Emergent BioSolutions Inc.
Form 10-K
March 10, 2008

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 10-K

(Mark One)

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2007

OR

O TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the transition period from to

Commission file number: **001-33137**

EMERGENT BIOSOLUTIONS INC.

(Exact Name of Registrant as Specified in Its Charter)

Delaware	**14-1902018**
(State or Other Jurisdiction of Incorporation or Organization)	(IRS Employer Identification No.)

2273 Research Boulevard, Suite 400

Rockville, Maryland	**20850**
(Address of Principal Executive Offices)	(Zip Code)

Registrant s Telephone Number, Including Area Code**(301) 795-1800**

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	Name of Each Exchange on Which Registered
Common stock, $0.001 par value per share	**New York Stock Exchange**
Series A junior participating preferred stock purchase rights	**New York Stock Exchange**

Securities registered pursuant to Section 12(g) of the Act: **None**

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of Securities Act. Yes O No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes O No

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes No O

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See definitions of large accelerated filer, accelerated filer, and smaller reporting company in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer O Accelerated filer Non-accelerated filer O Smaller reporting company O

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes O No

The aggregate market value of voting and non-voting common equity held by non-affiliates of the registrant as of June 29, 2007 was approximately $100,968,000 based on the price at which the common stock was last sold on that date as reported on the New York Stock Exchange.

As of February 29, 2008, the registrant had 29,750,237 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant s definitive proxy statement for its 2008 annual meeting of stockholders scheduled to be held on May 21, 2008, which is expected to be filed with the Securities and Exchange Commission not later than 120 days after the end of the registrant s fiscal year ended December 31, 2007, are incorporated by reference into Part III of this annual report on Form 10-K. With the exception of the portions of the registrant s definitive proxy statement for its 2008 annual meeting of stockholders that are expressly incorporated by reference into this annual report on Form 10-K, such proxy statement shall not be deemed filed as part of this annual report on Form 10-K.

BioThrax® and *spi*-VEC are our trademarks. Each of the other trademarks, trade names or service marks appearing in this annual report on Form 10-K are the property of their respective owners.

EMERGENT BIOSOLUTIONS INC.

ANNUAL REPORT ON FORM 10-K

FOR THE FISCAL YEAR ENDED DECEMBER 31, 2007

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This annual report on Form 10-K and the documents incorporated by reference herein contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 and Section 21E of the Securities Exchange Act of 1934, as amended, that involve substantial risks and uncertainties. All statements, other than statements of historical fact, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words anticipate, believe, estimate, expect, intend, may, plan, predict, project, will, would and similar exp to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

These forward-looking statements include, among other things, statements about:

- our ability to obtain new contracts with the U.S. government for sales of BioThrax® (Anthrax Vaccine Adsorbed), our FDA-approved anthrax vaccine, and our performance under those contracts, including the timing of deliveries;
- our plans for future sales of BioThrax;
- our plans to pursue label expansions and improvements for BioThrax;
- our plans to expand our manufacturing facilities and capabilities;
- the rate and degree of market acceptance and clinical utility of our products;
- our ongoing and planned development programs, preclinical studies and clinical trials;
- our ability to identify and acquire or in-license products and product candidates that satisfy our selection criteria;
- the potential benefits of our existing collaboration agreements and our ability to enter into selective additional collaboration arrangements;
- the timing of and our ability to obtain and maintain regulatory approvals for our product candidates;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our intellectual property portfolio; and
- our estimates regarding expenses, future revenues, capital requirements and needs for additional financing.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this annual report, particularly in the Risk Factors section, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

You should read this annual report, including the documents that we have incorporated by reference herein and filed as exhibits hereto, completely and with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements.

PART I

ITEM 1. BUSINESS

Overview

We are a profitable multinational biopharmaceutical company focused on the development, manufacture and commercialization of immunobiotics, consisting of vaccines and therapeutics that assist the body s immune system to prevent or treat disease. We manufacture and market BioThrax ®, also referred to as anthrax vaccine adsorbed, or AVA, the only vaccine approved by the U.S. Food and Drug Administration, or FDA, for the prevention of anthrax infection. We use internally generated cash flows from the sale of BioThrax to fund the development of a product pipeline that addresses a variety of infectious diseases and other medical conditions.

We develop immunobiotics for use against infectious diseases that have resulted in significant unmet or underserved public health needs and against biological agents that are potential weapons of bioterrorism and biowarfare. In addition to our licensed BioThrax product, we have product candidates in both advanced and earlier stages of development. Our advanced stage product candidates consist of an anthrax immune globulin therapeutic candidate, a typhoid vaccine candidate and a hepatitis B therapeutic vaccine candidate. Our earlier stage programs include botulinum vaccines, group B streptococcus vaccine and chlamydia vaccine candidates.

BioThrax is approved for pre-exposure prevention of anthrax infection by all routes of exposure, including inhalation. We are currently pursuing a label expansion for BioThrax as a post-exposure prophylaxis for anthrax infection in combination with antibiotic treatment, as well as a number of improvements for BioThrax, including an extension of expiry dating, a reduction in the number of required doses, and the addition of a second route of administration.

Revenues from product sales of BioThrax were $169.8 million in 2007, $148.0 million in 2006 and $127.3 million in 2005. The U.S. Department of Defense, or DoD, and the U.S. Department of Health and Human Services, or HHS, have been the principal customers for BioThrax. Since 1998, we have been a party to two procurement contracts for BioThrax with the DoD pursuant to which we have supplied over 10 million doses of BioThrax for immunization of military personnel, and the DoD has vaccinated more than 1.8 million military personnel with more than 7.1 million doses of BioThrax. We are not currently party to a procurement contract with the DoD. Since May 2005, we have supplied over 16 million doses of BioThrax to HHS for inclusion in the strategic national stockpile, or SNS. On September 25, 2007, we entered into a three-year agreement with HHS to supply 18.75 million doses of BioThrax to HHS for placement into the SNS, of which an additional 12.2 million doses remain to be delivered. We believe that in the future the DoD will procure additional doses of BioThrax directly from HHS to satisfy ongoing requirements for its active immunization program, and that these purchases may result in HHS procuring additional doses from us.

Our product candidates in advanced stages of development are:

Anthrax immune globulin therapeutic an intravenous therapeutic antibody product candidate for the treatment of post-symptomatic anthrax infection, which we are developing in part with funding from the National Institute of Allergy and Infectious Diseases of the National Institutes of Health, or NIAID, for which we expect to initiate a pivotal human trial and pivotal animal studies in 2008 and 2009;

Typhoid vaccine a single-dose, drinkable vaccine, for which we have completed a Phase I clinical program with trials in the United States, the United Kingdom and Vietnam, and are conducting a Phase II clinical program, which includes a recently completed clinical trial in Vietnam and planned clinical trials in the United States and in India; and

Hepatitis B therapeutic vaccine a multiple-dose, drinkable therapeutic vaccine for the treatment of chronic carriers of hepatitis B infection, for which we have completed a Phase I clinical trial in the United Kingdom and are conducting a Phase II clinical program.

Our product pipeline also includes the following earlier stage product candidates:

Group B streptococcus vaccine a multiple-dose, injectable vaccine for administration to women of childbearing age for protection of the fetus and newborn babies, for which we have successfully completed a Phase I clinical trial in the United Kingdom and are preparing to initiate a second Phase I clinical trial;

Next generation anthrax vaccine additional anthrax vaccine product candidates that would incorporate one or more advanced characteristics, such as a reduced number of doses, room temperature storage, novel adjuvants, recombinant subunits, an enhanced immune response, longer expiry dating, or a novel delivery method;

Botulinum vaccines two prophylactic vaccine product candidates to protect against illness caused by botulinum toxin which we are developing in collaboration with the United Kingdom Health Protection Agency, or HPA; and

Chlamydia vaccine an injectable vaccine for administration to adolescents designed to prevent illness caused by all clinically relevant strains of *Chlamydia trachomatis*.

We have established collaborations and funding arrangements for some of our product candidates. Our anthrax immune globulin therapeutic candidate is funded in part by NIAID under a development contract valued at up to $9.5 million that NIAID awarded us in the third quarter of 2007 to conduct animal efficacy studies and clinical trials, and under two grants valued at up to $3.8 million in the aggregate that NIAID awarded us in 2006 for non-clinical safety and efficacy studies and clinical trial planning for this product candidate. NIAID also has agreed to fund, manage and conduct a Phase I clinical trial of our group B streptococcus vaccine candidate. The Wellcome Trust provided funding for our Phase I and Phase II clinical trials of our typhoid vaccine candidate in Vietnam. In May 2006, we entered into a license and co-development agreement with Sanofi Pasteur, the vaccines business of Sanofi Aventis, under which we granted Sanofi Pasteur an exclusive, worldwide license

under our proprietary technology to develop and commercialize our Neisseria meningitis B vaccine candidate in exchange for payment to us of upfront and development fees, milestone payments and royalties.

We were incorporated as BioPort Corporation under the laws of Michigan in May 1998. In June 2004, we completed a corporate reorganization in which Emergent BioSolutions Inc., a Delaware corporation formed in December 2003, issued shares of class A common stock to stockholders of BioPort in exchange for an equal number of outstanding shares of common stock of BioPort. As a result of this reorganization, BioPort became our wholly owned subsidiary. We subsequently renamed BioPort as Emergent BioDefense Operations Lansing Inc.

Our Strategy

Our goal is to become a worldwide leader in developing, manufacturing and commercializing immunobiotics. Key elements of our strategy to achieve this goal are:

Focus on core capabilities in product development and manufacturing. We focus our efforts on immunobiotic product development and manufacturing, which we believe are our core capabilities.

Acquire additional late-stage product candidates. We seek to obtain product candidates through acquisitions and licensing arrangements with third parties, with a primary focus on late-stage development programs. This approach enables us to avoid the expense and time entailed in early-stage research activities and, we believe, minimize product development and commercialization risks and may enable us to accelerate product development timelines. Specifically, we are primarily seeking to acquire one or more additional product candidates that are either in Phase III clinical trials or well positioned for entry into Phase III clinical trials in the near term. Additionally, we may announce from time to time the acquisition or license of early stage product candidates or the entry into collaborations to continue to refresh the earlier phases of our product development programs.

Mitigate costs in advancing selected pipeline products by seeking governmental and other third party grants and support. We seek non-dilutive funding arrangements with government agencies and non-governmental organizations, or NGOs, including clinical trial sponsorship, grants and development contracts, to advance the development of our product candidates. For example, the Centers for Disease Control and Prevention, or CDC, is independently conducting a clinical trial to evaluate whether as few as three doses of BioThrax administered over six months, with booster doses up to three years apart, will confer an adequate immune response. In addition, NIAID has completed an independent animal efficacy study of BioThrax in combination with antibiotics as a post-exposure prophylaxis for anthrax infection. NIAID in collaboration with the BioMedical Advanced Research & Development Authority, or BARDA, of HHS also has awarded us funding for animal efficacy studies and clinical trials of our anthrax immune globulin therapeutic candidate. BARDA also has awarded funding of up to $11.5 million to support our post-exposure prophylaxis indication for BioThrax, of which $8.8 million was paid in the fourth quarter of 2007. The Wellcome Trust provided funding for our Phase I and Phase II clinical trials of our typhoid vaccine candidate in Vietnam. In addition, NIAID has agreed to fund, manage and conduct a Phase I clinical trial of our group B streptococcus vaccine candidate. We believe many of our product candidates may be of interest to governments and philanthropic organizations. We plan to continue to encourage government entities and NGO s to continue to conduct studies of, and provide financial support for the development of, our licensed product and product candidates.

Fund product development through internally-generated cashflows. We generate revenues and cash flows from sales of BioThrax. In turn, we use these cash flows to fund our development efforts, which we believe gives us an advantage over many of our competitors that rely primarily on external sources of funds. The revenues we derive from the sale of BioThrax help to insulate us from fluctuations in the capital markets and the uncertainties of development funding decisions by government agencies and NGO s. We are focused on increasing sales of BioThrax to the U.S. government, expanding the market for BioThrax to other customers and pursuing a label expansion and a number of improvements for BioThrax, including an extension of expiry dating, a reduction in the number of required doses and the addition of another route of administration. We seek to strike an appropriate balance between maintaining current profitability and continuing to invest in our product development pipeline, which we believe will maximize long term value.

Leverage internal manufacturing capabilities and infrastructure. Since 1998, we have manufactured BioThrax at our vaccine manufacturing facility Lansing, Michigan. The Lansing manufacturing facility is a multi-building vaccine production campus located on approximately 12.5 acres. To augment our existing manufacturing capabilities, we constructed a new 50,000 square foot manufacturing facility on our Lansing campus. We are currently conducting validation and qualification activities required for regulatory approval. We expect that this new facility will have the potential to reduce our manufacturing costs for BioThrax, while increasing dramatically our capacity to manufacture doses of BioThrax annually. This new facility will also allow us to manufacture other fermentation-based products, including production of our own vaccine candidates, as well as potentially allow us to provide contract manufacturing services for third parties.

