shift the risk of countermeasure research and development to the industry. Given the skepticism of the industry about the reliability of the government as a partner, shifting the risk to the industry -- with it risking its own capital to fund the R&D -- will be

difficult. But engaging the industry as entrepreneurs, rather than as defense contractors, is likely to be less expensive for the government and it's much more likely to secure the development of the medicines that we need.

If the government funds the research, the industry can expect to receive the operating margins that are typically paid to defense contractors - 8.5-9.5%. If the industry risks its own capital and funds the failures and cost overruns, the industry believes it would be justified demanding the operating margins that are typically paid in the commercial sector - 28-32%.

If the government funds the research, the industry expects that the government will control or own the patents associated with the medicines. If the industry funds the research, it believes it has claims on all the patents.

The only companies that are likely to accept a defense contractor model are companies with no approved products, no revenue from product sales, and no other source of capital to keep the lights on. For them government funding is "non-dilution" capital, meaning it's a form of capital that does not dilute the ownership shares of its current shareholders. Many biotech companies have stock trading in the low single digits, so they cannot issue another round of stock that would enrage the current shareholders. For them this government funding might validate the scientific platform of the company, generate some revenue, and hype the stock.

Biotech industry executives state in private that if their capital markets strengthen they will be even less likely to consider Bioterror countermeasure research. One CEO whose company has received an NIH grant for Bioterror countermeasure research stated in private that his company would never have considered this entanglement with the government if it had any other options to fund its research.

Our goal with BioShield II should be to engage the successful biopharma companies in this research -- companies that have brought products to the market -- and persuade them that the government will be a reliable partner. Then the risk of failure and cost overruns is shifted to the industry and we've engaged the companies with a track record of bringing products to the market. The government will need to provide substantial rewards if - and only if - the companies do succeed in developing the medicines we need, but then the government is only paying for results. When the government funds the research, it funds a process with no guarantees of any success. Providing the industry with substantial rewards for success is a model that engages the industry as entrepreneurs, drawing on the greatest strength our nation has in the war on terror.

Metrics for Success of Project BioShield

With the enactment of BioShield, it is critical for the Administration and Congress to agree on metrics for determining whether BioShield is sufficient. We also should immediately launch a comprehensive review of the policy options available to supplement it -- with this hearing a perfect start for such review.

In terms of metrics to measure the success of Project BioShield, let me suggest that we are on the right track if we see the following response:
1. Government, academia and industry set a long-term research and development agenda --

decades long -- that is commensurate with the full range of current and evolving bioterror threats;
2. The research and development agenda focuses in part on development of powerful research tools that will enable us to respond quickly to a new, unforeseen terror agent and not just to develop countermeasures for terror agents we know about today;
3. Government determines that the key to success in developing bioterror countermeasures is securing the enthusiastic engagement of private biopharma companies pursuing the research for their own good business reasons as "profit marking arsenals";
4. Government understands and accepts the entrepreneurial culture of the biopharma industry and sees that it is not an industry that can be recruited for bioterror countermeasure research on the defense contractor model
5. Government is able to overcome the suspicions of the biopharma companies and establish itself as a reliable long-term partner in bring bioterror countermeasure research to a successful conclusion and the Government reassures industry that what happened to Bayer in the Cipro case will never happen again;
6. We begin to see that a biodefense industry has become established, with its own capital funding from investors and retained earnings, its own lead companies, its own stock analysts, and its own legitimacy in the markets;
7. Successful biopharma companies are investing hundreds of millions of their own capital in bioterror countermeasure research and competing with one another to bring countermeasures to the market, small biotech companies are able to secure funding from investors for bioterror countermeasure research, and biotech companies are able to go public with IPOs for bioterror countermeasure research;
8. CFOs of biopharma companies see a reasonable opportunity to secure operating margins (rates of return) on their investment in bioterror countermeasure research that are commensurate with those that they seek and secure for other research;
9. We see company commitments to long-term research projects that might not yield a countermeasure for the 10-12 years -- the industry average;
10. Government understands that it can shift significant risk to the biopharma companies as long as it provides a reasonable rate of return if and when the companies successfully complete their research;
11. Government understands that is must remain focused on results -- countermeasures that can be stockpiled and deployed -- rather than process;
12. Government funded basic research is focused so that it does not compete with that of private companies and its inventions are transferred to company partners expeditiously on commercially reasonable terms;
13. Government makes the FDA animal model rule work effectively when bioterror countermeasures are brought to it for review and approval;
14. We see renewal in the U.S. vaccine industry, which has essentially been destroyed by government regulation;
15. We see companies launching major research projects to develop the next generation of antibiotics and antivirals, with major benefits for other infectious and contagious diseases, including HIV/AIDS, malaria, TB and antibiotic resistant pathogens; and
16. Government is not concerned that bioterror countermeasure research might yield collateral commercial market benefits to companies and considers this a positive development.

