Testimony of

The Honorable Joseph Lieberman #2

October 6, 2004

National Institutes of Health Reform

BioShield and BioShield II are directed at the biopharma companies. These companies have the expertise and experience needed to develop medical countermeasures; government does not. There remains an important role for government funded basic Bioterror research, principally through the National Institutes of Health. We need to be sure that these basic research investments implement a sophisticated strategy, with a clear understanding of how this research supports, and does not conflict with or duplicate, research that is more appropriately conducted by the biopharma companies.

The patent restoration provisions of BioShield II are especially critical to patents on basic research. Inefficiencies in the technology transfer process and the long-lead time necessary to translate basic research into FDA-approved products means that patents on basic research tend to be eroded. The patent term runs from the date of application, not the date of FDA approval, so if there are delays between the grant of a patent and FDA approval, much of it can be lost. If a patent has eroded 3-4 years, and additional erosion can be anticipated, it is likely that the patent will never be commercialized, it will block other researchers while it is in effect, and then it will die. Unpatentable inventions tend not to be commercialized by the biopharma industry.

As Anthony Fauci, the Director of NIAID, has acknowledged that "the path to product development has not been a part of [NIAID's] research strategy." NIH translates its basic research into commercial products through technology transfer licenses with biopharma companies. For a variety of reasons, including the imposition of the reasonable price clause, the threat of march-in rights, the NIH research tool guidelines and other policies, NIH's technology transfer program has not be notably successful.

A variety of measures should be considered to strengthen this critical program.
1. The commercialization efforts at NIH could be consolidated, centralized and restructured within a new National Center for Health Care Technology Development. It could be headed by a Director subject to Senate confirmation.
2. The Center's mission could be to increase the yield of our current investment in biomedical research and make the commercialization efforts more responsive to the medical needs in this country and more transparent to the taxpayers and their elected representatives.
3. The Center could oversee NIH's technology transfer programs, patenting and licensing of patents, and set a research and development strategy for NIH sponsored research.
4. The Center could gather and publish detailed measures of NIH's success in ensuring that its basic research is developed into commercial products.
5. The Center could be the liaison with the NIH grantees on all issues involving technology transfer.

6. Restrictions could be lifted that reduce the ability of NIH to act in a more entrepreneurial manner. This will allow NIH to foster the growth, by investing in and sponsoring technology that is emerging and entering into the commercial research market.
7. NIH and each Institute could consult with an industry advisory board to insure its research agenda is supportive of and not duplicative of industry research.
8. The process for selecting grantees could include assessments of the opportunities that may exist for commercialization of the sponsored research.
9. Grantees success in bringing technology to patients could be tracked so that the successful programs might be recognized, rewarded and copied by others
10. The Center could be charged with teaching what it learns to the research community in this country and around the world.

In addition, I have proposed I have proposed creating an American Center for Cures, which would be connected with the National Institutes of Health. Its job would not be to engage in much original research, but rather to better organize and fund work already being done in government and private laboratories across the country.

Right now, there is not only duplication of effort, but efforts are uncoordinated. Different laboratories may have keys to different pieces of the puzzle and be completely unaware of each other's work.

The Center for Cures would connect these efforts.

The Center for Cures would also work with the scientific community and the private sector to support the promising lines of research, even on those drugs and antibiotics that, while unprofitable, are indispensable if it is you or a family member who need them.

When leads looked promising, the Center would be able to commission large-scale research across disciplines to take advantage of advances not only in biology, but also in the physical sciences, computer science, and engineering.

The Center for Cures would also work with the pharmaceutical and biotechnology industries - especially smaller firms - to create incentives for innovation as well as cutting through bureaucracy to make it quicker and easier to get cures from the researcher's bench to the patient's bedside.

Responding to a Declaration of War

We should not need a 9/11 Commission report to galvanize the Administration and the Congress to respond to the unprovoked and deadly Bioterror attacks of three years ago. The threat could not be more obvious and what we need to do is also obvious. If we don't develop the diagnostics, therapeutics, and vaccines to protect those who might be exposed or infected, we risk public panic and quarantines. We have the world's preeminent biopharma industry and we need to put it to work in the national defense.

BioShield is a step in the right direction, but it is a small step that does not take us where we need to go. We need to follow the implementation of BioShield very carefully and set clear

metrics for determining its effectiveness. We should not wait to begin to review the policy options available to supplement BioShield. Senator Hatch and I will be proposing BioShield II and we will press for its consideration. We should press the biopharma industry to present its views on what it will take to engage it in this research and what it will take to establish a biodefense, research took, and infectious disease industry.

The American philosopher, George Santana said, "Those who cannot remember the past are condemned to repeat it." It's only been three years since the anthrax attack but I fear our memory of it already has faded. Let this hearing stand as a clear statement that some of us in the Congress remember what happened and are determined not to permit it to happen again. War has been declared on us and we need to act as if we noticed.