Market Opportunity

Vaccines have long been recognized as a safe and cost-effective method for preventing infection caused by various bacteria and viruses. Because of an increased emphasis on preventative medicine in industrialized countries, vaccines are now well recognized as an important part of effective public health management. According to a 2006 report issued by Frost & Sullivan, a market research organization, from 2002 to 2005, annual worldwide vaccine sales increased from $6.7 billion to $9.9 billion, a compound annual growth rate of approximately 14%. In this same report it is estimated that the worldwide sales of vaccines will grow at a compound annual rate of approximately 10.5% from 2005 through 2012. New vaccine technologies, coupled with a greater understanding of how infectious microorganisms, or pathogens, cause disease are leading to the introduction of new vaccine products. Moreover, while existing marketed vaccines generally are designed to prevent infections, new vaccine technologies have also led to a focus on the development of vaccines for therapeutic purposes. Potential therapeutic vaccines extend beyond infectious diseases to cancer, autoimmune diseases and allergies.

Most non-pediatric commercial vaccines are paid for directly by patients or paid for or reimbursed by managed care organizations, other private health plans or public insurers. With respect to certain diseases affecting general public health, particularly in developing countries, public health authorities or NGO s may fund the cost of developing vaccines against these diseases. According to a 2006 report issued by Frost & Sullivan, public purchases of vaccines, including immunization programs and government stockpiles, account for approximately 90% of the total volume of worldwide vaccine sales. Alternatively, private market purchases of vaccines represent only 10% of total worldwide vaccine sales and yet account for approximately 60% of total worldwide vaccine revenues in 2005.

The market for biodefense countermeasures, including vaccines and therapeutics, has grown dramatically as a result of the increased awareness of the threat of global terror activity in the wake of the September 11, 2001 terrorist attacks and the October 2001 anthrax letter attacks. The U.S. government is the principal source of worldwide biodefense spending. Most U.S. government spending on biodefense programs results from development funding awarded by NIAID, BARDA and the DoD, and procurement of countermeasures by HHS, the CDC and the DoD. The U.S. government is now the largest source of development and procurement funding for academic institutions and biotechnology companies conducting biodefense research or developing vaccines and immunotherapies directed at potential agents of bioterror or biowarfare.

The Project BioShield Act, which became law in 2004, authorizes the procurement of countermeasures for biological, chemical, radiological and nuclear attacks for the SNS, which is a national repository of medical assets and countermeasures designed to provide federal, state and local public health agencies with medical supplies needed to treat those affected by terrorist attacks, natural disasters, industrial accidents and other public health emergencies. Project BioShield provided appropriations of $5.6 billion to be expended over ten years. The Pandemic and All-Hazards Preparedness Act, passed in 2006, established BARDA as the agency responsible for awarding procurement contracts for biomedical countermeasures and providing development funding for advanced research and development in the biodefense arena, and supplements the funding available under Project BioShield for radiological, nuclear, chemical and biological countermeasures, and provides funding for infectious disease pandemics. Funding for BARDA is created by annual appropriations by Congress. Congress also appropriates annual funding for the CDC for the procurement of medical assets and countermeasures for the SNS and for NIAID to conduct biodefense research. This appropriation funding supplements amounts available under Project BioShield.

The DoD procures biodefense countermeasures that it administers primarily through the Military Vaccine Agency, or MilVax. MilVax administers various vaccination programs for military personnel, including vaccines for common infectious diseases, such as influenza, and vaccines to protect against specific bioterrorism threats, such as anthrax and smallpox. The level of spending by the DoD for MilVax is a function of the size of the U.S. military and the DoD s protocols with respect to vaccine stockpile management and active immunization. The DoD provides development funding for biodefense vaccines through its Joint Vaccine Acquisition Program, or JVAP. We believe that in the future the DoD will procure additional doses of BioThrax directly from HHS to satisfy ongoing requirements for its active immunization program and that these purchases may result in HHS procuring additional doses from us.

In addition to the U.S. government, we believe that other potential additional markets for the sale of biodefense countermeasures include:

state and local governments, which we expect may be interested in these products to protect emergency responders, such as police, fire and emergency medical personnel;

foreign governments, including both defense and public health agencies;

NGO s and multinational companies, including the U.S. Postal Service and transportation and security companies; and

health care providers, including hospitals and clinics.

Although there have been modest sales to these markets to date, we believe that they may comprise an important growth opportunity for the overall biodefense market in the future.

Scientific Background

The immune system provides protection against pathogens, such as bacteria and viruses, through immune responses that are generated by a type of white blood cell known as lymphocytes. Immune responses that depend on lymphocyte recognition of components of pathogens, called antigens, have two important characteristics. First, these immune responses are specific, which means that lymphocytes recognize particular antigens on pathogens. Second, these immune responses induce memory so that when the antigen is encountered again, the immune response to that antigen is enhanced. Generally, there are two types of specific immune responses: humoral immunity and cell-mediated immunity. Humoral immunity is provided by proteins, known as antibodies or immune globulins, that are produced by lymphocytes. Antibodies are effective in dealing with pathogens before the pathogens enter cells. Cell-mediated immunity is provided by lymphocytes that generally deal with threats from cells that are already infected with pathogens by directly killing infected cells or by interacting with other immune cells to initiate the production of antibodies or activating cells that kill and eliminate infected cells.

A vaccine is normally given to a healthy person as a prophylaxis in order to generate an immune response that will protect against future infection and disease caused by a specific pathogen. Following vaccination, the immune system s memory of antigens presented by a vaccine allows for an immune response to be generated against a pathogen in order to provide protection against disease. A therapeutic vaccine is slightly different in that it acts to strengthen or modify the immune response in patients already infected with bacterial and viral pathogens in order to clear the pathogens from the infected host. Without treatment, such patients can be subject to recurring bouts of the disease.

An immune globulin, also known as a polyclonal antibody, is a therapeutic that provides an immediate protective effect. Immune globulin is normally made by collecting plasma from individuals who have contracted a particular disease or who have been vaccinated against a particular disease and whose plasma contains protective antibodies, known as IgG, generated by a humoral immune response to pathogen exposure or vaccination. These antibodies are isolated by fractionation of the plasma, purified and then administered either intravenously or by intramuscular injection to patients. Because it normally takes several weeks to generate antibodies after vaccination, immune globulins are used in situations in which it is not possible to wait for active immunization to generate the protective immune response.

Products

The following table summarizes key information about our marketed product, BioThrax, and our other advanced and earlier stage product candidates. We use multiple technologies to develop our product candidates, including conventional and recombinant technologies. For each development program, we select and apply the technology that we believe is best suited to address the particular disease based on our evaluation of factors such as safety, efficacy, manufacturing requirements, regulatory pathway and cost. We currently hold all commercial rights to BioThrax and all of our immunobiotic product candidates, other than our recombinant botulinum vaccine, for which HPA has the non-exclusive right to make, use and sell to meet public health requirements in the United Kingdom, and our Neisseria meningitis B vaccine candidate that we are developing in collaboration with Sanofi Pasteur.

Immunobiotic Product or Product Candidate	Prophylactic or Therapeutic	Stage of Development
BioThrax (Anthrax Vaccine Adsorbed)	Pre-exposure prophylactic	FDA approved
	Post-exposure prophylactic*	Post-approval label expansion; animal efficacy and human safety and immunogenicity studies ongoing; BLA supplement planned
Next generation anthrax vaccine*	Pre-exposure prophylactic	Preclinical and Phase I
Anthrax immune globulin*	Therapeutic	Pivotal animal studies and pivotal human trial

		planned for 2008 and 2009
Typhoid vaccine	Prophylactic	Phase II
Hepatitis B therapeutic vaccine	Therapeutic	Phase II
Group B streptococcus vaccine	Prophylactic	Phase I
Botulinum vaccines*	Prophylactic	Preclinical
Chlamydia vaccine	Prophylactic	Preclinical
Neisseria meningitis B vaccine	Prophylactic	Preclinical; commercialization rights out-licensed to Sanofi Pasteur

* *We currently intend to rely on the FDA animal rule in seeking marketing approval for indications or product candidates marked with an asterisk. Under the animal rule, if human efficacy trials are not ethical or feasible, the FDA can approve drugs or biologics used to treat or prevent serious or life threatening conditions caused by exposure to lethal or permanently disabling toxic chemical, biological, radiological or nuclear substances based on human clinical data demonstrating safety and immunogenicity and evidence of efficacy from appropriate animal studies and any additional supporting data. For more information about the FDA animal rule, see Government Regulation Clinical Trials.*

No assessment of the safety or efficacy of our vaccine candidates can be considered definitive until all clinical trials needed to support a submission for marketing approval are completed. The results of our completed preclinical tests and Phase I clinical trials do not ensure that our planned later stage clinical trials for our vaccine candidates will be successful. A failure of one or more of our clinical trials can occur at any stage of testing.

BioThrax (Anthrax Vaccine Adsorbed)

Disease overview. Anthrax is a potentially fatal disease caused by the spore forming bacterium *Bacillus anthracis.* Anthrax bacteria are naturally occurring, and spores are found in soil throughout the world. Anthrax spores can withstand extreme heat, cold and drought for long periods and can survive without nutrients or air for extended periods. Anthrax infections occur if the spores enter the body through a cut, abrasion or open sore, or by ingestion or inhalation of the spores. Once inside the body, anthrax spores germinate into bacteria that then multiply. Anthrax bacteria secrete three proteins: protective antigen, lethal factor and edema factor, which individually are non-toxic but can become highly toxic if allowed to interact on the surface of human or animal cells.

Cutaneous anthrax, although rare in the United States, is the most common type of naturally acquired anthrax. Cutaneous anthrax is typically acquired through contact with contaminated animals and animal products. The fatality rate for untreated cases of cutaneous anthrax is estimated to be approximately 20%.

Inhalational anthrax is the most lethal form of anthrax. We believe that aerosolized anthrax spores are the most likely method to be used in a potential anthrax bioterrorism attack. Inhalational anthrax has been reported to occur from one to 43 days after exposure to aerosolized spores. Initial symptoms of inhalational anthrax are non-specific and may include sore throat, mild fever, cough, malaise, or weakness, lasting up to a few days. After a brief period of improvement, the release of anthrax toxins may cause an abrupt deterioration of the infected person, with the sudden onset of symptoms, including fever, shock and respiratory failure as the lungs fill with fluids. Hemorrhagic meningitis is common. Death often occurs within 24 hours of the onset of advanced respiratory complications. The fatality rate for inhalational anthrax is estimated to be between 45% and 90%, depending on whether aggressive, early treatment is provided.

Market opportunity and current treatments. To date, the principal customer for anthrax countermeasures has been the U.S. government, specifically the DoD and HHS. We believe that federal, state and local governments and allied foreign governments are significant potential customers for anthrax countermeasures.

The only FDA-approved product for pre-exposure prophylaxis of anthrax infection is BioThrax. The only FDA-approved products for post-exposure prophylaxis of anthrax infection are antibiotics, which are typically administered over a 60-day period. Antibiotics are effective against anthrax post-exposure by killing the anthrax bacteria before the bacteria can release anthrax toxins into the body. However, antibiotics are not effective against anthrax toxins once the toxins are present in the body. Nor are antibiotics effective against anthrax spores that are in the body and dormant following exposure. Anthrax spores may remain in the body for extended periods, which can potentially germinate into bacterium following the end of antibiotic treatment and lead to infection. Infection may also occur if patients do not adhere to the prolonged course of antibiotic treatment or are not able to remain on antibiotics for extended periods of time. In addition, antibiotics may not be effective against antibiotic resistant strains of anthrax. Because of these limitations, the CDC recommends administering BioThrax in combination with antibiotics under an investigation new drug application, or IND, with informed consent of the patient as a post-exposure prophylaxis for anthrax

infection as an emergency public health intervention.

Although BioThrax is not currently approved by the FDA for post-exposure prophylaxis, as discussed below, we are actively pursuing a label expansion for this indication. We are also developing an anthrax immune globulin therapeutic product candidate and we recently acquired a monoclonal anthrax antibody product candidate, both of which are deigned for post-exposure use. Several other companies also are developing post-exposure anthrax therapeutic products.

Our total revenues from BioThrax sales were $169.8 million in 2007, $148.0 million in 2006 and $127.3 million in 2005.

Description and benefits of BioThrax. BioThrax is the only FDA-approved vaccine for the prevention of anthrax infection. It is approved by the FDA as a pre-exposure prophylaxis for use in adults who are at high risk of exposure to anthrax spores. BioThrax is manufactured from a sterile culture filtrate, made from a non-virulent strain of *Bacillus anthracis,* and contains no dead or live bacteria. Based on its current product labeling, BioThrax is administered by subcutaneous injection in three initial doses followed by three additional doses, with an annual booster dose recommended thereafter. The three initial doses are given two weeks apart over a thirty-day period followed by three additional doses given at six, 12 and 18 months following the first vaccination. BioThrax includes aluminum hydroxide, or alum, as an adjuvant. BioThrax is not currently approved as a post-exposure prophylaxis. Following the October 2001 anthrax letter attacks, however, the CDC provided BioThrax under an IND protocol for administration on a voluntary basis to Capitol Hill employees and certain others who may have been exposed to anthrax.