These are ambitious metrics for success, and I am open to hearing the Administration's own proposed metrics. What we cannot afford to do is simply to spend two years trying to implement BioShield without applying metrics of success to every stage in the process.

In terms of exploring the policy options for BioShield II, the bills that Senator Hatch and I have introduced are comprehensive and ambitious. There are other possible options that might be appropriate. We are happy to work with the Administration and appropriate committees of the Congress to review them. At a minimum, this review should focus on liability, intellectual property, tax, antitrust and research tool issues and should engage the Justice, Commerce, Treasury Departments, Homeland Security, Defense, and Health and Human Services Department.

Implementation of Project BioShield

The industry will now watch how HHS implements BioShield and how NIH responds to the march-in petition. I anticipate that the implementation of BioShield will be a painful process as HHS experiences the depth of industry skepticism about this research and this market. In fact, it's not clear which is more threatening form an industry perspective - no market or an exclusively government market. I anticipate that HHS will find that it will only be able to engage biopharma companies that have little or no success in securing development of FDA-approved products and that are dependent on government funding for the research. If HHS is able only to engage these companies, and able only to engage companies as defense contractors, it's prospects for securing development of the full range of medical countermeasures we need will be bleak.

HHS will be setting its long-term agenda of development projects. It has yet to be seen how HHS will set the mix of diagnostics, therapeutics, and vaccines. Many believe that diagnostics and therapeutics are more important priorities than vaccines. Former Soviet bioweaponeer Ken Alibek and his colleague Charles Bailey argue that "vaccines are not a realistic prophylaxis for civilian populations, because they would be only be effective in very narrowly defined circumstances. They argue that even if we had vaccines for the top six Bioterror pathogens, it is "highly unlikely that a decision would be made to vaccinate the entire population against each" of them. They argue that vaccines are "unlikely ever to be used..." They recommend we focus on medicines to treat the late stages of these diseases. Given the delay that may arise between an attack and the recognition of it as an attack, this would seem to be the most important priority for BioShield.

One key implementation issue has already arisen. My staff has heard that HHS is saying that it won't guarantee procurement of a medical countermeasure under BioShield unless the FDA has granted IND (investigational new drug) status to the medicine. It has referred companies to NIH for funding to take the product to that stage of development. This interpretation makes no sense and may substantially inhibit the effectiveness of BioShield. The concept behind BioShield is that the government will provid detailed specifications regarding the market for a medical countermeasures so companies can assess whether to risk their capital to develop the countermeasure. This concept applies to research and procurement of any medicine, including those that are long-term research projects that might take many years to reach the IND stage. Because BioShield is a procurement bill, not a research funding bill, and only guarantees

procurement if and only if the country develops the product the government needs, there is little risk in applying BioShield to pre-IND research. Many companies have no interest in negotiating a research funding grant from NIH -- they'd rather rely on investor funding or retained earnings -- or might not receive a grant.