Appendix

Defense Science Board "stoplight chart" - The Projected Evolution of Diagnostics, Vaccines, and Therapeutics Against Major Bioagents with Strategic R&D and Supply Actions (Summer 2000)

"Move on BioShield to Aid Biodefense Industry," Senator Joe Lieberman and Senator Orrin Hatch, The Hill (May 19, 2004)

Chronology: Incentives for Research to Develop Countermeasures to Bioterror Pathogens

Outline: Biological, Chemical, and Radiological Weapons Countermeasures Research Act of 2003, S. 666 (Senators Lieberman and Hatch)

BioPharma vs. Defense Contractor Operating Margins

Interview--Serguei Popov, Journal of Homeland Security (November 13, 2000)

Move on BioShield to Aid Biodefense Industry
Senator Joseph Lieberman and Senator Orrin Hatch
May 19, 2004 -- The Hill

Anthrax hit the Senate in October, 2001 and Senators and staff took CIPRO to prevent infection. There was no panic and no one fell ill. This may have lulled us into a false sense of complacency. In fact, we are woefully unprepared with diagnostics and medicines to respond to a bioterror attack. Four years ago the Defense Science Board found that we had only one of the 57 bioterror medical countermeasures we most need. Today we have two. If we don't have diagnostics, drugs, and vaccines, next time we could see panic. Our country simply does not have the medicines we need to respond to a bioterror assault, neither in the short term nor the long run.

So what must we do? For openers, one way we should enlist our innovative biotech industry into the business of developing diagnostics, vaccines, antibiotics, and other medical countermeasures that would control the massive disease and death we might see from a biological weapons attack. Funding basic research is no longer enough. We also need diagnostics and medicines ready to use.

Right now, our biotech industry is not conducting the necessary R&D to develop these countermeasures, primarily because there is no private sector commercial market for these

products. Because we hope and pray that we'll never face an attack, government emergency stockpiles are the only market. So, we must create the equivalent of a private sector commercial market for which the bio-pharmacological industry will want to invest their own and investors' capital to develop bioterror countermeasures. The industry must be provided tax incentives so small biotech firms can form the capital to fund this research. It must be assured of intellectual property protections for those worried the federal government might in a crisis confiscate a countermeasure. And, it must have liability protections because many of these countermeasures cannot be fully tested in clinical trails.

Last year, we reintroduced the Biological, Chemical, and Radiological Weapons Countermeasures Research Act, an ambitious bill we first introduced in 2002 that would create the right conditions and incentives for private sector R&D on bioterror countermeasures. Once those incentives are in place, the industry and its investors would be paid if, and only if, they successfully develop the countermeasures we need. This approach shifts the risks off the taxpayer and onto the industry for the inevitable research failures. The government pays only for success, not process.

Furthermore, this breakthrough research won't be wasted if there is no bioterror attack. We desperately need to develop new antibiotics to replace those for which resistance is emerging. Even if no bioterror attack ever occurs, the work of the biotech industry could make significant progress toward finding cures for infectious diseases that are ravaging millions of people

Our bill complements the Administration's Project Bioshield. Project BioShield follows our lead by setting the terms in advance for government markets - our concept. It would give bio-pharmacological companies reliable commitments regarding the market they will tap if they risk their own capital to develop countermeasures. In all likelihood, Project Bioshield would result in the development of some new Bioterror antidotes. We believe Congress should pass Project BioShield immediately. It's a step in the right direction.

We believe that more can and should be done to provide additional incentives to help infuse the biodefense industry with the talent and capital necessary to give us all the bioterror medicines we need. Bioterror is an evolving threat that could, over time, require development of dozens, perhaps hundreds, of medical countermeasures. The Lieberman-Hatch bill would pave the way for industry involvement sufficient to meet the potential need.

We will know that we've established a biodefense industry when hundreds of millions of dollars in company and investor capital are available to fund countermeasure research, and investors see a reasonable opportunity to profit to the same degree they do on investments in other biomedical research.

We urge Congress to move expeditiously on the President's BioShield bill and then take up BioShield II, a bill we'll introduce once BioShield is enacted. It will be based on our own bipartisan legislation. That combination will advance the process of building a biodefense industry to protect us from future biological attacks.

In the long run, we may face no greater threat than a bioterror pathogen. Now is the time to come together to ensure that we are ready with the medical countermeasures - and the public health infrastructure - to prevent panic and minimize what could otherwise be massive loss of life. We will continue to work with President Bush, our colleagues in the Congress, and other interested parties on this important matter.

Chronology: Incentives for Research to Develop Countermeasures to Bioterror Pathogens

Summer 2000 -- Defense Science Board finds that we have only 1 of the 57 bioterror countermeasures we most need
October 5, 2001 -- Bob Stevens, a photo editor at American Media in Boca Reton, Florida, dies of inhalation anthrax.
October 7, 2001--U.S. Centers for Disease Control and Prevention (CDC) reported that investigators had detected evidence that the deadly anthrax bacterium was present in the building where Stevens had worked.
October 12, 2001 -- NBC employee in New York exposed to anthrax.
October 15, 2001 -- Anthrax laced letter opened in Senator Daschle's Office in the Hart Senate Office Building. ABC News finds anthrax in its offices in New York.

October 18, 2001 -- CBS news finds anthrax in its offices in New York.

October 19, 2001 -- New York Post finds anthrax at its offices in New York.

October 21-22, 2001 -- Washington, D.C. area postal workers are diagnosed with inhalation anthrax after two others had died.

October 31, 2001 -- New York supply clerk Kathy Nguyen dies of inhalation anthrax.

November 21, 2001 -- Connecticut woman, Dottie Lungren, dies of inhalation anthrax.