The NIH originally approved the manufacture and sale of BioThrax by the Michigan Department of Public Health in 1970. In 1972, responsibility for approving biological products transferred from the NIH to the FDA. Following that transfer of responsibility, the FDA established procedures for reviewing the safety and efficacy of biological products, including BioThrax, that had been previously approved by the NIH. The FDA set out to categorize the products according to evidence of safety and effectiveness and determine if the products should remain approved and on the market. In December 1985, the FDA issued a proposed rule containing a finding that BioThrax was safe and effective. However, the FDA did not finalize that proposed rule pursuant to applicable notice and comment requirements. In December 2005, based on a review of data from the study used to support the original marketing approval of BioThrax and other studies of the use of BioThrax in humans, including studies by the CDC and the DoD, the FDA issued a final order regarding BioThrax. In the final order, the FDA affirmed the approval of BioThrax and found, among other things, that:

- BioThrax is safe and effective;
- the study used to support the original marketing approval of BioThrax constituted a well controlled human efficacy study in which BioThrax was 92.5% effective in preventing inhalational and cutaneous anthrax;
- as reported by the Institute of Medicine, studies in humans and animal models support the conclusion that BioThrax is effective against anthrax strains that are dependent upon the anthrax toxin as a mechanism of virulence by all routes of exposure, including inhalation;
- periodic evaluations of reports in the vaccine adverse event reporting system database maintained by the CDC and the FDA confirm that BioThrax continues to be safe for its intended use; and
- as reported by an independent advisory panel to the FDA, the CDC data suggest that BioThrax is fairly well tolerated with systemic reactions and severe local reactions being relatively rare.

In a study published in 2002, the Institute of Medicine, which is a component of The National Academy of Sciences and provides independent, unbiased, evidence-based advice on matters pertaining to public health, found that BioThrax is an effective vaccine for protection against anthrax, including inhalational anthrax, caused by any known or plausible engineered strains and that no convincing evidence exists that people face an increased risk of experiencing short-term life-threatening or permanently disabling adverse effects from BioThrax or developing any adverse effects from long-term use of BioThrax.

As with any pharmaceutical product, the use of vaccines carries a risk of adverse health effects that must be weighed against the expected health benefit of the product. The adverse reactions that have been associated with the administration of BioThrax are similar to those observed following the administration of other adult vaccines and include local reactions, such as redness, swelling and limitation of motion in the inoculated arm, and systemic reactions, such as headache, fever, chills, nausea and general body aches. In addition, some serious adverse events have been reported to the vaccine adverse event reporting system database maintained by the CDC and the FDA with respect to BioThrax. The report of any such adverse event to the vaccine adverse event reporting system database is not proof that the vaccine caused such an event. These putative serious adverse events, including diabetes, heart attacks, autoimmune diseases, including Guillian Barre syndrome, lupus and multiple sclerosis, lymphoma and death, have not been causally linked to the administration of BioThrax.

BioThrax development activities. We are actively pursuing label expansions and improvements for BioThrax, including the following:

Extend expiry dating. The current FDA-approved expiry dating of BioThrax is three years. In December 2006, based on data generated from our ongoing stability studies, we submitted a supplement to our biologics license application, or BLA, for BioThrax to extend the expiry dating from three years to four years, which, if granted, would allow BioThrax to be stockpiled for a longer period of time. This application is still pending and we continue to discuss with FDA the requirements for approval of this supplement. We are unable to predict whether or when this application might be approved.

Add second route of administration. We have applied to the FDA using interim data from the CDC study to add a second route of administration of BioThrax to include intramuscular injection in addition to subcutaneous injection. We believe that intramuscular injection may result in fewer local reactions than subcutaneous injection. We may be required to wait for full study data to be submitted to the FDA before consideration of our application.

Reduce doses for pre-exposure prophylaxis. We have applied to the FDA to reduce the number of required doses of BioThrax for pre-exposure prophylaxis from six to five, with an annual booster dose thereafter. Our application is based on an analysis of interim data from an ongoing clinical trial being conducted by the CDC to evaluate whether as few as three doses of BioThrax, administered over six months, with booster doses up to three years apart, will confer an adequate immune response. The FDA has requested additional data, some of which may not be available until we receive final data from the CDC dose reduction trial, which we expect at the end of 2008. The FDA may not approve dose reduction based on interim data. If the final data from the CDC dose-reduction trial support a further reduction of doses, we plan to file an additional BLA supplement with FDA for approval of a three-dose regimen, with booster doses thereafter up to three years apart.

Expand label indication to include post-exposure prophylaxis. We plan to seek approval of BioThrax in combination with antibiotic therapy as a post-exposure prophylaxis for anthrax infection. In October 2007, we completed a human clinical trial of BioThrax for the post-exposure indication using the anticipated dosing schedule of three doses of BioThrax given two weeks apart. The purpose of this trial was to collect data that, in combination with data from our non-clinical studies, will be used to design our pivotal human clinical trial for this indication. We are currently conducting non-clinical studies for the post-exposure indication pursuant to the FDA animal rule. In these studies, we are evaluating the effect of a humanized dose of BioThrax in combination with antibiotics compared to antibiotics alone in rabbits exposed by inhalation to anthrax spores. We also plan to conduct one or more pivotal studies in non-human primates. The timing of such studies depends on the development of a non-human primate model by NIAID. In 2005, NIAID completed a proof-of-concept study in which rabbits infected with anthrax were treated with the antibiotic levofloxacin or with levofloxacin in combination with two doses of BioThrax in one of three dose amounts. One of the dose amounts tested was a dilution of BioThrax designed to elicit an immune response that is proportional to the effect of an undiluted dose in humans. This is referred to as a humanized dose. Only 44% of the rabbits treated with antibiotics alone survived, while 100% of the rabbits treated with either humanized doses or undiluted doses of BioThrax in combination with levofloxacin survived. In the trial, there were statistically significant increases in survival rates for rabbits treated with all dose amounts of BioThrax in combination with the antibiotic compared to rabbits treated with levofloxacin alone. These results were consistent with an earlier animal test conducted by the U.S. Army Medical Research Institute of Infectious Diseases, or USAMRIID, involving the administration of BioThrax in combination with an antibiotic to non-human primates infected with anthrax. We believe that the data from our rabbit and non-human primate efficacy studies, together with the human immunogenicity data, if favorable, will be sufficient to support the filing with the FDA of a BLA supplement for marketing approval of BioThrax for the post-exposure indication. In February 2007, the FDA granted Fast Track designation for BioThrax as a post-exposure prophylaxis for anthrax infection. In September 2007, BARDA awarded us up to $11.5 million in development funding for this indication, $8.8 million of which was paid in the fourth quarter of 2007.

Next Generation Anthrax Vaccine

We have established a program to develop additional anthrax vaccine product candidates that would incorporate advanced characteristics, including one or more of the following: reduced number of doses, room temperature storage, enhanced immune response, longer expiry dating, or novel delivery method. We are evaluating candidates based on recombinant protective antigens, or rPA, of *Bacillus anthracis,* as well as a candidate based on *Bacillus anthracis* toxoid technology.

Our most advanced product candidate in this program is based on BioThrax combined with an adjuvant, known as VaxImmune ™ (CPG adjuvant), which we licensed from Coley Pharmaceuticals which was recently acquired by Pfizer, Inc. The DoD s Defense Advanced Research Projects Agency, or DARPA, previously funded a double-blind Phase I clinical trial of BioThrax plus VaxImmune vaccine candidate pursuant to a collaboration among DARPA, Pfizer and us. That trial, which was completed in 2005 and involved 69 healthy volunteers, was designed to evaluate the safety and immunogenicity of this product candidate compared to BioThrax alone and to VaxImmune alone. In this Phase I trial, the product candidate was administered in three doses by intramuscular injection at two week intervals. In this trial, the BioThrax VaxImmune combination vaccine candidate elicited an enhanced immune response. The immunogenicity results from this trial were statistically significant.

The results of a clinical trial are statistically significant if they are unlikely to have occurred by chance. We determined the statistical significance of the trial results based on a widely used, conventional statistical method that establishes the *P* value of the results. Under this method, a *P* value of 0.05 or less represents statistical significance. Immune responses observed in a group of vaccine trial participants can be compared with those observed in other groups of trial participants or with an assumed response rate. Immunogenicity alone does not establish efficacy for purposes of regulatory approval. Immunogenicity data only provide indications of efficacy and are neither required nor sufficient to

enable a product candidate to proceed to Phase II clinical development. Phase I clinical trials are required to establish the safety of a product candidate, not its immunogenicity, before Phase II clinical trials may begin.

The immunogenicity parameters for this trial were the mean peak antibody concentration in trial participants who received the BioThrax Vaximmune combination vaccine candidate as compared to trial participants who received BioThrax alone and the median time to achieve mean peak immune response. In this trial, the mean peak concentration of antibodies to anthrax protective antigen in participants who received the product candidate was approximately 6.3 times higher than in participants who received BioThrax alone. This result was statistically significant, with a *P* value of less than 0.001. Participants who received BioThrax alone achieved a mean peak concentration of antibodies to anthrax protective antigen approximately 42.5 days after first injection. Participants who received the BioThrax VaxImmune combination product candidate achieved this same mean antibody concentration approximately 21 days earlier. This result was statistically significant, with a *P* value of less than 0.001. In this trial, there was a slightly higher frequency of moderate injection site reactions and systemic adverse events in the volunteers who received the product candidate as compared to volunteers who received BioThrax alone or VaxImmune alone. One volunteer withdrew from this trial because of an adverse event. There were no serious adverse events reported that the trial investigators considered related to the product candidate, to BioThrax or to VaxImmune.

Anthrax Immune Globulin

We are developing a human anthrax immune globulin therapeutic product as a treatment for patients who present with symptoms of anthrax disease. We expect that, if approved, this product would be prescribed as a single-dose intravenous infusion either as a monotherapy or in conjunction with an antibiotic. We are developing our anthrax immune globulin therapeutic product candidate using plasma produced by healthy donors who have been immunized with BioThrax. We have engaged Talecris Biotherapeutics, Inc. to fractionate, purify and fill our anthrax immune globulin therapeutic product candidate at its FDA-approved facilities. We have manufactured two full-scale lots of this product candidate under current good manufacturing practices, or cGMP, using a validated and approved process at Talecris. We plan to rely on the FDA s animal rule to support approval of our anthrax immune globulin therapeutic product candidate. We currently are conducting efficacy studies of this product candidate in infected rabbits, and we plan to conduct further efficacy studies in infected non-human primates in 2008 and 2009. In March 2007, we filed an IND for a Phase I clinical trial to evaluate the safety and pharmacokinetics of our anthrax immune globulin therapeutic candidate in healthy human volunteers. We expect to commence this trial in 2008. NIAID has provided us grant funding of up to $13.4 million for a combination of initiatives, including studies designed to assess the tolerability, pharmacokinetics and efficacy of this product candidate in infected rabbits, the development and validation of product assays, and a human clinical trial to evaluate safety and pharmacokinetics. We believe that favorable data from the animal efficacy studies and safety and pharmacokinetic data from the human clinical trial would be sufficient to support an application to the FDA for marketing approval of this product candidate.

Anthrax Monoclonal

In addition to our anthrax immune globulin product candidate, which is a polyclonal antibody therapeutic, we recently acquired a monoclonal antibody therapeutic from AVANIR Pharmaceuticals. This human monoclonal antibody product candidate is being developed as an intravenous treatment for patients who present with symptoms of anthrax disease and is being funded in part with a grant from NIAID to support efficacy testing in non-human primates and the establishment of cGMP manufacturing process.

We believe that anthrax therapeutics would be eligible to be procured by HHS under Project BioShield for inclusion in the SNS prior to receiving marketing approval, provided that the product candidate is deemed to be licensable**.**

Typhoid Vaccine

Disease overview. Typhoid, also known as typhoid fever, is caused by infection with the bacterium *Salmonella enterica (type typhi).* Typhoid is characterized by fever, headache, constipation, malaise, stomach pains, anorexia and myalgia. Severe cases of typhoid can result in confusion, delirium, intestinal perforation and death. Typhoid is transmitted by consuming contaminated food or drinks. Contamination usually results from poor hygiene and sanitation. Typhoid is often endemic in developing countries in which there is limited access to treated water supplies and sanitation.

Prevalence, market opportunity and current treatment. Typhoid fever continues to be a public health problem in many developing countries with an estimated 22 million cases of typhoid occurring per year worldwide, resulting in approximately 200,000 deaths annually. Increasing multi-drug resistance of typhoid reduces effective treatment options, increases treatment costs and results in higher rates of serious complications and deaths. According to the CDC, approximately 400 cases of typhoid are reported annually in the United States, of which approximately 70% are contracted abroad. The CDC recommends that all persons from the United States traveling to developing countries consider receiving a typhoid vaccination, with travelers to Asia, Africa and Latin America deemed to be especially at risk. According to the U.S. Office of Travel and Tourism, over 30 million people travel annually to typhoid endemic areas. This travelers market represents our primary target market. Potential additional markets include U.S. military personnel deployed in regions where typhoid is endemic as well as children and adults living in these areas.