Perhaps this interpretation arises from the extremely limited funding for BioShield. The Tufts Center for the Study of Drug Development estimates that industry expends more than $800 million on average to develop a new chemical entity. It is clear that the $5.6 billion funding for BioShield procurement represents a fraction of what will be needed to develop all of the medical countermeasures we will need to prepare for a Bioterror, chemical or radiological attack. (By way of contrast, the government spent nearly $7 billion in just one year developing the missile defense system. Many believe we are much more likely to see a Bioterror than a missile attack.) As a way to ration its scarce funds, the IND requirement might be necessary, but as a development strategy it does not fully exploit the potential embodied in BioShield to shift the risk to the industry to fund the research in exchange for a specified reward for successful R&D projects.

The first Request for Proposal (RFP) for biodefense subsequent to the enactment of BioShield was issued on August 18 for immunotherapeutic antitoxins (e.g. monoclonal antibodies, polyclonal antibodies, and human immune globulin), other protein products (e.g. mutated toxins), and small molecule entity treatments (e.g. protease inhibitors) for the treatment of inhalational anthrax. The RFP calls for the procurement of 10,000 -200,000 therapeutic courses of treatment, contingent upon the outcome of an initial procurement of "10 grams" of the product for the government to test - a surprisingly small amount. Many in industry found this RFP surprising, with its focus on an initial purchase of such small amounts of the product which will serve as a significant deciding factor in determining the fate of further acquisition of the product. This approach seems rather plodding, attenuated and cautious.

More troubling, there is no clear timeline for procurement of additional courses of treatment nor is there a predictable outcome for a contractor awarded only the initial phase of the contract. There seems to be no limitation on the company selling the same product in other markets, including allies or civilian markets.
The RFP indicates that even though the company, at the time of award, has obtained an IND from the FDA to proceed with human clinical trials, HHS will be reviewing the IND data on its own and conduct its own comparative testing, after which it might conclude that it will not go forward with a contract with the company. Given FDA's special expertise on these matters and their designated mission to protect public health by ensuring safety and efficacy of medical products, it is not clear what other government agency might find to trump the FDA determination. Does HHS have a specific animal model or in vitro test that they find particularly relevant, different from any communicated by the FDA during the IND process that the company hasn't performed? It is not clear why HHS requires only that the IND be filed, and not requiring that it be approved at the time of application. It is not clear in the RFP how soon HHS will make its final determination. Will it wait until the FDA has approved or denied an IND for all companies who submitted proposals, or for some subset? What if the FDA approval of the IND sets standards for the clinical trial in excess of those upon which the bid price is premised?
Other terms of the RFP are less surprising. The intellectual property associated with the product

appears to remain the property of the company. The contract asks for offers from companies for the fixed total contract price (with some items being cost reimbursable that needlessly subjects the winner to implement very burdensome cost accounting processes, thus further discouraging industry participation), more than one contract might be issued, and the company must first submit a "complete IND" application to the FDA for the initiation of human clinical trails. INDs can only be obtained after the company has completed toxicity and other laboratory tests that demonstrate that the product is "reasonably safe to give to human subjects in clinical trails." The RFP requires that the company show "proof of concept in small animals." The contractor must commit to securing final FDA approval for the product. The contractor shall be required "to attempt to obtain clinical trial insurance" but can request HHS to invoke the Safety Act for the work, thereby leaving a bidder's position on liability to be tenuous at best. The company is required to establish a security plan for the development, manufacturing, storage and distribution of the product. The company is required to maintain a production line for the product through the life of the contract. The experience of the bidders is one relevant factor in determining which will be selected. About 100 complex FAR provisions will be included in the contract, all with their own interpretations and enforcement issues. Strangely the contract takes advantage of none of the special contracting authority found in BioShield, which can be used to cut through some of burdensome and intimidating FAR contracting provisions.