December 4, 2001 -- Senator Lieberman introduces S. 1764, a comprehensive set of incentives for research on countermeasures for bioterror agents

October 15, 2002 -- First Anniversary of Daschle Office anthrax attack - no Administration proposal submitted to the Congress

October 17, 2002 -- Senators Lieberman and Hatch introduce S. 3148, a refined version of S. 1764

January 29, 2003 -- President Bush in his State of the Union Address calls for Congress to enact Project BioShield; it is modeled on one of twelve key provisions in S. 3148 (guaranteed procurement incentives)

March 19, 2003 -- Senators Lieberman and Hatch introduce S. 666, a further refined version of S. 3148

March 25, 2003 -- Senator Gregg introduces S. 15 -- the text of BioShield as submitted by the President

May 15, 2003 -- H.R. 2122 introduced -- the House version of BioShield

June 10-July 18, 2003 -- Three House Committees report H.R. 2122

July 16, 2003 -- House passes H.R. 2122

September 2, 2003 -- Senator Gregg introduces S. 1504 -- legislation similar to S. 15

October 15, 2003 -- Second Anniversary of the Daschle Office anthrax attack

November 24, 2003 -- President signs Department of Defense Authorization Act, H.R. 1588, Public Law 108-136, which contains a version of BioShield

May 19, 2004 -- Senate passes S. 15 on a vote of 99-0 with an amendment (a complete substitute) based on the House-passed bill. Amendment No. 3178. S. 15 is now pending in the House.

July 14, 2004 -- House passes S. 15 414-2. It goes to the President for his signature.

July 21, 2004 -- President signs BioShield into law as Public Law 108-276

Senators Lieberman and Hatch have announced that they will introduce BioShield II, which will re-propose eleven incentives from S. 1764, S. 3148, and S. 666 that were not included in BioShield.

BIOLOGICAL, CHEMICAL AND RADIOLOGICAL WEAPONS
COUNTERMEASURES RESEARCH ACT OF 2003, S. 666
Senators Lieberman and Hatch

The legislation proposes incentives that will enable biotechnology and pharmaceutical companies to take the initiative -- for good business reasons -- to conduct research to develop countermeasures, including diagnostics, therapeutics, and vaccines, to treat those who might be exposed to or infected by biological, chemical or radiological agents and materials in a terror attack.

The premise of this legislation 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.

For biotechnology companies, incentives for capital formation are needed because most such companies have no approved products or revenue from product sales to fund research. They rely on investors and equity capital markets to fund the research. These companies must focus on research that will lead to product sales and revenue and end their dependence on investor capital. When they are able to form the capital to fund research, biotech companies tend to be innovative and nimble and focused on the intractable diseases for which no effective medical treatments are available. Special research credits for pharmaceutical companies are also needed.

For both biotech and pharmaceutical companies, there is no established or predictable market for these countermeasures. Investors and companies are justifiably reluctant to fund this research, which will present technical challenges similar in complexity to development of effective treatments for AIDS. Investors and companies need assurances that research on countermeasures

has the potential to provide a rate of return commensurate with the risk, complexity and cost of the research, a rate of return comparable to that which may arise from a treatment for cancer, MS, Cystic Fibrosis and other major diseases or from other investments.

President Bush's BioShield initiative is designed to establish and predictable market for these countermeasures. This legislation provides a template for implementation of BioShield and supplements it with additional incentives to ensure that the industry is enthusiastically engaged in this vital research.

The legislation provides tax incentives to enable companies to form capital to conduct the research and tax credits usable by larger companies with tax liability with respect to which to claim the credits. It provides a guaranteed and pre-determined market for the countermeasures and special intellectual property protections to serve as a substitute for a market. Finally, it establishes liability protections for the countermeasures that are developed.

Section 3 of the legislation is drafted as an amendment to the Homeland Security Act of 2002 (HSA)(P.L. 107-296). Section 2 sets forth findings and sections 4-9 are drafted as amendments to other statutes.

1. Setting Research Priorities (Section 1811 of HSA): The Department of Homeland Security sets the countermeasure research priorities in advance. It focuses the priorities on threats for which countermeasures are needed, and with regard to which the incentives make it "more likely" that the private sector will conduct the research to develop countermeasures. It is required to consider the status of existing research, the availability of non-countermeasure markets for the research, and the most effective strategy for ensuring that the research goes forward. The Department then provides information to potential manufacturers of these countermeasures in sufficient detail to permit them to conduct the research and determine when they have developed the needed countermeasure. The Department is responsible for determining when a manufacturer has, in fact, successfully developed the needed countermeasure.

2. Registration of Companies (Section 1812 of HSA): Biotechnology and pharmaceutical companies register with the Department to become eligible for the incentives in the legislation. They are obligated to provide reports to the Department as requested and be open to inspections. The Department certifies which companies are eligible for the incentives.

Once a company is certified as eligible for the incentives, it becomes eligible for the tax incentives for capital formation, and if it successfully develops a countermeasure that meets the specifications of the Department, it becomes eligible for the procurement, patent, and liability provisions.

3. Diagnostics (Sections 1813 and 1814 of HSA): The incentives apply to development of detection systems and diagnostics, as well as drugs, vaccines and other needed countermeasures.

4. Research Tools (Section 1815 of HSA): A company is also eligible for certification for the tax and patent provisions if it seeks to develop a research tool that will make it possible to quickly develop a countermeasure to a previously unknown agent or toxin, or an agent or toxin not targeted by the Department for research.

5. Capital Formation for Countermeasures Research (Section 1821 of HSA; also section 4 of the legislation): The legislation provides that a company seeking to fund research is eligible to elect from among four tax incentives. The companies are eligible to:

(a). Establish an R&D Limited Partnership to conduct the research. The partnership passes through all business deductions and credits to the partners.
(b). Issue 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.
(d). Receive a special tax credit for research conducted at a non-profit and academic research institution.

A company must elect only one of these incentives and, if it elects one of these incentives, it is then not eligible to receive benefits under the Orphan Drug Act. The legislation includes amendments (Section 9 of this legislation) to the Orphan Drug Act championed by Senators Hatch, Kennedy and Jeffords (S. 1341). The amendments make the Credit available from the date of the application for Orphan Drug status, not the date the application is approved as provided under current law.