One oral typhoid vaccine and one injectable typhoid vaccine are currently approved for administration in both the United States and Europe and are primarily sold for use in the travelers market. The approved oral typhoid vaccine is available in liquid and capsule formulations. Both formulations require multiple doses to generate a protective immune response. The capsule formulation requires a booster every five years thereafter. The liquid formulation has been reported to provide 77% of recipients in clinical trials with protection three years after vaccination. The approved injectable vaccine requires only a single dose. However, it is not effectively immunogenic in children, requires a booster dose every three years thereafter and was effective in only 55% to 75% of recipients in clinical trials. Both approved vaccines have good safety profiles with relatively few adverse events reported. Antibiotics are used to treat typhoid after infection and usually lead to recovery commencing within four days. Without antibiotic therapy, the CDC estimates that the mortality rate for typhoid could be as high as 20%. Although vaccines are available, the World Health Organization, or WHO, has stated that improved vaccines against typhoid fever are desirable, especially for children 2 years of age and older.

Description and development status. We are developing a live attenuated typhoid vaccine that contains deletions in two genes of the *Salmonella typhi* bacterium designed to eliminate virulence. We have designed our vaccine candidate to be administered in a single drinkable dose prior to travel to countries where typhoid is endemic. We believe that, if approved, the method of administration of our vaccine candidate would provide a competitive advantage compared to both currently approved typhoid vaccines. If we are unable to establish that our typhoid vaccine product candidate can induce a sufficient immune response after one drinkable dose, this competitive advantage will not be realized.

We have completed the following clinical trials of our typhoid vaccine candidate in the United States and Europe:

- An open-label, non-placebo controlled, pilot study conducted in the United Kingdom in nine healthy adult volunteers. The purpose of this study was to evaluate the safety and immunogenicity of our vaccine candidate. In this study, our vaccine candidate was immunogenic, eliciting both cell mediated and humoral immune responses, and well tolerated.
- A double-blind, placebo controlled, single dose escalating Phase I clinical trial conducted in the United States in 60 healthy adult volunteers. The purpose of this trial was to evaluate the safety, tolerability and immunogenicity of three dose levels of our vaccine candidate. In this trial, our vaccine candidate was immunogenic and well tolerated at all dose levels. The immunogenicity parameter for this trial was the proportion of trial participants with an immune response to the product candidate on day seven after dosing or day 28 after dosing. To be considered adequately immunogenic, 50% of the participants receiving a vaccine dose had to satisfy the primary immunogenicity endpoint. We performed analyses on both an intent to treat and a per protocol basis. Intent to treat analysis is based on the participants who receive a dose of vaccine. A per protocol analysis is based on the participants who complete a trial and substantially comply with the trial protocol. In both the intent to treat population and the per protocol population, 100% of the trial participants in the highest dose group and 56% of the participants in the lowest dose group had an immune response on day seven or day 28. The immune response rate for the highest dose group was statistically significantly greater than the immune response rate for the lowest dose group. The *P* value was 0.0068 in the intent to treat population and 0.0073 in the per protocol population.
- An open-label, non-placebo controlled, single dose Phase I clinical trial conducted in the United States in 32 healthy adult volunteers. The purpose of this trial was to evaluate the safety and immunogenicity of two different presentations of the vaccine candidate, one using bottled water and another using tap water. We vaccinated 16 subjects with each presentation. Because one subject who received the tap water presentation of the vaccine candidate was excluded from the trial results due to a lack of post-baseline immunology data, the tap water presentation data reflected data from only 15 subjects. The immunogenicity parameter for this trial was the proportion of trial participants with an immune response to *Salmonella typhi* following administration of a single dose of the vaccine candidate. The immune response rate was 94% for the participants who received the bottled water presentation and 93% for the participants who received the tap water presentation. The response rate for both groups was statistically significantly higher than the assumed response rate of 50%. The *P* value was 0.0005 for the participants who received the bottled water presentation and 0.001 for the participants who received the tap water presentation. Because the two presentations were similarly immunogenic and both were well tolerated by trial participants, we selected the tap water presentation for further development based on its relative convenience.

In these three clinical trials, our typhoid vaccine candidate demonstrated immunogenicity response levels following a single drinkable dose similar to those seen with multiple doses of the currently approved oral vaccine. As a result of these trials, we were able to establish the dose and regimen for our vaccine candidate with a formulation that we believe is appropriate for commercialization and intend to move the development program forward into Phase II safety and immunogenicity trials in the target populations that will be the focus of the Phase III efficacy trials to follow.

We have completed the following clinical trials of our typhoid vaccine candidate in endemic areas:

A single-blind, placebo controlled Phase I clinical trial of our vaccine candidate in Vietnam in 27 healthy adult volunteers using the dose and regimen established in our Phase I clinical trials in the United States. The Wellcome Trust provided funding for the Phase I trial in Vietnam. The purpose of the trial was to evaluate the safety and immunogenicity of the vaccine candidate when administered as a single oral dose in adults living in an endemic area. Based on initial data from this trial, the vaccine candidate met the criterion for immunogenicity, with approximately 68% of subjects who received the vaccine candidate mounting a humoral antibody response. The vaccine candidate was well tolerated by trial participants, with no serious adverse events reported.

A single-blind randomized, placebo controlled, Phase II clinical trial of our vaccine candidate in Vietnam in 151 healthy children between the ages of 5 and 14 years. A total of 101 children received the vaccine candidate and 50 children received placebo. This was our first trial involving a pediatric population. We conducted this trial in collaboration with the Wellcome Trust, Oxford University and the Hospital for Tropical Diseases, Ho Chi Minh City, Vietnam. The Wellcome Trust provided funding for this trial. The purpose of this trial was to evaluate the safety and immunogenicity of the vaccine candidate in children in an endemic area. The immunogenicity parameter for this trial was the percentage of trial participants with an immune response to *Salmonella typhi* following administration of a single oral dose of the vaccine candidate. In this trial, 93% of the children receiving a vaccine dose developed an immune response as measured by increases in *Salmonella typhi* LPS-specific IgG antibody levels, which is suggestive of systemic protective immunity, and 94% of the children receiving a vaccine dose developed an immune response as measured by increase in *Salmonella typhi* LPS-specific IgA antibody levels, which is suggestive of mucosal protective immunity. In the aggregate, 97% of the children receiving a vaccine dose developed an immune response, which was statistically significantly greater than the percentage of children receiving placebo who developed an immune response. The vaccine candidate was well tolerated by trial participants, with no serious adverse events reported.

The remainder of our planned clinical development program for this vaccine candidate consists of the following:

Phase II clinical trial. We plan to conduct a randomized, double-blind, placebo-controlled, dose escalation Phase II clinical trial in the United States in healthy adults to evaluate the immunogenicity, safety and tolerability of our typhoid vaccine at a range of dose levels. Clinical trial supplies for this study were manufactured at a new manufacturing facility under scaled up conditions.

Phase II clinical trial. We plan to conduct a Phase II clinical trial in India in children under five years of age as a step towards conducting a Phase III clinical trial in an area where the incidence of disease is prevalent. The purpose of this Phase II trial is to evaluate the safety and immunogenicity of our vaccine candidate in the target population in preparation for our planned Phase III clinical study.

Disease surveillance study. We plan to conduct a disease surveillance study in India to confirm that a sufficient number of subjects will be included in the Phase III trial. The Wellcome Trust has provided funding for this surveillance study.

Phase III clinical trial. We plan to conduct a single-blind Phase III clinical trial in India, where typhoid is endemic. The purpose of this trial will be to evaluate the efficacy of our vaccine candidate in children who are likely to be exposed to the typhoid bacterium. We expect to undertake the primary analysis of the data from the trial after approximately one year, which, if the results are favorable, we plan to use to support the filing with the FDA of a BLA for marketing approval of our vaccine candidate. We plan to continue to monitor the incidence of typhoid in the trial participants for several years after vaccination.

Tolerability and immunogenicity study. Concurrently with our planned Phase III clinical trial in India, we plan to conduct a Phase III clinical trial in the United States or Europe in healthy volunteers. The purpose of this trial will be to evaluate the safety and immunogenicity of our vaccine candidate to support marketing approval in the United Sates and Europe.

Since typhoid fever in Asia is largely a disease of children, we are conducting our Phase II, and plan to conduct our Phase III, clinical trials in children in endemic areas because there are no agreed immune correlates of efficacy for live attenuated typhoid vaccines, and it is not practicable to demonstrate clinical efficacy in travelers from the United States or Europe due to the prohibitively large number of subjects that would be needed. The currently approved typhoid vaccines relied on similar clinical trials for regulatory approval. We plan to seek additional grant funding for the further development of this product candidate.

Hepatitis B Therapeutic Vaccine

Disease overview. Hepatitis B is a highly infectious virus transmitted from person to person by contact with blood and bodily fluids. Most hepatitis B infections in adults result in acute hepatitis, with the immune system eventually clearing the infection. However, in approximately

8% to 10% of infected adults and a much larger proportion of infected children, the immune system fails to clear the virus, resulting in immune tolerance of the virus and chronic infection. In addition, pregnant women suffering from hepatitis B can pass the infection on to their babies during childbirth. Babies born infected rarely clear the infection, with over 90% becoming chronically infected. According to the WHO, as many as 40% of people with chronic hepatitis B infection develop serious liver disease, including cirrhosis and liver cancer.

Prevalence, market opportunity and current treatment. Chronic infection with the hepatitis B virus is a global problem, with an estimated 350 million chronically infected individuals worldwide. The WHO estimates that approximately one million people per year worldwide die from complications of hepatitis B infection. Infection rates are highest in the developing world, posing an infection risk to travelers from industrialized countries. Infection is less common in the United States and Europe. In the United States, there are an estimated 1.2 million people with chronic hepatitis B infection, resulting in approximately 4,000 to 5,000 deaths annually.

Prophylactic vaccines based on recombinant protein subunit preparations are effective in preventing hepatitis B infection. Childhood vaccination with these vaccines is common in industrialized countries and in some of the developing world. Childhood immunization programs have reduced the number of carriers of chronic hepatitis B infection by up to 90% in parts of the world where hepatitis B is most common. In the United States, infection rates for acute hepatitis B have decreased by approximately 77% over the past 20 years. However, these existing vaccines have not proven to be effective in treating people with chronic hepatitis B infection. As a result, there remain a large number of people who are chronically infected with hepatitis B and require treatment to prevent the development of liver disease and to reduce the risk of transmitting the infection to others.

There is no vaccine currently on the market that is licensed as a therapeutic treatment for chronic hepatitis B infection. Currently available therapies for this patient population consist mainly of antiviral drugs and immunotherapies, such as interferons. However, these treatments are subject to a number of shortcomings. Both of these treatments can only be used in a subset of patients, and their efficacy is limited. In addition, the use of antiviral drugs may lead to the development of resistant forms of the virus, and interferons have side effects that reduce patient compliance.

Description and development status. We are developing a live attenuated therapeutic vaccine for treatment of patients with chronic hepatitis B infection. We have designed our vaccine candidate to be administered in multiple drinkable doses over several months. It may require further booster doses. Because chronic carriers have weak cellular immune responses to the hepatitis B virus, they cannot clear the virus. Our vaccine candidate is intended to redirect the immune system to make strong cellular responses to a hepatitis B antigen known as the hepatitis B core protein in chronic carriers, which we believe will lead to a suppression of viral replication and associated liver damage.

Our vaccine candidate uses our proprietary *spi*-VEC (attenuated salmonella vaccine vector) oral delivery system technology to deliver the hepatitis B core antigen to the human immune system. s*pi*-VEC is based on our live attenuated typhoid vaccine and employs recombinant technology to insert the gene for hepatitis B core into the live attenuated *Salmonella* bacteria. The bacteria produce the antigen once inside the patient. Because we are relying on recombinant technology to insert the gene for hepatitis B core into a vector delivery system, we do not need to separately purify the hepatitis B core antigen.

We have completed a program of pharmacology and toxicity studies of our hepatitis B therapeutic vaccine candidate in animals. In mice that were administered our vaccine candidate, the hepatitis B core antigen was produced and immune responses were elicited against the antigen. In separate toxicity studies also conducted in mice, our vaccine candidate was non-toxic.