In addition, many of the standard "special contract requirements" are not appropriate for biodefense contracts and should be tailored accordingly. For example, the requirement for incorporation of the technical proposal into a contract would make this information publicly available. Not only does this pose the risk of exposing proprietary data to competitors, but it also creates a national security risk, allowing potential development by terrorist organizations of strains that can evade the specific countermeasure which is being developed for stockpiling and make such countermeasure ineffective.

Responses to the RFP are due October 19, 2004 and we will then see whether this HHS approach is proving to be effective in securing the engagement of biopharma companies with a proven track record of bringing products to market. We must then wait for the first procurement under Project BioShield to go forward.

We anticipate that the implementation process will be a difficult one as HHS learns more about what terms and limitations are acceptable to the companies it wishes to bid and which are considered threatening or unduly burdensome. Given the operating margins for these companies, the fixed price for these contacts might be a huge issue. When the Joint Vaccine Acquisition Program (JVAP) at the Department of Defense put out a solicitation for the procurement of seven vaccines, not a single established pharmaceutical company chose to bid.

BioShield II Provisions

The BioShield II legislation we will introduce will be based on S. 666, legislation Senator Hatch and I introduced on March 19, 2003, and from which BioShield was taken. While BioShield establishes a predictable and guaranteed government market for medical countermeasure for Bioterror pathogens, BioShield II will include tax incentives to form capital for biopharma companies to conduct research to develop these countermeasures, protect and enhance intellectual property associated with these countermeasures and address other issues that affect

the companies' inclination to conduct this research.

The premise of this legislation, as it was with BioShield, is that direct government funding of this research is likely to be much more expensive and risky to the government and less likely to produce the countermeasures we need to defend America. Shifting some of the expense and risk of this research to entrepreneurial private sector firms is likely to be less expensive and much more likely to produce the countermeasures we need to protect ourselves in the event of an attack.

The legislation will provide that a company seeking to fund research is eligible to elect from among three tax incentives:
(a). Establishment of an R&D Limited Partnership to conduct the research. The partnership passes through all business deductions and credits to the partners.
(b). Issuance of a special class of stock for the entity to conduct the research. The investors would be entitled to a zero capital gains tax rate on any gains realized on the stock.
(c). Receive a special tax credit to help fund the research
The first two provisions help small biotech companies to form capital to fund the research. These companies cannot use tax credits because they have no revenue from product sales and no income tax liability with respect to which to claim a tax credit.

The legislation will provide that a company that successfully develops a countermeasure is eligible to elect one of two patent incentives:
(a). The company is eligible to receive a patent for its invention with a term as long as the term of the patent when it was issued by the Patent and Trademark Office, without any erosion due to delays in the FDA approval process.
(b). The company is eligible to extend the term of any patent owned by the company for two years. The patent may not be one that is acquired by the company from a third party. In S. 666, this wild card patent provision is only available to companies with $750 million or less in paid-in capital.
In addition, a company that successfully develops a countermeasure is eligible for a 10-year period of market exclusivity on the data supporting FDA approval of the countermeasure.

The legislation will provide for protections against liability for the company that successfully develops a countermeasure. It will grant companies with a limited exemption from the antitrust laws as they seek to expedite research on countermeasures. It will include special incentives are incorporated to ensure that manufacturing capacity is available for countermeasures. And it will apply all of the incentives to the development of research tools.

Given the reluctance of the biopharma industry to participate in the legislative process on BioShield, it's been difficult to determine whether enactment of these BioShield II incentives will be sufficient to establish a biodefense industry. I believe that doing less will not be sufficient, but I acknowledge that even if we enact every provision in BioShield II, we may not meet all of the metrics of success that I have proposed.

We should not stop until we have reached our goal - to establish a well capitalized and expert biodefense industry to develop these medical countermeasures. We must recognize that our challenge is not simply to procure and stockpile a few diagnostics, therapeutics and vaccines.

The Bioterror threat is evolving rapidly and over time we will need to develop many additional medicines. We need a biodefense industry ready, willing, and able to accomplish this mission.