6. Countermeasure Purchase Fund (Section 1822 of HSA): The legislation provides that a company that successfully develops a countermeasure -- through FDA approval -- is eligible to sell the product to the Federal government at a pre-established price and in a pre-determined amount. The company is given notice of the terms of the sale before it commences the research.

7. Intellectual Property Incentives (Section 1823 of HSA; also section 5 of this legislation): The legislation provides that a company that successfully develops a countermeasure is eligible to elect one of two patent incentives. The two alternatives are as follows:

(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. This alternative is available to any company that successfully develops a countermeasure irrespective of its paid-in capital.
(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. This is included as a capital formation incentive for small biotechnology companies with less than $750 million in paid-in capital, or, at the discretion of the Department of Homeland Security, to any firm that successfully develops a countermeasure.

In addition, a company that successfully develops a countermeasure is eligible for a 10-year period of market exclusivity on the countermeasure.

8. Liability Protections (Section 1824 of HAS; also Section 10 of the legislation): The legislation provides for protections against liability for the company that successfully develops a countermeasure.

9. Accelerated Approval of Countermeasure (Section 1831 of HSA): The countermeasures are considered for approval by the FDA on a "fast track" basis.

10. Special Approval Standards (Section 6 of this legislation: The countermeasures may be approved in the absence of human clinical trails if such trails are impractical or unethical.

11. Limited Antitrust Exemption (Section 7 of this legislation): Companies are granted a limited exemption from the antitrust laws as they seek to expedite research on countermeasures.

12. Biologics Manufacturing Capacity and Efficiency (Section 1832 and 1833 of HSA; and section 8 of this legislation): Special incentives are incorporated to ensure that manufacturing capacity is available for countermeasures.

13. Strengthening of Biomedical Research Infrastructure (Section 1834 and 1835 of HSA): Authorizes appropriations for grants to construct specialized biosafety containment facilities where biological agents can be handled safely without exposing researchers and the public to danger (Section 216). Also reauthorizes a successful NIH-industry partnership challenge grants to promote joint ventures between NIH and its grantees and for-profit biotechnology, pharmaceutical and medical device industries with regard to the development of countermeasures and research tools (Section 217).

14.Annual Report (Section 1841 of HSA): The Department is required to prepare for the Congress an annual report on the implementation of these incentives.

15. International Conference (Section 1842 of HSA): The Department is required to organize an annual international conference on countermeasure research.

Contacts: Chuck Ludlam, chuck_ludlam@lieberman.senate.gov and 202-224-4041 (Senator Lieberman); Bruce Artim, bruce_artim@judiciary.senate.gov and 202-224-5251 (Senator Hatch)

BioPharma vs. Defense Contractor Operating Margins

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 drastically less than the operating margin for non-biodefense research, it is not likely that these companies will choose to undertake biodefense research.

The operating margin for the major defense contractors listed below was 8.5% in 2001 and 9.5% in 2002.

Defense Contractor Operating Margins
2001 2002
Boeing
company 6.7% 7.2%
military 10.8% 11.8%
General Dynamics

company 12.9% 11.4%
marine systems 8.6% 7.9%
info systems 9.3% 11.8%
combat systems 10.8% 11.1%
L-3 Communications 4.4% 9.9%
Lockheed Margin
company 3.7% 8.5%
systems integration 9.3% 9.9%
aeronautical systems 7.8% 6.9%
Northrop Grumman
company 7.4% 8.1%
electronic systems 7.6% 8.1%
ships 1.0% 6.5%
integrated systems 8.6% 10.1%
Ratheon
company 12.0% 11.4%
electronic systems 13.7% 13.5%
C3l systems 10.5% 10.0%
Rockwell Collins
company 16.3% 14.7%
Teledyne
Company 4.9% 5.6%
Average 8.5% 9.6%

The operating margin for the successful biotechnology companies listed below was 31.8% in 2001 and 28% in 2002. This operating margin is 3.74 times and 2.91 times as great for 2001 and 2002 respectively as the operating margin for the defense contractors listed above.

U.S. Biotechnology Operating Margins
2001 2002
Amgen 44.2% 41.8%
Biogen 34.5% 26.3%
Cephalon 25.9%
Chiron 19.5% 24.3%
Genentech 22.7% 24%
Genzyme 22.3% 21.8%
Gilead 17.4%
IDEC 48.1% 52.9%
MedImmune 31.1% 17.2%
Average 31.8% 28.0%

The operating margin for the successful pharmaceutical companies listed below was 29.5% in 2001 and 26.5% in 2002. This operating margin is 3.47 and 2.76 times as great for 2001 and 2002 respectively as the operating margin for the defense contractors listed above.

U.S. Pharma Operating Margins
2001 2002
Bristol-Myers 33.2% 21.9%
Eli Lilly 32.3% 29.5%
Merck 21.0% 19.0%
Pfizer 34.2% 36.1%
Schering Plough 30.0% 27.7%
Wyeth 26.1% 24.5%
Average 29.5% 26.5%

Operating margin is profit before tax. The operating margin for the defense contractors has been adjusted for good will. Operating margin is calculated by dividing a company's operating profit by net sales. It is also known as operating profit margin or net profit margin. Operating profit it typically assessed before taking into account interest and taxes.

Compiled from publicly available information with assistance from Michael King, Banc of America Securities LLC.