In February 2004, we completed an open-label, dose escalating Phase I clinical trial of our vaccine candidate in the United Kingdom in 30 healthy adult volunteers. The purpose of this trial was to evaluate the safety and immunogenicity of two dose levels of our vaccine candidate. In this trial, we administered the two doses of vaccine over a period of approximately two months. The primary immunogenicity parameter for this trial was the proportion of trial participants with an immune response to the product candidate on day 28 after dosing or day 84 after dosing. In this trial, 50% of the participants in the low dose group and 40% of the participants in the high dose group demonstrated an immune response on day 28 or day 84. The results in the low dose group reflect a confidence interval of 19.0% to 81.0%. The results in the high dose group reflect a confidence interval of 18.5% to 61.5%. These confidence intervals indicate a 95% likelihood that the true value is within the range specified. The secondary immunogenicity endpoint for this trial was the proportion of participants who demonstrated the type of immune response known to be important in promoting clearance of the hepatitis B virus at any point during the trial. In this trial, 100% of the participants in the high dose group and 90% of the participants in the low dose group demonstrated such a response. We did not conduct a statistical analysis of the results from the secondary immunogenicity endpoint. The vaccine candidate was well tolerated by trial participants, with no serious adverse events

reported.

In the fourth quarter of 2006, we initiated a Phase II clinical trial of our vaccine candidate in trial participants chronically infected with the hepatitis B virus in the United Kingdom. The protocol provides for a placebo controlled, randomized, dose escalating study to be conducted in 45 chronic carriers of hepatitis B. We subsequently expanded this trial to Serbia to increase the rate of participant recruitment. If necessary, we may expand the trial to additional sites around the world to accelerate subject recruitment. The primary purpose of this trial is to evaluate the safety and tolerability of six monthly doses of our vaccine candidate.

The secondary purpose is to investigate whether the vaccine candidate can reduce the hepatitis B viral DNA load, a recognized surrogate endpoint for treatment of hepatitis B using current therapeutics. If the results of this Phase II clinical trial are favorable, we expect to submit an IND to the FDA to conduct one or more clinical trials of this vaccine candidate in the United States as may be appropriate to support approval of the product in the United States as well as in Europe. The FDA IND must become effective before we can conduct any clinical trials in the United States.

Group B Streptococcus Vaccine

Disease overview. Group B streptococcus is a bacterium that causes illness in newborn babies, pregnant women, the elderly and adults with other illnesses, such as diabetes or liver disease. Group B streptococcus is the most common cause of sepsis and meningitis in newborns in the developed world and is a frequent cause of pneumonia in newborns. It affects more babies than any other newborn health problem. Group B streptococcus bacteria can cause bladder and womb infections in pregnant women that in turn lead to infection of the fetus and premature delivery and stillbirth. In pregnant women carrying the group B streptococcus bacteria, the baby may become infected either before or during birth.

In the United States, approximately half of all neonatal group B streptococcus infections occur in newborns less than seven days old and are categorized as early onset disease. Infections in babies between seven days and three months old are categorized as late onset disease. Early onset disease is often associated with complicated or premature deliveries and usually results in pneumonia and the blood infection septicemia in the baby. It is also associated with meningitis. Approximately 5% of babies with early onset disease die. A high number of survivors of early onset disease are left with significant permanent disabilities, including sight or hearing loss and mental retardation. The majority of late onset cases occur in the first month of life. Late onset disease usually results in meningitis. Up to 5% of babies with late onset disease die. A high number of survivors of late onset disease are left with permanent disabilities, with up to one-third suffering long-term mental or physical handicaps. Group B streptococcus infections in the elderly cause blood infections, skin or soft tissue infections and pneumonia.

Prevalence, market opportunity and current treatment. Concern about the number of group B streptococcus neonatal infections prompted the CDC to recommend routine screening of pregnant women for group B streptococcus bacteria and preventative antibiotic treatment at the time of labor for women found to be infected. In the absence of antibiotic treatment, the CDC estimates that the risk is one in 200 of delivering a baby with group B streptococcus infection. While the level of group B streptococcus disease decreased in the United States from 1.7 cases per 1,000 live births in 1993 to 0.4 cases per 1,000 live births in 2002, the CDC projects that there are approximately 2,750 neonatal infections each year in the United States. In a study of 338 of these cases of neonatal infections, the death rate was approximately 6%. The NIH has identified prevention of group B streptococcus infection in newborns as a major vaccine objective. We expect the target market for our vaccine candidate to be women of childbearing age.

Approximately 10% to 30% of women are found to be carrying the bacterium as a normal component of the vaginal microflora. The existing method of prevention of group B streptococcus infection in neonates is the targeted administration of intravenous antibiotics to women during labor. However, this approach is invasive and only partially effective. In addition, antibiotics create the risk of possible adverse reactions and may lead to the development of antibiotic resistant strains of the bacteria. Direct vaccination of newborns is not effective because their immune systems are too immature to respond effectively to the vaccine. Antibiotics are used to treat babies after infection.

Approximately 17,500 cases of group B streptococcus infection occur each year in the U.S. population over one year of age, with most occurring in those over age 50. According to the CDC, the average death rates for invasive infections are approximately 8% to 10% for adults 18 to 64 years of age and 15% to 25% for adults 65 years of age and over. Antibiotics are used to treat infected individuals.

Description and development status. We are developing a recombinant protein subunit group B streptococcus vaccine initially for administration to women of childbearing age for protection of the fetus and newborn babies. We are designing our vaccine candidate to be administered by injection with an alum adjuvant in a three-dose regimen. We expect that a booster dose may also be required. We anticipate that the vaccine will elicit an antibody response resulting in the production of antibody in the mother, which may then cross the placenta to protect the fetus and the newborn baby by passive immunity.

We have identified several novel surface associated proteins and are working on the development of two of these proteins as components of our vaccine candidate. We believe that a combination of proteins will be required to provide effective protection. We have conducted preclinical studies in which we evaluated the safety and immunogenicity of these proteins. Based on the results of these preclinical studies, we have initiated a clinical development program. We have completed an open-label, dose escalating Phase I clinical trial of the first protein component of our vaccine candidate in the United Kingdom in 47 healthy adult volunteers. The purpose of this trial was to evaluate the safety and immunogenicity of this protein as an individual recombinant protein. The protein was administered with alum as an adjuvant and tested at four different dose levels. Subjects received two doses of vaccine given 28 days apart.

In this trial, the protein was immunogenic at all dose levels tested. We performed analyses on both intent to treat and a per protocol basis. In both the intent to treat population and the per protocol population, the immune response rate was 83% at the lowest dose tested and 100% at the highest dose tested. The response rate for both the highest dose group and the lowest dose group was statistically significantly higher than the assumed response rate of 50%. For the lowest dose group, the *P* value was 0.0386 in both the intent to treat population and the per protocol population. For the highest dose group, the *P* value was 0.0039 in the intent to treat population and 0.0078 in the per protocol population. The vaccine candidate was well tolerated by trial participants at all dose levels tested, with no serious adverse event s reported. None of the subjects withdrew due to an adverse event.

In the fourth quarter of 2006, we entered in to a clinical trial agreement with NIAID under which NIAID has agreed to fund, manage and conduct a Phase I clinical trial of our group B streptococcus vaccine product candidate. In the proposed study, NIAID would test the same recombinant subunit antigen we evaluated in our Phase I trial in the United Kingdom alone and in combination with a second recombinant subunit antigen. The second recombinant subunit antigen would also be tested separately. The trial is to be conducted at a NIAID clinical research site, with NIAID serving as the IND sponsor. An IND must become effective before the clinical trial may begin.

Botulinum Vaccines

Disease overview. Botulism is a frequently fatal disease caused by botulinum toxins produced by the bacterium *Clostridium botulinum.* *Clostridium botulinum* is widely distributed in soil and aquatic environments throughout the world. Botulinum bacteria produce seven distinct serotypes, each of which elicits a distinct antibody response. Naturally occurring outbreaks of botulism in humans have been reported from exposure to four of the seven serotypes: A, B, E and F. Botulism normally occurs when an individual consumes contaminated food containing botulinum toxin. Once consumed, the toxin rapidly attacks nerve cells, resulting in paralysis of peripheral muscles, including the muscles involved in respiration. Botulism can also be contracted if botulinum bacteria contaminate wounds or colonize in the intestine of infants, which is referred to as infant botulism. Botulinum toxins are among the most potent and dangerous of potential biological weapons. Exposure to very small quantities of botulinum toxin can cause the rapid onset of life threatening paralytic disease syndrome. It has been estimated that a single gram of toxin evenly dispersed and inhaled could kill more than one million people.

Prevalence, market opportunity and current treatment. As with anthrax countermeasures, we believe that the U.S. government and foreign, state and local governments will be the principal potential customers for botulinum countermeasures, including both vaccines and therapeutics. Because botulinum toxin is stable when purified and extremely potent when administered in very small quantities, it has the potential to be used as a biological weapon, either through deliberate contamination of food supply or drinking water or as an aerosol.

Currently, there is no FDA-approved botulinum vaccine on the market, although the DoD has provided development funding to various competitors of ours for the development of a recombinant botulinum vaccine that addresses two of the seven serotypes of botulinum neurotoxin. These two botulinum serotypes, A and B, are responsible for approximately 85% of all cases of botulism. Because of the rapid onset of symptoms following infection with the botulinum toxin, prophylactic vaccines, which take several weeks to create an effective protective immune response, are not useful as post-exposure treatments for botulism. In addition, antibiotics are not effective post-exposure treatments since they work by killing the botulinum bacteria that produce the toxin, but do not act directly against the botulinum toxin. Currently, the only FDA-approved treatment for botulism is a human botulinum IG product for the treatment of infant botulism caused by type A or type B *Clostridium botulinum.* The supply of this product is limited. The product was derived from plasma taken from individuals who had been vaccinated with an experimental pentavalent botulinum toxoid vaccine that is no longer in production. In addition, the CDC manages a supply of experimental botulinum IG derived from equine plasma. However, the experimental equine IG is subject to important shortcomings. First, because the human body recognizes the equine IG as a foreign substance, its efficacy may be limited. In addition, the antibody immune response against the equine IG can lead to potential severe side effects, including anaphylactic shock, if the equine IG is administered more than once. To screen for sensitivity to the equine IG, patients are given small challenge doses of the equine IG before receiving a full dose. HHS has awarded a development and supply contract to a competitor of ours for development and supply of a botulinum IG derived from equine plasma that addresses five of the seven serotypes of botulinum neurotoxin.

Description and development status. We are developing two vaccine candidates to protect against illness caused by botulinum toxin. The first is a recombinant protein subunit trivalent botulinum vaccine for protection against botulinum serotypes A, B and E in collaboration with HPA. We hold an exclusive license from HPA to the recombinant technology that we are using in the development of our vaccine candidate. HPA is also providing us with process development and toxicology expertise, access to its facilities and specialized manufacturing capabilities. We are designing this vaccine candidate to be administered by intramuscular injection with an alum adjuvant in a three-dose regimen. Our recombinant vaccine candidate is based on a fragment of the botulinum toxin that we have selected as an antigen because we believe it to be non-toxic and immunogenic.

We are producing this recombinant antigen in an *E. coli* expression system. We believe that our technology will allow us to develop a stable product with possible cross-protection against a range of toxin subtypes and ease of formulation into a multivalent vaccine. We have established a small scale production process for botulinum serotypes A, B, and E and have conducted proof-of-concept studies of this vaccine candidate in mice for all three of these serotypes. In these studies, the vaccine elicited antibodies and provided protection against challenge with the botulinum toxin. We anticipate that the manufacture of our recombinant vaccine in a cGMP facility will not require the high level of containment that is required for the production of conventional, non-recombinant toxoid vaccines that involve cultivation of the disease-causing organism.

Our second vaccine candidate is also a trivalent botulinum toxoid vaccine using a combination of botulinum serotypes A, B and E. Initially our candidate was developed using botulinum serotype B derived from the starting material from a pentavalent botulinum toxoid vaccine developed by the Michigan Department of Public Health and serotype A from HPA. We are designing this vaccine to be administered by injection with an alum adjuvant. We anticipate that several doses will be needed to elicit a strong immune response. We are performing development activities at existing HPA facilities, which we expect may expedite production of clinical material for the vaccine. HPA is also providing us with process development and specialized manufacturing capabilities for the vaccine. We have completed a proof-of-concept study of this vaccine candidate in mice, which confirmed the suitability of the vaccine for further development. Should we recieve U.S. government funding, we plan to file an IND to initiate a Phase I clinical trial to evaluate the safety of this vaccine candidate in healthy volunteers. Our regulatory plan also includes reliance on safety and immunogenicity data from the pentavalent botulinum toxoid vaccine previously manufactured by the State of Michigan, including the results of a Phase II safety and immunogenicity clinical trial conducted by the DoD from July 1998 to May 2000, animal efficacy data and use of the pentavalent vaccine by the CDC in immunizing at risk laboratory personnel.

In addition to our botulinum vaccine programs, we are developing a human botulinum immune globulin candidate in collaboration with HPA as an intravenous therapeutic for symptomatic botulinum exposure. We believe that botulinum immune globulin has the potential to provide immediate protection from the effects of botulinum toxin.

We plan to rely on the FDA animal rule in connection with the development of our botulinum-related product candidates. We have applied for U.S. government funding to support the further development of our botulinum-related product candidates. We will continue to assess, and may alter, our future development plans for these products based on the U.S. government s interest in providing development funding for, and procuring, botulinum countermeasures.