To do this, we need to reassure the biopharma industry that the government will be a reliable partner in this research and persuade the industry that what happened to Bayer in the Cipro procurement will not happen to them. Most of all, we need to engage the successful biopharma companies - the ones that have a track record of bringing safe and effective medicines to market. We need to engage these companies as entrepreneurs, not as defense contractors. Acting as entrepreneurs, deploying their own or investor's capital, we can shift some of the risk of this research to the industry. If we seek to engage these companies as defense contactors, it's likely to cost more with fewer prospects for securing the development of the medicines we need.

The single most controversial proposal in BioShield II will be the wild card patent extension. There will be substantial debate on this proposal and both sides have legitimate concerns. In favor of it is the concern that without it we will not be able to establish a biodefense industry. Against it is the concern that it will unfairly raise health care costs to consumers and health care entities. The Congress has looked at similar points before and decided to extend patents on drugs as an incentive for companies to conduct pediatric clinical trials and secure appropriate pediatric labels. In this case Congress judged that the patent extensions were worth their cost. The details of how the wild card patent provision would work are also important and we are open to discussing them. In the end, Congress will have to weigh the competing considerations and judge whether we should include the wild card patent as an incentive.

If BioShield II is insufficient to accomplish these goals, we need to develop BioShield III. We must do whatever it takes to ensure that we have the medical countermeasures available if and when there is a Bioterror attack. The consequences of failing to do this could be catastrophic. We cannot settle for some effort to develop these countermeasures - we need results, not process.

Who Should Be In Charge?

BioShield is being implemented by the Department of Health and Human Services. The bills that Senator Hatch and I have introduced place the implementation responsibility with the Department of Homeland Security. The Department of Defense is a third alternative, but its efforts to develop Bioterror medical countermeasures have been a scandalous failure. We need a frank and full review of which agency has the best culture and expertise to lead this vital effort.

HHS has a complicated and often contentious relationship with the biopharma industry. The industry has had frequent policy conflicts with the Food and Drug Administration, The Center for Medicare Services and the National Institutes of Health. Over many decades we've seen HHS focused on keeping unsafe and ineffective products off the market, reducing the government reimbursement for medicines, and policies that are hostile to patents. The original version of BioShield submitted to the Congress by the Administration was laced with provisions that the industry viewed as dysfuncational, unworkable, and hostile. Given this history and culture, it is not clear that HHS can effectively work with the industry on a massive industrial development program with regard to Bioterror countermeasures. HHS does substantial scientific and contracting expertise.

The Department of Homeland Security appears to be developing a culture that focuses intensively on the bottom line with no time taken for ideological diversions. It has no history of conflicts with the biopharma industry. It does not now possess substantial scientific and contracting expertise.

The issue of who is in charge is central to all of our homeland security issues. That's why I first proposed that we create a Department of Homeland Security. We should review carefully the effectiveness of HHS in implementing BioShield, its metrics for determining whether BioShield is sufficient, and its review of the policy options for supplementing BioShield. If HHS does not perform well in these roles, we should consider whether the Department of Homeland Security might provide better leadership.

Research Tools

We will never be able to anticipate all of the pathogens that might be utilized by terrorists. Our medicine chest will never have all the medicines we need for all the possible terrorist pathogens. The ultimate and only effective bioterror defense are "research tools" powerful enough so that we can develop and deploy a new countermeasures quickly after an attack has occurred. We need this power to respond to Mother Nature's new concoctions, like SARS, but it's also the only defense against exotic terror pathogens we'll never see in advance of an attack. As stated by the leading biodefense think tank,

The process of moving from 'bug to drug' now takes up to ten years. The U.S. biodefense strategy must act as one of its key strategic goals the radical shortening of this process.

The development of research tools is a central focus of the bills that Senator Hatch and I have introduced and it will be a central focus in BioShield II and all of the incentives in BioShield II will apply to the development of research tools.