Interview--Serguei Popov
Journal of Homeland Security (November 13, 2000)

Serguei Popov is a former scientist in the Russian biological warfare program. After obtaining a degree in biochemistry, he served as a division head in Vector and Obolensk, branches of the Soviet program dedicated to developing genetically enhanced bioweapons. His position allowed him to expand his research into the fields of molecular biology and microbiology. Dr. Popov worked at Vector from 1976 to 1986, then at Obolensk until 1992, when he defected to Britain and later traveled to the United States. He now works for Hadron, Inc., in microbiology and pharmacology.

Homeland Defense: How did you first become involved in the Soviets' biological warfare program?

Serguei Popov: I found work by speaking to Lev Sandakchiev, who later became in charge of Vector Institute. Lev wasn't my friend but I knew him very well. My wife was a student of his at that time, so there was a close connection. Of course, I had no knowledge of what specific programs they had decided to run, but in 1975, Sandakchiev wanted me very much to join his institute. And shortly thereafter I became a scientist for him at Vector.

Homeland Defense: What were some of your earliest projects at Vector?

Serguei Popov: With my background in biochemistry and nucleic acid chemistry, I primarily studied DNA. At that time, it was not a very advanced science, but it was exciting and we tried to create artificial DNA fragments and artificial genes. That was my goal, actually, for the next several years, to make artificial genes. I eventually became the head of a department, with about 50-60 people working with me, half of whom were researchers.

Our approaches were straightforward, using mainly chemical synthesis. It was certainly easier than other available procedures. And chemical synthesis was attractive because it promised to do whatever we wanted. And of course Sandakchiev was interested. That same year, 1976, I became a department head--a department whose whole purpose was to learn how to design artificial genes.

Homeland Defense: Could you describe the different levels of security in your program?

Serguei Popov: Early on, I was already at security level three, but there were at least four levels of security. At level one, the explanation, called "an open legend," was that there was no biological weapons program at all. The work at the institute was completely academic and open. At level two, there was "a closed legend" explaining that there was a strictly defensive weapons program. At the third level, a particular person was provided with a description of some programs there were and what were the true purposes of these programs. But even this wasn't the complete truth. The real truth was at level four, which I viewed only briefly much later on. I read these types of documents on only one occasion.
Level number four described the purpose of specific programs and their interconnections. I read some of them, but I didn't know the whole picture. And I believe that below level four, there was yet another level with a full description of all the bioweapons programs. That was for the government. I didn't have that big picture. I think that Ken Alibek had that big vision. I have just fragments of that vision.

Homeland Defense: When did you realize you were involved in biological weapons production?

Serguei Popov: It happened both gradually and immediately. With a program like Vector, you know something is going on, but no one tells you what you are going to do, or what the precise purpose of your program is. People get involved step by step, in such a way that there is no way back. You sign papers, and you commit yourself.

Homeland Defense: How did the conditions at Vector compare to the working conditions in Biopreparat?

Serguei Popov: There were subtle differences between the Siberian institution of Vector and the other institutions of Biopreparat. Lev Sandakchiev was a pure scientist and had never been involved previously in biological weapons programs. So, the approach of Vector was the scientific approach. In contrast, the people who organized the Obolensk Institute had experience in biological weapons. The whole mentality was different. In Siberia, there was more a sense of freedom, adventure, excitement, and a sense of discovery. The other place, as I understand it, was much more depressing.

Homeland Defense: At that time, did they tell you the United States was involved in offensive biological weapons?

Serguei Popov: Yes, they did. They always did. And there was no way to explore that point of view, even if we believed otherwise. It was an official statement and no one doubted it.

Homeland Defense: Did they also tell you the United States was working on genetically enhanced weapons?

Serguei Popov: That wasn't difficult to believe either. The United States is the biggest country, with some of the best scientists, you know. So I had no doubts.

Homeland Defense: So when did you realize the U.S. was out of the biological warfare program?

Serguei Popov: Not until I came to this country. I knew what was written about the U.S. program. But I had a suspicion that nothing was happening in this country when I visited England in 1979. When I visited England, it didn't take long to pick it up.

Homeland Defense: Dr. Popov, this interview in generally targeted for the benefit of two groups: individuals with strong scientific background, and at the opposite end of the spectrum, policy makers with little background in the sciences but strong interests in the subject matter. But there is likely one question in particular that both sides could agree on in terms of importance. In our discussions with Dr. Alibek, agents like plague, anthrax and smallpox all sounded like very effective weapons.

Serguei Popov: Oh, they are.

Homeland Defense: What then was the purpose of taking this next step, which was really leading-edge science? Why genetic engineering?

Serguei Popov: The answer changed over time. Originally, the Soviet military wanted Vector and Obolensk to produce genetically engineered weapons because they wanted classical agents with new properties like higher pathogenicity and unusual symptoms. And ultimately, we did develop improved classical weapons, with new, unusual properties and resistance to antibiotics.

But it proved to be an illogical way to construct a weapon. There was a belief that new weapons, completely new weapons, without known protection and with new properties, could be superior. The classical agents were there, and they were effective, but initially the military wanted even more effective [ones].

Homeland Defense: Now, Dr. Alibek told us last month about how Biopreparat developed plague that was resistant to our ten most common antibiotics. They couldn't find a strain of plague resistant to ten, so they took one strain, made it resistant to five, and another to another five. Were you just looking for more effective ways to achieve the same result?

Serguei Popov: Not exactly. When we talk about the whole program of genetically engineered weapons, it was a combination of several projects. For example, projects like "Bonfire" were specifically aimed at developing antibiotically resistant strains.
But there was a much bigger program, called "Factor." It was a program to create strains with the ability to produce certain biologically active substances as new pathogenic factors. It was not about an improvement of what was generally known. But the final goal of Factor was to create strains with completely new properties.