Chlamydia Vaccine

Disease overview. Chlamydia is the most prevalent sexually transmitted bacterial disease in the world. It is caused by infection with the bacterium *Chlamydia trachomatis. Chlamydia trachomatis* can cause urogenital disorders such as uritheritis, cervicitis, pelvic inflammatory disease, ectopic pregnancy and infertility among females and is the leading cause of non-gonococcal uritheritis and epidemiditis in males. *Chlamydia trachomatis* also causes the ocular disease trachoma, which is a form of vesicular conjunctivitis. Trachoma is the leading cause of preventable blindness worldwide.

Prevalence, market opportunity and current treatment. The WHO estimates that approximately 92 million new cases of *Chlamydia trachomatis* infection occur annually worldwide, of which approximately four million occur in North America. *Chlamydia trachomatis* infections are the most commonly reported notifiable disease in the United States, with an estimated 2.8 million Americans becoming infected with *Chlamydia trachomatis* each year. Epidemiological studies indicate that in the United States *Chlamydia trachomatis* infections are most prevalent among young sexually active individuals between the ages of 15 to 24. There is no vaccine currently on the market for *Chlamydia trachomatis.* However, screening tests and effective antibiotic treatments have been effective at containing *Chlamydia trachomatis* in the United States and Europe. Although *Chlamydia trachomatis* infection can be treated with antibiotics, control measures based on antimicrobial treatment alone are difficult due to the incidence of infection, the percentage of asymptomatic infections and deficiencies in diagnosis.

Description and development status. We are developing a recombinant protein subunit chlamydia vaccine for all clinically relevant strains of *Chlamydia trachomatis,* including strains that cause ocular disease. We are designing our vaccine candidate to be administered by injection with a novel adjuvant in a three-dose regimen. We are currently evaluating in-license opportunities for the adjuvant. We have cloned our vaccine candidate and produced it in *E. coli.* In studies in mice, our vaccine candidate protected against both upper reproductive tract disease and lower reproductive tract infection induced by *Chlamydia trachomatis.* In addition, the fertility of mice immunized with our vaccine candidate was equivalent to that observed in healthy animals.

Meningitis B Vaccine

Disease overview. Meningococcal disease is a life threatening condition caused by infection with the bacterium *Neisseria meningitidis. Neisseria meningitidis* is classified into 12 groups based on differences in the surface coating of the bacterium that elicit distinct immune responses. According to the WHO, group B is the most common cause of endemic meningitis in industrialized countries, accounting for 30% to 40% of cases in North America and 30% to 80% of cases in Europe.

Meningococcal disease has a fatality rate of approximately 10%. The infection can develop very rapidly and cause death within 24 hours of the symptoms first becoming apparent. Children from six months to two years of age are at the highest risk of group B meningococcal infection, with teenagers also at enhanced risk.

Prevalence, market opportunity and current treatment. The WHO estimates that approximately 1.2 million cases of bacterial meningitis occur annually worldwide, resulting in approximately 135,000 deaths. The WHO estimates that approximately 500,000 of these cases and 50,000 of these deaths are caused by the bacterium *Neisseria meningitidis.* In the United States, 2,333 cases of meningococcal disease were reported in 2001, with approximately one-third due to group B. In 2003, 1,756 cases of meningococcal disease were reported in the United States. Currently, there is no meningitis vaccine on the market that is protective against group B meningococcal infection. Current meningitis B treatments include antibiotics and clinical support. The rapid progression of the infection means that antibiotic therapy can be ineffective in preventing serious morbidity and mortality.

Description and development status. We are developing a recombinant protein subunit meningitis B vaccine for babies, children and adolescents. We are designing our vaccine candidate to be administered by injection with an alum adjuvant in a two-dose regimen for children under age five and a single-dose regimen for children over age five. We do not expect that a booster dose will be required. We anticipate that the vaccine will consist of two or three protein antigens. We are currently evaluating a pool of more than 40 protein candidates in a number of preclinical studies. We are producing recombinant proteins in *E. coli.* We have entered into a collaboration agreement with Sanofi Pasteur for this vaccine candidate.

Collaboration. In May 2006, we entered into a license and co-development agreement effective April 1, 2006 with Sanofi Pasteur, the vaccines business of Sanofi Aventis, pursuant to which we granted Sanofi Pasteur an exclusive, worldwide license to develop and commercialize a meningitis vaccine that contains program antigens evaluated and selected under the agreement. We retain the right and obligation to conduct development activities through Phase I clinical trials. Under specified circumstances, we also retain the right to exploit antigens that have been terminated from development under the agreement on an exclusive basis and other specified antigens on a co-exclusive basis. Sanofi Pasteur has agreed to use commercially reasonable efforts to develop and commercialize a meningitis B vaccine in the United States, the European Union and other major market countries.

A steering committee made up of an equal number of representatives from us and Sanofi Pasteur oversees all development and commercialization activities under the agreement. The steering committee has the authority to make strategic decisions by unanimous vote relating to the development of a meningitis vaccine. Sanofi Pasteur has ultimate decision-making authority over matters that are not resolved at the steering committee and executive officer levels, but does not have the unilateral authority to amend the agreement or the development plan in a manner that would alter our rights or obligations. In addition, Sanofi Pasteur has the right to make all strategic decisions relating to the development of any combination product and has sole discretion over the commercialization of any meningitis vaccine developed under the agreement.

Under the agreement, Sanofi Pasteur paid us an initial fee of 3 million. In addition, Sanofi Pasteur has agreed to pay all expenses incurred by us under the development program, and we have received approximately 7.4 million since the inception of this arrangement. We are also eligible to receive payments of up to a maximum of 73 million upon the achievement of specified research, development and commercialization milestones. Sanofi Pasteur has agreed to pay royalties to us based on net sales by Sanofi Pasteur, its affiliates and sublicensees of licensed products from the collaboration, including specified minimum royalties with respect to sales of any combination product. In addition, Sanofi Pasteur has agreed to pay us a portion of specified sublicense income received by Sanofi Pasteur or its affiliates.

The term of the agreement ends, on a country-by-country basis, upon the later of ten years from first commercial sale or the expiration of the last-to-expire patent covering a licensed product in such country. Sanofi Pasteur may terminate the agreement for convenience upon six months prior written notice. Sanofi Pasteur also may terminate the agreement upon any change of control involving us or as a result of our uncured material breach of the agreement or bankruptcy.

Manufacturing

We conduct our primary vaccine manufacturing operations at a multi-building campus on approximately 12.5 acres in Lansing, Michigan. To augment our existing manufacturing capabilities, we have constructed a new 50,000 square foot manufacturing facility on our Lansing campus. We substantially completed construction of this facility in 2006, and are currently conducting validation and qualification activities required for regulatory approval. This new facility is a large scale manufacturing plant that we can use to produce multiple fermentation based vaccine products, subject to complying with appropriate change-over procedures.

We also own two buildings in Frederick, Maryland that are available to support our future manufacturing requirements. We are also performing initial engineering designs and preliminary utility build out of one of these buildings. We may elect to lease all or a substantial portion of, or sell, one of these facilities to third parties.

We manufacture BioThrax at our facilities in Lansing, Michigan using well established vaccine manufacturing procedures. We currently rely on contract manufacturers and other third parties to manufacture the supplies for our other vaccine and therapeutic product candidates we require for our preclinical studies and clinical trials. We typically acquire these supplies on a purchase order basis. We anticipate that we may use our existing plant facilities in Michigan, including our recently commissioned pilot plant and, when completed and approved, our planned new plant facilities in Michigan to support both continued process development and the manufacture of clinical supplies of our product candidates. However, we also expect that we will continue to use third parties for production of preclinical and clinical supplies of some of our product candidates. We believe that manufacturing our products and product candidates independently will provide us cost savings and greater control over the manufacturing and regulatory approval and oversight processes accelerate product development timelines and allow us to expand our base of manufacturing know-how that we can then apply to the development and manufacture of future product candidates.

Hollister-Stier Laboratories LLC performs the contract filling operation for BioThrax vials at its FDA-approved facility located in Spokane, Washington. Hollister-Stier has agreed to meet all of our firm purchase orders for contract filling of BioThrax based on a good faith annual estimate that we provide prior to each calendar year. In addition, Hollister-Stier has agreed to accommodate fill requests in excess of our annual estimate, subject to its available production capacity. Our contract with Hollister-Stier expires December 31, 2010.

Talecris Biotherapeutics has agreed to perform plasma fractionation and purification and contract filling of our anthrax immune globulin therapeutic candidate at its FDA-approved facilities located in Melville, New York and Clayton, North Carolina. Subject to limited exceptions, we have agreed to obtain all manufacturing requirements for our anthrax immune globulin therapeutic candidate exclusively from Talecris. While our agreement with Talecris remains in effect, Talecris has agreed not to market, sell or acquire any competing product that contains anthrax immune globulin as an active ingredient. Talecris has agreed to perform plasma fractionation and purification and contract filling for the manufacture of our anthrax immune globulin therapeutic candidate for preclinical or animal studies, for clinical use or for non-clinical testing required for clinical trials and for commercial sale. We have agreed to pay Talecris royalties on net sales on a country-by-country basis for commercial product manufactured by Talecris under the contract. Our contract with Talecris expires December 31, 2013 or five years following initiation of commercial manufacturing. We have the option to extend the term for an additional five-year period upon notice to Talecris at least 12 months prior to the expiration of the initial term. After three years following initiation of commercial manufacturing, either party may terminate the contract upon two years advance notice. We have the right to terminate the contract, under specified circumstances, if we discontinue our production of anthrax immune globulin source plasma or the development of our anthrax immune globulin therapeutic candidate.

We used a contract manufacturer for the supply of our typhoid vaccine candidate for the Phase I and Phase II trials in Vietnam. We may use a different contract manufacturer for the supply of this vaccine candidate for the Phase II study in India, for the Phase III clinical supply, and for commercial manufacturing. We also plan to use a contract manufacturer for the clinical and commercial supplies of our group B streptococcus vaccine candidate.

We also expect that we will rely on third parties for a portion of the manufacturing process for commercial supplies of other product candidates that we successfully develop, including fermentation for some of our vaccine product candidates and contract fill and finish operations. The manufacture of immunobiotic products and the scale-up process necessary to manufacture quantities of immunobiotics sufficient for commercial launch are complex. If we are unable to secure a relationship with third party contract manufacturers that can provide sufficient supplies for the commercial launch of our product candidates, our ability to capture market share may be adversely affected.

In addition, we rely on third parties for supplies and raw materials used for the production of BioThrax and our immunobiotic product candidates. We purchase these supplies and raw materials from various suppliers in quantities adequate to meet our needs. We believe that there are adequate alternative sources of supply available if any of our current suppliers were unable to meet our needs.

Marketing and Sales

We currently market and sell BioThrax directly to the U.S. government with a small, targeted marketing and sales group. We plan to continue to do so and expect that we will use a similar approach for sales to the U.S. government of any other biodefense product candidates that we successfully develop. We plan to expand our sales and marketing organization as we broaden our sales activities of biodefense products at the state and local level, where we expect there will be interest in these products to protect emergency responders such as police, fire and emergency medical personnel, and other personnel whose occupation may cause them to be at a high risk of exposure to biothreats.

We have established marketing and sales offices in Singapore and Munich, Germany, and a joint venture in Malaysia, to target sales of biodefense products to foreign governments. We have augmented our international efforts by engaging third party marketing representatives to identify potential opportunities to sell BioThrax in the Middle East, India, Australia, and several countries in Southeast Asia and Europe.

We expect to increase our sales and marketing resources to market and sell commercial products for which we retain commercialization or co-commercialization rights. We generally expect to retain commercial rights for our product candidates that we successfully develop in situations in which we believe it is possible to access the market through a focused, specialized sales force. In particular, we believe that such a sales force could address commercial markets that overlap with markets for our biodefense products, such as the market for typhoid vaccines and other vaccines for travelers to developing countries. We anticipate that our internal marketing and sales organization will be complemented by selective co-promotion and other arrangements with leading pharmaceutical and biotechnology companies, especially in situations in which the collaborator has particular expertise or resources for the commercialization of our products or product candidates or to access particular markets.

We have entered into an agreement with Ninebio Sdn. Bhd. to form a joint venture in Malaysia that will focus on creating critical biologics infrastructure and supplying biodefense countermeasures, including BioThrax and other medical and complementary products and services to the Government of Malaysia. It is anticipated that the joint venture will also supply such products and services to certain member countries of the Organisation of the Islamic Conference and other countries within Asia. 9Bio is a Malaysian Government owned company and one of the National Institutes of Health under the Ministry of Health. The Government of Malaysia, through 9Bio, has selected us as one of its principal partners to assist, as a contract service provider, in building vaccine development and manufacturing infrastructure. The joint venture will be majority owned by us.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our technologies, knowledge, experience, and resources provide us with competitive advantages, we face potential competition from many different sources, including commercial pharmaceutical and biotechnology companies, academic institutions, government agencies and private and public research institutions. GlaxoSmithKline, Sanofi-Aventis, Wyeth, Merck and Novartis generated over 80% of total worldwide vaccine revenues in 2005. The concentration of the industry reflects a number of factors, including:

- the need for significant, long-term investment in research and development;
- the importance of manufacturing capacity, capability and specialty know-how, such as techniques, processes and biological starting materials; and
- the high regulatory burden for prophylactic products, which generally are administered to healthy people.