One obstacle to the development of research tools to expedite the development of Bioterror countermeasures is the NIH Research Tool Guidelines. Finalized in 1999, the guidelines find that "intellectual property restrictions can stifle the broad dissemination of new discoveries and limit future avenues of research and product development." It defines a "research tool" in "its broadest sense to embrace the full range of tools that scientists use in the laboratory, including cell lines, monoclonal antibodies, reagents, animal models, growth factors, combinatorial chemistry and DNA libraries, clones and cloning tools (such as PCR), methods, laboratory equipment and machines." A more sweeping definition is hard to imagine. With regard to these tools, the guidelines find that patents, and "reach-through royalty or product rights, unreasonable restraints on publication and academic freedom, and improper valuation of tools impede the scientific process whether imposed by a not-for-profit or for-profit provider of research tools." While the NIH guidelines only apply to recipients of government funding, the guidelines states that "it is hoped that other not-for-profit and for-profit organizations will adopt similar policies and refrain from seeking unreasonable restrictions or conditions when sharing materials."

The practical result of the guidelines is that any private company that seeks to develop research tools must be wary of working with any institution or individual that receives NIH grants. This estranges the industry from the academic community with regard to the development of these

tools. In many cases, the innovative research of academics had led to the private sector development of tools by companies whose business plan was to create such tools, not develop therapeutics. Now it is much less likely that the work of academics regarding research tools will ever be commercialized. This could not be worse timing - what we need to prepare for a Bioterror attack is a well capitalized research tool industry. Accordingly, our bills waive the application of the research tool guidelines to tools relevant to the development of Bioterror countermeasures. These tools are the gold standard for preparedness for a Bioterror attack.

Finally, the Food and Drug Administration has published a rule that permits Bioterror medical countermeasures to be developed relying on tests in animals rather than humans. This is necessary as it is not ethical to test a Bioterror pathogen on a human subject and there is no patient population available with a naturally occurring incidence of these diseases. One major issue for the development of these countermeasures is whether animal models exist for the diseases for which we need to develop countermeasures. If there is no animal model for a disease, it is not likely that biopharma companies will begin a research project to develop a countermeasure when there is no path to FDA approval. In addition, there is a growing shortage of animals. We need to take decisive action to ensure that this research tool does not prove to be a major bottle neck in the R&D to develop Bioterror countermeasures.

Third World Diseases and Antibiotic Resistant Pathogens

As we draft BioShield II, we are actively exploring the scientific and economic implications of applying BioShield and BioShield II to infectious diseases generally, not just pathogens deemed to be "terror weapons."

As a matter of science, the research and development on countermeasures to bioweapons is inextricably linked to research directed to pathogenic virus, bacteria and fungus that cannot be weaponized. Consequently, it makes sense to enact incentives for research that addresses the pathology, diagnosis or therapeutics that relates to virus bacteria or fungus whether it has been or could be weaponized or not. Research on infectious diseases seeks to understand how organisms cause disease, the immune system responds to pathogens, and antibiodies and other medicines protect against them. This research is broadly applicable to both bioterror and non-bioterror pathogens. In the end, we need broad-spectrum antibiotics, anti-virals that can be utilized against a variety of viruses, and vaccines that can be adapted to a variety of organisms.

As enacted into law, BioShield could be applied to the development of new antibiotics, which can serve as a Bioterror countermeasure. The Administration's draft of BioShield provided that if there was a "significant commercial market for the product other than as a homeland security threat countermeasure" BioShield would not apply (S. 15, section 203, as introduced on March 11, 2003). This anti-dual use provision, which would have squandered the potential benefits of this legislation for the development of new antibiotics and other dual-use medicines, was deleted in the final version of the bill. We need these antibiotics as countermeasures for Bioterror pathogens and we especially need them to respond to Bioterror pathogens that are engineered to be antibiotic resistant.