Homeland Defense: Did Factor also work with the classical agents?

Serguei Popov: Yes. The initial vision was that the old classical biological weapons would acquire new, unusual properties so that, for example, prophylaxis would be difficult. Project goals included high virulence, high stability, and surprising new outcomes for the disease in order to confuse treatment. To achieve those goals, there were several directions. The first was to express short biologically active peptides. Then there was an attempt to introduce toxin genes into those strains. The toxin genes could be short peptide toxins or they could be proteins.

Homeland Defense: In follow-up, you commented on the plague issue, that somehow there was recent success in achieving the properties. Is that what you're suggesting?

Serguei Popov: Yes. I know at least two examples of plague and smallpox strains which acquired new properties.

Homeland Defense: And what would those properties be?

Serguei Popov: A gene responsible for hemorrhage formation was included in one viral strain and diphtheria toxin gene in another bacterial strain. Later, the Obolensk Institute published their results on anthrax with hemolysin gene. That was the third example. But again, in [the] case of diphtheria toxin, we were more interested in the outcome. The idea was that the vaccine directed against plague would not be effective. When we talked about those problems, there is no clear way to achieve those goals. That's why the programs constantly changed. The final purpose was the same but the way to achieve success varied.

Homeland Defense: For the benefit of the non-scientific audience, could you describe what a peptide basically is?

Serguei Popov: A peptide is a short protein fragment. Peptides are of the same origin and display properties of proteins. But peptides are more direct in their action and properties. They may target specific functions. We have an example of small peptides like endorphins or enkephalins. Those peptides are approximately 30 amino acids long, and it is about 10 to 20 times [fewer] amino acids than in an average protein. The peptides can interact with a receptor, and they could be produced in a biological way. It's difficult to produce morphine or other drugs through genetic means. But endorphin peptides have similar properties. In the case of peptides, you make a very small DNA chain that codes for the peptide, and you introduce that gene into the genome of any agent. That's, in general, all you need.
Small peptides that are neuro-active were capable of changing behavior. Some peptides also created changes of behavior and could have other activities, because they were multifunctional peptides. One example of this was vasopressin, which affects blood pressure. Some peptides were toxins, while others offered a completely new approach for causing autoimmune diseases.

Homeland Defense: What do you think about press reports which suggest it's possible to take the toxin from cobra venom and splice it into strains of influenza?

Serguei Popov: Those are all an exaggeration, but the idea is correct. I would doubt that cobra venom would be good for biological expression. Toxins must meet numerous specific

requirements. But the simplest is that they should be easy to reproduce in biologically active ways. Many toxins are also big molecules, requiring energy and specific biological machinery to build and deliver them to their specific targets. If you consider the simplest toxin, it should be short, it should not be sensitive to the environment, and it should be stable when created inside the body.

Homeland Defense: Did you have any success in creating these?

Serguei Popov: Well, essentially, yes. There are several toxins which are very effective, like peptide toxins from cone snails (conotoxins). However, there were some problems. One of them was that those toxins required two specific cystine bridges. Without those bridges they weren't biologically active, and that was a complication.

Homeland Defense: But you successfully produced those toxins?

Serguei Popov: Finally, yes. The work on inserting them into smallpox virus continued till the program was terminated.

Homeland Defense: Was it your goal to produce the toxins in quantities sufficient by themselves, or was it always part of your plan for one organism to produce the toxins inside the host?

Serguei Popov: The final goal of Factor was to create microorganisms that produce these toxins inside the host. But there was another program that dealt directly with toxins themselves. It was closely linked to Factor because when we studied the action of toxins engineered into microbes, we had to know their behavior, meaning we needed them in control experiments. The goal of genetically engineering the weapons was to create strains of microorganism producing toxins, such as viruses coding for toxins and ultimately producing toxins.

Homeland Defense: Were you successful? You were talking about genetically engineering strains of the classic biological weapons, so that they were more effective, had different properties, and presented themselves in new, challenging ways. But did you ultimately produce an anthrax or smallpox agent with new properties?

Serguei Popov: Yes; for example, plague with diphtheria toxin has been produced. But the whole program was a difficult task. Some approaches proved to be more successful than others. One tactic, immune mimicry, was to induce an immune response against myelin (found in the body's nervous system). Because the cloned myelin protein (or its fragment) would be very close in structure to the body's, host responses against the infection would be directed against the body's own myelin. As a general principle it's been discussed for many years, but it's a very difficult practical task to pull off. Damaged myelin interferes with the transmission from the brain to the peripheral nerves. Most likely its destruction by a microbial agent would induce paralysis and death.
For example: You get the flu, and then you get a complication from the flu. In that case, the immune system, which struggled with flu virus, could target your body as well as flu. When your body tries to heal itself, it actually does the reverse.
In Obolensk, we did extensive experimentation with different bacteria carrying a myelin gene. We finally found that an agent called Legionella created very strong immunological responses.

The myelin peptide it produced was very immunogenic because the immune system was activated by the infectious process. That's what resulted in paralysis and death of infected experimental animals. And what is important as well, a lethal dose was much lower, only a few Legionella cells.

Homeland Defense: Were you able to do that in animal models, like primates?

Serguei Popov: No, just guinea pigs. We were initially ordered to do it, and we did not expect any technical difficulty, but the program had been abruptly stopped at the level of primates.

Homeland Defense: And how long would it take before the target was affected?

Serguei Popov: Essentially, it's two weeks.

