Biodefense: Next Steps
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Testimony

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

Before I begin, I would like to acknowledge the dedication of the Members of this Subcommittee to the improvement of current US biodefense preparedness capabilities. In particular, I would like to thank Acambis's constituent Senator, the Honorable Edward Kennedy, for his continued support of our smallpox vaccine programs, and for his leadership in introducing Project Bioshield together with Senator Gregg, moving it forward until it was signed in July 2004. Senator Gregg, I would also like to applaud your introduction of S3 along with your colleagues, Senate Majority Leader Frist and Senators Sessions, De Wine, Santorum, McConnell, De Mint and Allen. It is with your dedicated leadership that we can ensure the United States—and the world—can be shielded from the ever-present threat of bioterrorism.

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

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

has also supplied ACAM2000 to a number of foreign countries for emergency-use stockpiles.

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

Scientific Progress: Cell-Cultured Smallpox Vaccine

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

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

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

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

As Members of the Subcommittee are well aware, concerns about the lack of countermeasures extend far beyond known bioterrorism agents and covers a long list of infectious diseases. Nature has been the most efficient purveyor of new biological threats, such as pandemic influenza, SARS and West Nile. I would submit that because of the benefits of advanced science, the US government must encourage innovation of new

production methods such as cell-culture to improve domestic preparedness for biodefense and infectious disease.

Ensuring Continued Scientific Progress of Biodefense Countermeasures

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

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

I can say with all certainty that we would not have a partial U.S. stockpile of cell-cultured smallpox vaccines without the hard-work and dedication of our government and partners, particularly during the critical years following 9/11.

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

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

First, it is important that the final dose order be consistent with original plans negotiated between the manufacturer and federal government. In the case of ACAM2000, in initial

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

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

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

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

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

Since it is Acambis' intention to file a Biologics License Application for ACAM2000 in 2005 for FDA licensure, a warm-base program would allow for steady replacement of the older vaccines with ACAM2000. Once the smallpox vaccine stockpile is fully FDA licensed, the government would no longer need to be concerned with informed consent or issuing orders under Bioshield, which would ultimately speed up the process of vaccination in the event of an attack.

Acambis presented a recommendation for warm-based manufacturing to the CDC in December 2004, and is currently awaiting a decision on whether the distribution of fiscal

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

The Need for Stable and Commercially Viable Funding Arrangements

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

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

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

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

A final solicitation to acquire this vaccine for the Strategic National Stockpile is expected in 2005 under Project Bioshield. If the value or size of this solicitation were to be below the 50 to 60 million doses originally projected by the NIH and the Congressional Budget

Office, it may be difficult to dedicate staff and facilities to the project at the cost of pursuing other commercial opportunities, and it would certainly make other manufacturers wary of committing to develop countermeasures to other bioterrorism agents. Most importantly, such a decision would leave a huge segment of the population without access to the vaccine they need.

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

Concluding Remarks

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

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

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