We also need new antibiotics to respond to a public health crisis in our hospitals - one documented in great depth by the Infectious Diseases Society of America in Bad Bugs, No Drugs

(July, 2004). IDSA finds that about 70% of the two million bacterial infections in America each year are resistant to at least one antibiotic. If our current range of antibiotics loses its effectiveness - and signs of resistance to our last line of antibiotics, vancomycin, are appearing - then we will face a public health crisis even if there is never a Bioterror attack. The relentless rise of antibiotic resistance in bacteria and the exit of all of the major Pharma companies conducting R&D in this area due to lack of incentives will leave us vulnerable in the extreme by the end of the decade. At some point society will be badly bitten by this trend, with pandemic influenza being the most likely candidate in the short term. I fear that someday we'll be forming another 9/11 commission after large numbers of Americans (and others around the world) die as a result of failure of our government to engage the problem proactively.

While BioShield could apply to the development of new antibiotics, it is not likely that new antibiotics will be listed as a priority of the Administration for Project BioShield. BioShield focuses on procurement by the government of medical countermeasures, so it is likely that it will mostly or entirely be utilized for procurement of countermeasures where the government is the sole market. There is a substantial civilian market for antibiotics, with the government only a marginal player. It makes more sense to deploy the tax, intellectual property, and other incentives in BioShield II to this research. This would both be consistent with our needs for Bioterror preparedness and provide a much-needed benefit to our public health infrastructure.

In terms of infectious disease generally, it is likely that the biopharma companies that we might engage in developing Bioterror countermeasures will have expertise, and capital from investors for research on a broad range of infectious diseases, going well beyond those that might be weaponized. In fact, it may well be easier for these companies to form or deploy capital for this research if it involves development of medicines where the Federal government is not the sole or principal market. In the end, we need to establish an Infectious Disease Industry, not just a BioDefense Industry. We need companies capable of development effective platforms that have a broad application to a variety of infectious diseases -- research tools of immense power and importance. We certainly need many more companies with expertise in developing vaccines. So, it makes little economic sense to stovepipe these lines of research, providing incentives for research to develop medicines for only a select few pathogens we label as "bioterror pathogens." It is also true that in some cases we may not know if a particular pathogen can be weaponized. For example, some believe SARS could be weaponized.

Accordingly, it makes good sense to apply BioShield II to research and development of countermeasures for "infectious" diseases even if they might not be pathogens that can be weaponized. BioShield could also be applied to these countermeasures with a proviso that the government could organize a procurement fund comprised of its own funds, funds form international public health agencies like the Global Alliance for Vaccines and Immunization (GAVI), foundation funding, and other sources. This is an issue that we need to explore with organizations such as the IDSA, The international Aids Vaccine Initiative, the Alliance for Microbicide Development, the Alan Guttmacher Institute, the AIDS Vaccine Advocacy Coalition, Biotech Ventures for Global Health, the Aeras TB Foundation, AmFAR, the Global Alliance for TB Drug Development, the Malaria Vaccine Initiative (MVI), International Partnership for Microbicides, Medicines for Malaria, and similar groups.

The need for additional research to develop therapies, cures, and vaccines for infectious disease - both Bioterror and natural - is clear. Worldwide, seventeen million deaths annually are caused by infectious and parasitic diseases, 33% of the total and 71% of all deaths among children under 5 years of age. This compares with fourteen million deaths from famines, wars, violence and aging, the same number from circulatory and obstructive pulmonary disease, and five million due to cancer. AIDS is out of control in many countries and mutating to create new strains. In the end, we may lose one hundred million people to AIDS. Malaria is developing resistance to the newest prophylaxis - with nearly three million deaths a year. Antibiotic resistant TB is surging - with over three million deaths a year. One million die each year of hepatitis B and one billion are infected. 165,000 each year die of hookworm and roundworm. We have seen waves of emerging diseases, including AIDS, SARS, West Nile virus, Lyme disease, and hantavirus. The public health agenda - for bioterrorism and beyond - is compelling and amply justifies enactment of new incentives for development of effective medical countermeasures.