Homeland Defense: And there would be no symptoms before that?

Serguei Popov: No, there wouldn't, and there would be no agent in your body. It will be completely clear.

Homeland Defense: Doctor Popov, this sounds like a topic that very few people in the areas of biological warfare and homeland defense have discussed. It also sounds like a very challenging weapon to guard against. Could you offer any additional explanations on this subject?

Serguei Popov: Certainly. In general, there is a basic technique to make a viral or bacterial genome easier to manipulate genetically. First you take a gene of interest and you put it in a suitable biological vehicle, often called a vector. Here the gene can be changed, and new properties can be added. More importantly, the vector could be introduced into a bacterial strain, so that the bacteria will carry it, and will acquire the properties to produce the substance the gene codes for. Usually, the bacterial host is harmless, but it can be pathogenic. The gene product can be pathogenic as well. In the above case of the myelin peptide, [the] immune system eliminates the bacteria that produced it, but the peptide triggers a slow destructive immune response. And you are right when you say people in biodefense have never considered this approach.
Let me provide you with another example of a new bioweapon idea, which was under development when I left Russia. Imagine plague carrying a whole copy of a virus. You would expect that people infected with genetically engineered strains of plague would be treated for plague. But the antibiotic treatment would actually make the patient worse because of the antibiotic-induced release of the virus from its copy. A virus infection on top of a bacterial infection may be a situation you will never be able to properly deal with.

Homeland Defense: So you don't have the virus until you kill the bacteria?

Serguei Popov: No, you don't.

Homeland Defense: In the exercise we did in May, called "Topoff," in Denver, we did the simulation of a plague attack, and they chose plague because treatment, in theory, is simple. You just need to provide people with antibiotics. But in your scenario, it wouldn't matter. No matter

how effective we are at controlling it, the more antibiotics you pass out, the more viruses you release?

Serguei Popov: Exactly. Each disease has completely different symptoms and incubation periods, which means treated people will appear healthy and think they are fine. But the treated people are still sick. They simply don't know it. And a new viral disease can appear after a few days in cases of recombinant plague, or two or three weeks in case of recombinant Legionella. People will experience paralysis, and their central nervous system will cease to function.

Homeland Defense: And how long does it take for this paralysis to take effect?

Serguei Popov: It's difficult to say, but the disease itself in animals is quite fast (a few days).

Homeland Defense: Some of the peptides you've mentioned are extremely novel. But in looking at some of your viral agents, was it more in your interest to create new properties, or to perpetuate existing systems?

Serguei Popov: Initially, the purpose was to bring new properties to existing strains. But the whole program shifted development in the 1980s into new strains. We struggled with the problem of small peptides creating new properties, putting them into active strains. We began to ask ourselves, "Why should we insert peptides into classical strains when we could put them in new strains with new properties, and it could become a weapon even more difficult to deal with or cure?" So the whole plan of the program was shifted to making new virulent strains. In this area, I was relatively successful in making autoimmune peptides effective.

Homeland Defense: Was your specialty in bacterial vectors, or did you look at viral vectors?

Serguei Popov: I studied viral vectors originally. But after I was transferred to the Obolensk Institution, I worked on bacterial vectors as well.

Homeland Defense: You stated earlier that one of the goals of Project Bonfire was vaccine resistance. How much success did your program have in developing a strain of anthrax resistant to vaccinations?

Serguei Popov: I heard a story in 1986 about developing an anthrax resistant strain expressing hemolysin, but [at] that time it wasn't considered a very productive way of doing vaccine resistance against anthrax, and that was in place a long time ago. I did not think they would find anything very exciting about this. Surprisingly, it finally worked.

Homeland Defense: Out of curiosity, was tularemia an interest of your program?

Serguei Popov: Well it was, but it was considered an old workhorse, an old vehicle. In terms of genetic engineering with tularemia, there was little activity.

Homeland Defense: How about mycoplasm?

Serguei Popov: We didn't try that. I know that they looked at it, but that was in a different institute.

Homeland Defense: Did your program share work with allied countries, or was it only with Russian scientists?

Serguei Popov: No, my program only employed Russians. And there was no change in this policy up until 1992, when I left Russia.

Homeland Defense: So you did no work except for biological weapons work?

Serguei Popov: Yes, but it was not easy to distinguish between pure science and military science applications. In a way, everything had military usage. Anything considered "pure science" was questionable. Take an example of a recombinant interferon project I was in charge of at Vector. It was believed to be a potent antiviral drug for troops' protection.

Homeland Defense: How much control did the Soviet Union have over your life? Was your travel restricted?

Serguei Popov: Traveling abroad was completely impossible. I managed it once and that was it. But travel inside the country was restricted in terms of procedures. You had to be back in the lab by certain times. That type of thing took place frequently.

Homeland Defense: When you began this in the 1970s and 1980s, you were involved in what we would call leading-edge technologies. Only Russia, the United States, and maybe a few other countries like the United Kingdom could reasonably succeed in this area. Because of the biotechnology revolution, do you think this type of research is continuing today in other countries like Iran, China, India, or North Korea?

Serguei Popov: I think the answer to your question is: no doubt. But the knowledge is not there, I hope. Creating biological agents is not only technology and procedures. But the most important thing is what to do, and how to achieve success.

Homeland Defense: Do you believe it's possible some of these countries have recruited former colleagues of yours to work for them in this area?

Serguei Popov: Oh, I'm pretty sure they did.

Homeland Defense: And how many people worked in your program at Vector, at your level and with your expertise?
Serguei Popov: It's hard to estimate. I know there were several institutions, with several labs in each. There were probably a few thousand researchers. But at my level, there were maybe several dozen, as of 1992.