These factors have created a significant barrier to entry into the vaccine industry.

Many of our competitors, including those named above, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. These companies also compete with us in recruiting and retaining qualified scientific and management personnel, as well as in acquiring products, product candidates and technologies complementary to, or necessary for, our programs. Smaller or more narrowly focused companies, including Cangene, Human Genome Sciences, Acambis, Avant Immunotherapeutics, Dor BioPharma, Dynport Vaccine Company LLC, Elusys, Bavarian Nordic, Pharmathene and Avecia, may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies or through significant development or procurement contracts with governmental agencies or philanthropic organizations.

Our biodefense product candidates face significant competition for U.S. government funding for both development and procurement of medical countermeasures for biological, chemical and nuclear threats, diagnostic testing systems and other emergency preparedness countermeasures.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer side effects, are more convenient or are less expensive than any products that we may develop. In addition, we may not be able to compete effectively if our products and product candidates do not satisfy government procurement requirements, particularly requirements of the U.S. government with respect to biodefense products.

Any immunobiotic product candidate that we successfully develop and commercialize is likely to compete with currently marketed products, such as vaccines and therapeutics, including antibiotics, and with other product candidates that are in development for the same indications.

Specifically, the competition for BioThrax and our product candidates includes the following:

BioThrax. Although BioThrax is the only product approved by the FDA for human use for the prevention of anthrax infection, we face significant potential competition for the supply of this vaccine to the U.S. government. Various agencies of the U.S. government are providing funding to our competitors for development of an anthrax vaccine based on recombinant protective antigen. Avecia is currently developing a recombinant protective antigen based anthrax vaccine. HHS has issued an RFP for grants to develop and procure a recombinant protective antigen based anthrax vaccine which could reduce demand for BioThrax. In addition, HPA manufactures an anthrax vaccine for use by the government of the United Kingdom. Other countries as well may have anthrax vaccines for use by or in development for their own internal purposes.

Anthrax immune globulin and monoclonal therapeutic. Cangene is currently developing an anthrax immune globulin based on plasma collected from military personnel who have been vaccinated with BioThrax; Human Genome Sciences is developing a monoclonal antibody to *Bacillus anthracis,* referred to as ABthrax, as a post-exposure therapeutic for anthrax infection; Elusys Therapeutics is developing a monoclonal antibody to *Bacillus anthracis*, known as Anthim , as a pre-exposure and post-exposure prophylaxis for anthrax infection, as well as an active treatment of disease; and PharmAthene and Medarex are collaborating to develop a human antibody to *Bacillus anthracis,* known as Valortim, to protect human cells from damage by anthrax toxins. The FDA has granted Fast Track designation and orphan drug status for ABthrax and Valortim. HHS awarded contracts to Human Genome Sciences and Cangene in 2005 to supply their anthrax therapeutics for evaluation of efficacy as a post-exposure therapeutic for anthrax infection.

Botulinum. In April 2005, the DoD provided additional funding to DynPort Vaccine Company LLC for the continued development of a recombinant bivalent botulinum vaccine for protection against botulinum serotypes A and B. This vaccine is called bivalent because it addresses two of the seven serotypes of botulinum neurotoxin. In June 2006, HHS awarded a five-year development and supply contract with a base value of $362 million to Cangene for a heptavalent botulinum immune globulin derived from equine plasma. The contract provides for the supply of 200,000 doses of a botulinum immune globulin for the SNS.

Typhoid vaccine. One oral typhoid vaccine and one injectable typhoid vaccine are currently approved and administered in the United States and Europe. In addition, combination vaccines are available for the prevention of hepatitis A and typhoid infections. Antibiotics typically are used to treat typhoid after infection. Avant Immunotherapeutics Inc. has announced it has an oral, single dose, live attenuated typhoid vaccine candidate in Phase II clinical development with funding from NIAID.

Hepatitis B therapeutic vaccine. Currently available therapies for this patient population consist mainly of antiviral drugs and immunotherapies, such as interferons. There are multiple follow on antivirus and immunotherapies as well as therapeutic vaccines being developed by potential competitors.

Group B streptococcus vaccine. The existing method of prevention of group B streptococcus infection in neonates is the targeted administration of intravenous antibiotics to women during labor. A number of competitors have passive immune vaccines in preclinical development.

Chlamydia vaccine. There is no vaccine currently on the market for chlamydia. Although we are not aware of any competing chlamydia vaccine candidate in clinical development, competitors may have chlamydia vaccine candidates in preclinical development. Screening tests and targeted antibiotic treatments have been effective at containing chlamydia in the United States and Europe, which may have the effect of decreasing demand for a vaccine.

Meningitis B vaccine. Currently, there is no meningitis vaccine on the market that is protective against group B meningococcal infection. Novartis markets a meningitis B vaccine in New Zealand to people under the age of 20 and is also developing a broad coverage protein subunit vaccine candidate. Current meningitis B treatment strategies include antibiotics and clinical support.

Intellectual Property and Licenses

Our success, particularly with respect to our commercial business, depends in part on our ability to obtain and maintain proprietary protection for our product candidates, technology and know-how, to operate without infringing the proprietary rights of others and to prevent others from infringing our proprietary rights. Our policy is to seek to protect our proprietary position by, among other methods, filing U.S. and foreign patent applications related to our proprietary technology, inventions, and improvements that are important to the development of our business. U.S. patents generally have a term of 20 years from the date of nonprovisional filing. We also rely on trade secrets, know-how, continuing

technological innovation and in-licensing opportunities to develop and maintain our proprietary position.

As of February 22, 2008, we owned or licensed exclusively a total of 14 U.S. patents and 27 U.S. patent applications relating to our biodefense and commercial product candidates, as well as numerous foreign counterparts to many of these patents and patent applications. Our patent portfolio includes patents and patent applications with claims directed to compositions of matter, pharmaceutical formulations and methods of use.

We consider of great importance the patent rights that we own or exclusively licensed from HPA relating to our recombinant bivalent botulinum vaccine candidate and our botulinum toxoid vaccine.

We consider the following patents that we own or have licensed exclusively to be most important to the protection of our commercial vaccine candidates that are in clinical development.

Typhoid vaccine. We hold three U.S. patents relating to our typhoid vaccine candidate. These patents have claims to the composition of matter of the vaccine candidate and methods of use of live attenuated *Salmonella typhi* bacteria as vaccines for the treatment and prevention of typhoid and for the delivery of vaccine antigens. In addition, we have three pending U.S. patent applications with claims to additional compositions and methods of therapy that are generally related to our typhoid vaccine candidate. Our issued U.S. patents expire, and, if issued, our U.S. patent applications would expire, between 2015 and 2020. We hold 46 foreign counterparts to our issued U.S. patents relating to our typhoid vaccine candidate, including counterparts under the European Patent Convention and in Japan, that expire, and 15 foreign patent applications that, if issued, would expire, between 2015 and 2020. Additional patents relating to our typhoid vaccine and delivery of vaccine antigens are discussed below under STM technology.

Hepatitis B therapeutic vaccine. Our hepatitis B therapeutic vaccine candidate uses our proprietary *spi*-VEC oral delivery system technology to deliver hepatitis B core antigen to the human immune system. *spi*-VEC is based on our live attenuated typhoid vaccine candidate and employed recombinant technology to insert the gene for hepatitis B core antigen into the live attenuated *Salmonella* bacteria. As a result, the patents relating to our typhoid vaccine candidate also protect our hepatitis B therapeutic vaccine candidate. In addition, we hold one U.S. patent with claims to the use of attenuated *Salmonella* organisms for the delivery of hepatitis B vaccine antigens, which expire in 2019.We also have three pending U.S. patent applications relating to our hepatitis B therapeutic vaccine candidate, which if issued also would expire in 2019. We have five foreign patent applications relating to our hepatitis B therapeutic vaccine candidate that, if issued, would expire in 2019.

Group B streptococcus vaccine. We hold three U.S. patents relating to our group B streptococcus vaccine candidate with claims to the composition of matter of the vaccine candidate and methods of use for the prevention or treatment of infection caused by *Streptococcus agalactiae.* In addition, we have seven pending U.S. patent applications with claims to additional compositions and methods of therapy relating to our group B streptococcus vaccine candidate. Our issued U.S. patents expire, and, if issued, our U.S. patent applications would expire, between 2019 and 2027. We hold 82 foreign counterpart patents relating to our group B streptococcus vaccine candidate, including counterparts under the European Patent Convention and in Japan, that expire, and 34 foreign patent applications that, if issued, would expire, in 2019.

STM technology. We own three U.S. patents with claims to methods for the identification of virulence genes using our signature tagged mutagenesis, or STM, technology, which we used to identify and develop the gene mutations that form the basis of our typhoid vaccine and hepatitis B therapeutic vaccine candidates. We also own 16 foreign counterpart patents, including counterparts under the European Patent Convention and in Japan. These patents relating to the STM method will expire in 2015. We also hold 16 foreign patent applications that, if issued would expire in 2015. Our rights under these patents are licensed on a limited non-exclusive basis to third parties to practice the STM method with respect to specific microorganisms, not including *Salmonella typh*i or hepatitis virus.

The patent positions of companies like ours are generally uncertain and involve complex legal and factual questions. Our ability to maintain and solidify our proprietary position for our technology will depend on our success in obtaining effective claims and enforcing those claims once granted. We do not know whether any of our patent applications or those patent applications that we license will result in the issuance of any patents. Our issued patents and those that may issue in the future, or those licensed to us, may be challenged, invalidated or circumvented, which could limit our ability to stop competitors from marketing related products or the length of term of patent protection that we may have for our products. In addition, our competitors may independently develop similar technologies or duplicate any technology developed by us, and the rights granted under any issued patents may not provide us with any meaningful competitive advantages against these competitors. We may become subject to patent interference proceedings or claims that our products infringe or violate the intellectual property rights of third parties. Furthermore, because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that, before any of our products can be commercialized, any related patent may expire or remain in force for only a short period following

commercialization, thereby reducing any advantage of the patent.

We also rely on trade secrets relating to manufacturing processes and product development to protect our business. Because we do not have patent protection for BioThrax or for the label expansions and improvements that we are pursuing for BioThrax, our only intellectual property protection for BioThrax is confidentiality regarding our manufacturing capability and specialty know-how, such as techniques, processes and biological starting materials. However, these types of trade secrets can be difficult to protect. We seek to protect this confidential information, in part, with agreements with our employees, consultants, scientific advisors and contractors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our consultants or contractors use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

We are a party to a number of license agreements under which we license patents, patent applications, and other intellectual property. We enter into these agreements to augment our owned intellectual property. These agreements impose various diligence and financial payment obligations on us. We expect to continue to enter into these types of license agreements in the future. The only existing licenses that we consider to be material to our current product portfolio or development pipeline are our agreements with HPA, which are described below. We also have a license agreement with the Bavarian State Ministry of the Environment, Public Health and Consumer Protection, or StMUGV, relating to a viral vector technology that we may use in the development of future product candidates, which is also described below.

HPA agreements. In November 2004, we entered into two separate license agreements with HPA for our botulinum toxoid vaccine and our recombinant bivalent botulinum vaccine candidate. Under the license agreements, we obtained the exclusive, worldwide right to develop, manufacture and commercialize pharmaceutical products that consist of botulinum toxoid components or recombinant botulinum toxin components for the prevention or treatment of illness in humans caused by exposure to the botulinum toxin, subject to HPA s non-exclusive right to make, use or sell recombinant botulinum products to meet public health requirements in the United Kingdom.

The licensed patent portfolio includes three U.S. patents with claims to the composition of matter of recombinant components of *Clostridium botulinum,* and the use of such components in vaccines for the treatment or prevention of *Clostridium botulinum* infection or toxicity. These patents expire in 2016. Additional composition of matter and method of use claims are pending in four U.S. patent applications, which if issued as patents also would expire in 2016. The licensed portfolio also includes five foreign patents and three foreign applications, which if issued would expire in 2016.

Under each license agreement, we are required to pay HPA royalties on sales of the licensed product by us, our affiliates or third party sublicensees in the major market countries of the United States, United Kingdom, France, Germany, Italy and Japan, and a separate royalty on sales of the licensed product by us and our affiliates in any other country.

Under each license agreement, we are generally obligated to use commercially reasonable efforts to respond to applicable solicitations or procurement proposals from, and to enter into contracts with, governmental agencies in each of the major market countries with respect to the licensed product. We may satisfy this obligation by filing an IND with respect to a licensed product by November 2009. If we fail to file an IND within that time period under either of the license agreements, we are obligated to pay HPA an annual fee until an IND has been filed.