Homeland Defense: Russia has ostensibly been opened to travel, but we assume someone with your skills would probably have been discouraged from leaving. Can you tell us about how you came out?

Serguei Popov: Well, of course it wasn't the straight way. When I recognized that everything was collapsing and the KGB was having problems maintaining control, I decided it was a good time to get out. My problem, however, was that I had no money at all, not even to buy food. My only

connection outside Russia was in England. I had visited England once in 1979 and I had some good friends over there in the scientific community. In fact, that's why [the] Soviets didn't let me join the communist party in the Soviet Union.
So I wrote those friends by sending them email and faxes. Finally, they found some money for me to conduct research, but still didn't have money for tickets. At the time, I only had four dollars in my pocket.
But the Royal Society promised to pay me in England. So I negotiated a short-term pass to England, and the KGB agreed to let me go. They may have agreed because they wanted the money that would come from the science I promised them. So they let me go. I just didn't go back.

Homeland Defense: Do you feel like you've been threatened since then? Did they follow you?

Serguei Popov: They followed my wife. When I left my home, I had to leave my family and my children in the Soviet Union for about a year. She knew I was going. But that was the only way to earn money, so that we could purchase their passports.

Homeland Defense: When you left, were you debriefed by British or American intelligence services?

Serguei Popov: Nobody was interested. Not a single person. Only much later, in Dallas, Texas, was I debriefed.

Homeland Defense: So where have you been working and what have you been doing since you left Russia in 1992?

Serguei Popov: Well, first I came to England. The Medical Research Council arranged for me to study molecular biology in Cambridge, and I studied HIV virus for six months there. Then I traveled to Dallas, and I researched microbiology and pharmacology. And today I work for Hadron.

Homeland Defense: So to the best of your knowledge, the genetically engineered agents were not weaponized by the military?

Serguei Popov: That is correct, but with a few exceptions. I think plague with diphtheria toxin was weaponized. That's my impression. The antibiotic-resistant strains of plague and anthrax were also weaponized. But as far as the Factor program is concerned, not very much was weaponized. I also know that hemorrhage gene was introduced into smallpox virus; I don't know the final results.

Homeland Defense: Did you work on the smallpox virus yourself?

Serguei Popov: Yes. But that project belonged primarily to another person. And I don't know if they decided to continue this work.

Homeland Defense: There have been rumors of combining smallpox and Ebola after some fashion. Some have suggested making an agent as contagious as smallpox and as deadly [as] Ebola. Is such a thing possible?

Serguei Popov: This idea could be accomplished on a genetically defined level, or by simply combining both. The physical combination was the subject of discussion. But not everybody liked it because of the difficulties involved.

Homeland Defense: Did you hear about this in Russia or after you came here?

Serguei Popov: From 1986 I heard some rumors on these types of agents. Both bacterial and viral combinations were discussed, but I was not included in these talks. To be honest, I had little interest in this area.

Homeland Defense: You mentioned the development of "subtle agents," using biopeptides and bioregulators. Did Vector also work on similar agents that would affect people from a psychological perspective?

Serguei Popov: Yes, endorphins, enkephalins, and other neuromodulating peptides. It has been discovered that personalities could be adjusted with these agents. For example, you could make people more aggressive. Or you could create feelings of insomnia, where people wanted to sleep, but would never feel tired.

Homeland Defense: In your program, who decided where the work would go? Was it the military, the government, or the scientists?

Serguei Popov: Factor was literally created overnight in a Moscow kitchen by some military officers, sometime around 1978. From that point on, it became an official program, but they always took feedback from scientists. They realized it was the perfect way to make new agents, which could be essentially undetectable, and furthermore could get around the biological weapons treaty. Many of the agents created by Factor would be very dangerous, but they would not be illegal.

Editor's note: The Journal of Homeland Defense disagrees with the Soviet claim that such activity was legal. The Biological and Toxin Weapons Convention prohibits any type of activity (development, production, or stockpiling) regarding the offensive use of biological or toxin weapons. Article I from the convention is provided at the end of the interview for the readers' perusal.

Homeland Defense: You've mentioned quite a few unsettling agents in today's discussion. But we want to be clear on this subject: were any of these agents weaponized in mass quantities?

Serguei Popov: No, they were not. We ceased this work around 1991, after funding was cut.

Homeland Defense: What happened to the research related to these projects?

Serguei Popov: Everything was archived and put into storage, and I believe it is still there.

Homeland Defense: This information sounds sensitive, if not dangerous. Do you know if this data is currently secure?

Serguei Popov: To the best of my knowledge the information is still safe.

Homeland Defense: What about your former colleagues? Do you believe any of this work you've discussed is still going on?

Serguei Popov: Yeah, I'm pretty sure. I don't have any direct evidence. But recently I've begun looking up what my former colleagues have published. All I found were a few lousy, lousy papers. This suggests they are currently working on something they cannot publish. And that's a good indication the program is still functioning.

Homeland Defense: Those papers are just cover stories?

Serguei Popov: Yes. That's all they are allowed to publish.

Homeland Defense: Finally, we should mention that this is your first public interview since you departed the Soviet Union. You said that the U.S. Intelligence Community debriefed you. Were the people who conducted this interview fully qualified to conduct your briefing? Did they have the proper scientific background to fully appreciate the nature of your previous work with the Soviet Union?

Serguei Popov: No, they did not sound like scientists. However, I told them about the directions of my work in the Soviet Union. They were mainly concerned with the issues of possible terrorist attack using bioweapons.