In November 2004, we also entered into two separate development agreements with HPA pursuant to which HPA agreed to conduct specified tests, studies and other development activities with respect to the botulinum toxoid product and the recombinant botulinum product in accordance with mutually-agreed development plans. We have paid minimum contractual commitments of $1.0 million under each development agreement to compensate HPA for this development work. HPA also agreed to provide us with clinical supplies of the botulinum toxoid product and the recombinant botulinum product for clinical trials.

The term of each development agreement lasts until the development activities are completed. Each of the development agreements automatically terminates if the applicable license agreement is terminated. The term of each license agreement lasts until the expiration of all of our royalty obligations under the applicable license agreement. We are obligated to pay royalties under each license agreement, on a product-by-product and country-by-country basis, until the later of seven years from first commercial sale of the first licensed product in that country and the expiration of the last-to-expire licensed patent in that country. HPA may terminate each license agreement if we terminate the applicable development agreement without cause before we have paid, or if HPA terminates such development agreement due to our failure to pay, the minimum commitment amount set forth in such development agreement.

MVA platform technology. In July 2006, in connection with our acquisition of ViVacs GmbH, or Vivacs, a German limited liability company, we acquired a license agreement with StMUGV that provides us the non-exclusive, worldwide right to develop and produce viruses and viral products, including recombinant viral vectors, using the modified vaccinia Ankara virus, or MVA. Under the license agreement, we are required to pay StMUGV a percentage of the net revenue or license fees, that we receive from products developed using MVA that are used for research or other purposes and a percentage of the license fees that we receive from products developed using MVA that are licensed as starting material for the production of a smallpox vaccine.

The license agreement does not have a specified term. In addition, StMUGV may terminate the license agreement upon the insolvency or liquidation of our wholly owned subsidiary, Emergent Product Development GmbH, formerly ViVacs GmbH. Our MVA platform technology, which is based on these licensed rights, could potentially be used as a viral vector for delivery of multiple vaccine antigens for different disease-causing organisms using recombinant technology. We are currently exploring potential product candidates based on our MVA platform, include a broadly cross protective influenza vaccine candidate.

Government Regulation

The FDA and comparable regulatory agencies in state and local jurisdictions and in foreign countries impose substantial requirements for the preclinical and clinical development, manufacture, distribution and marketing of pharmaceutical and biological products, including immunobiotics. These agencies and other federal, state and local entities regulate research and development activities and the testing, manufacture, quality control, safety, effectiveness, labeling, storage, distribution, recordkeeping, approval, advertising, sale, promotion, import, and export of our product and product candidates.

U.S. Government Regulation

In the United States, BioThrax and our product candidates are regulated by the FDA as biological products. Biologics are subject to regulation under the Federal Food, Drug, and Cosmetic Act, or the FDCA, the Public Health Service Act, or the PHSA, the regulations promulgated under the FDCA and the PHSA and other federal, state, and local statutes and regulations. Violations of regulatory requirements at any stage may result in various adverse consequences, including delay in approving or refusal to approve a product. Violations of regulatory requirements also may result in enforcement actions, including withdrawal of product approval, labeling restrictions, seizure of products, fines, injunctions or civil or criminal penalties.

The process required by the FDA under these laws before our product candidates may be marketed in the United States generally involves the following:

- preclinical laboratory and animal tests;
- submission to the FDA of an IND, which must become effective before clinical trials may begin;
- completion of human clinical trials and other studies to establish the safety and efficacy of the proposed product for each intended use;
- FDA review of facilities in which the product is manufactured, processed, packed and held to determine compliance with cGMP requirements designed to assure the product s continued quality; and
- submission to the FDA and approval of an NDA in the case of a drug, or a BLA in the case of a biologic, containing preclinical and clinical data, proposed labeling, and information to demonstrate that the product will be manufactured to appropriate standards of identity, purity and quality.

The research, development and approval process requires substantial time, effort and financial resources, and approvals may not be granted on a timely or commercially viable basis, if at all.

Preclinical Studies and the IND

Preclinical studies include laboratory evaluation of the product candidate, its chemistry, formulation and stability, as well as animal studies to assess its potential safety and efficacy. We submit the results of the preclinical studies, together with manufacturing information, analytical data and any available clinical data or literature to the FDA as part of an IND, which must become effective before we may begin human clinical trials. The IND submission also contains clinical trial protocols, which describe the design of the proposed clinical trials. The IND becomes effective 30 days after the FDA receives the filing, unless the FDA, within the 30-day time period, raises concerns or questions about the conduct of the preclinical trials or the design of the proposed clinical trials as outlined in the IND. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin. In addition, an independent Institutional Review Board charged with protecting the welfare of human subjects involved in research at each medical center proposing to conduct the clinical trials must review and approve any clinical trial. Furthermore, study subjects must provide informed consent for their participation in the clinical trial.

Clinical Trials

Human clinical trials are typically conducted in three sequential phases, which may overlap:

In a Phase I clinical trial, the drug or biologic is initially administered into healthy human subjects or subjects with the target condition and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion.
In a Phase II clinical trial, the drug or biologic is administered to a limited subject population to identify possible adverse effects and safety risks, the efficacy of the product for specific targeted diseases and dosage tolerance and optimal dosage.
A Phase III clinical trial is undertaken if a Phase II clinical trial demonstrates that a dosage range of the drug or biologic is effective and has an acceptable safety profile. In a Phase III clinical trial, the drug or biologic is administered to an expanded population, often at geographically dispersed clinical trial sites, to further evaluate dosage and clinical efficacy and to further test for safety.

Clinical trials must be conducted in compliance with good clinical practice, or GCP, requirements. In addition, federal law now requires the listing, on a publicly-available website, of registry and results information for most clinical trials that we conduct. The federal requirements for submission of results information will be phased-in over the next three years. Some states have similar clinical trial reporting laws.

In the case of product candidates that are intended to treat rare life-threatening diseases, such as infection caused by exposure to the anthrax toxin, conducting controlled clinical trials to determine efficacy may be unethical or infeasible. Under regulations issued by the FDA in 2002, often referred to as the animal rule, approval of such products can be based on clinical data from trials in healthy subjects that demonstrate adequate safety and immunogenicity and efficacy data from adequate and well controlled animal studies. Among other requirements, the animal studies must establish that the biological product is reasonably likely to produce clinical benefits in humans. Because the FDA must agree that data derived from animal studies may be extrapolated to establish safety and effectiveness in humans, these studies add complexity and uncertainty to the testing and approval process. In addition, products approved under the animal rule are subject to additional requirements including post-marketing study requirements, restrictions imposed on marketing or distribution or requirements to provide information to patients.

Marketing Approval

In the United States, if a product is regulated as a drug, an NDA must be submitted and approved before commercial marketing may begin. If the product is regulated as a biologic, a BLA must be submitted and approved before commercial marketing may begin. The NDA or BLA must include a substantial amount of data and other information concerning the safety and effectiveness and, in the case of a biologic, purity and potency of the product candidate. Both NDAs and BLAs must contain data and information on the finished product, including manufacturing, product stability and proposed product labeling.

Each domestic and foreign manufacturing establishment, including any contract manufacturers we may decide to use, must be listed in the NDA or BLA and must be registered with the FDA. The FDA generally will not approve an application until the FDA conducts a manufacturing inspection, approves the applicable manufacturing process for the drug or biological product and determines that the facility is in compliance with cGMP requirements. If the manufacturing facilities and processes fail to pass the FDA inspection, we will not receive approval to market these products.

The FDA may deny an NDA or BLA if the applicable regulatory criteria are not satisfied or may require additional clinical data. Even if additional clinical data is submitted, the FDA may ultimately decide that the NDA or BLA does not satisfy the criteria for approval. If the FDA approves a product, it may limit the approved therapeutic uses for the product as described in the product labeling, require that contraindications, warning statements or precautions be included in the product labeling, require that additional studies be conducted following approval as a

condition of the approval, impose restrictions and conditions on product distribution, prescribing or dispensing in the form of a risk management plan or risk evaluation and mitigation strategy, or otherwise limit the scope of any approval or limit labeling. Once issued, the FDA may withdraw product approval if compliance with regulatory standards is not maintained or if problems occur after the product reaches the market. In addition, the FDA may require testing and surveillance programs to monitor the effect of approved products that have been commercialized. The FDA has the power to prevent or limit further marketing of a product based on the results of these post-marketing programs.

Fast Track Designation

In February 2007, the FDA granted Fast Track designation for BioThrax as a post-exposure prophylaxis for anthrax infection. The FDA s Fast Track programs, one of which is Fast Track designation, are designed to facilitate the development and review of new drugs and biologics that are intended to treat serious or life-threatening conditions and that demonstrate the potential to address unmet medical needs for the conditions. Fast Track designation applies to a combination of the product and the specific indication for which it is being studied. Thus, it is the development program for a specific drug or biologic for a specific indication that receives Fast Track designation. The sponsor of a product designated as being in a Fast Track drug development program may engage in early communication with the FDA, including timely meetings and early feedback on clinical trials. Products in Fast Track drug development programs also may receive priority review or accelerated approval and sponsors may be able to submit portions of an application before the complete application is submitted. The FDA may notify a sponsor that its program is no longer classified as a Fast Track development program if the Fast Track designation is no longer supported by emerging data or the designated drug development program is no longer being pursued.

Ongoing Regulation

Any products manufactured or distributed by us pursuant to FDA clearances or approvals are subject to pervasive and continuing regulation by the FDA, including:

- recordkeeping requirements;
- periodic reporting requirements;
- cGMP requirements related to all stages of manufacturing, testing, storage, packaging, labeling and distribution of finished dosage forms of the product;
- reporting of adverse experiences with the drug or biologic; and
- advertising and promotion restrictions.

The FDA s rules for advertising and promotion require in particular that we not promote our products for unapproved uses and that our promotion be fairly balanced and adequately substantiated. We must also submit appropriate new and supplemental applications and obtain FDA approval for certain planned changes to the approved product, product labeling or manufacturing process.

Drug and biologics manufacturers and their subcontractors are required to register their establishments with the FDA and state agencies. The cGMP requirements for biological products are extensive and require considerable time, resources, and ongoing investment to comply. The regulations require manufacturers to establish validated systems to ensure that products meet high standards of sterility, purity and potency. The requirements apply to all stages of the manufacturing process, including the synthesis, processing, sterilization, packaging, labeling, storage and shipment of the biological product. The regulations require investigation and correction of any deviations from cGMP and impose documentation requirements upon us and any third party manufacturers that we may decide to use. Manufacturing establishments are subject to periodic unannounced inspections by the FDA and state agencies for compliance with cGMP. The FDA is authorized to inspect manufacturing facilities without a warrant at reasonable times and in a reasonable manner. We or our present or future suppliers may not be able to comply with cGMP and other FDA regulatory requirements.

In addition, cGMP requirements are constantly evolving, and new or different requirements may apply in the future. We, our collaborators or third party contract manufacturers may not be able to comply with the applicable regulations. After regulatory approvals are obtained, the subsequent discovery of previously unknown problems, or the failure to maintain compliance with existing or new regulatory requirements, may result in:

restrictions on the marketing or manufacturing of a product;

warning letters;

withdrawal of the product from the market;

refusal to approve pending applications or supplements to approved applications;

voluntary or mandatory product recall;

fines or disgorgement of profits or revenue;

suspension or withdrawal of regulatory approvals;

refusal to permit the import or export of products;

product seizure; and

injunctions or the imposition of civil or criminal penalties.

BioThrax Lot Release and FDA Review

Because of the complex manufacturing processes for most biological products, the FDA requires that each product lot of an approved biologic, including vaccines, undergo thorough testing for purity, potency, identity and sterility. Before a lot of BioThrax can be used, we must submit a sample of the vaccine lot and a lot release protocol to the FDA. The lot release protocol documents reflect the results of our tests for potency, safety, sterility and any additional assays mandated by our BLA for BioThrax and a summary of relevant manufacturing details. The FDA reviews the manufacturing and testing information provided in the lot release protocol and may elect to perform confirmatory testing on lot samples that we submit. We cannot distribute a lot of BioThrax until the FDA releases it. The length of the FDA review process depends on a number of factors, including reviewer questions, license supplement approval, reviewer availability, and whether our internal testing of product samples is completed before or concurrently with FDA testing.

Regulation of Immune Globulin Products

Products derived from humans, including our immune globulin therapeutic candidates, are subject to additional regulation. The FDA regulates the screening and vaccination of human donors and the process of collecting source plasma. FDA regulations require that all donors be tested for suitability and provide informed consent prior to vaccination or collection of source plasma for the immune globulin. The vaccination and collection of source plasma may also be subject to Institutional Review Board approval or to an IND, depending on factors such as whether donors are to be vaccinated according to the vaccine s approved schedule. The FDA also regulates the process of testing, storage and processing of source plasma, which is used to manufacture immune globulin candidates for use in clinical trials and, after approval by the FDA, for commercial distribution.

Legislation and Regulation Related to Bioterrorism Counteragents and Pandemic Preparedness

Because some of our products or product candidates are intended for the treatment of diseases that may result from acts of bioterrorism or for pandemic preparedness, they may be subject to the specific legislation and regulation described below.

Project BioShield

The Project BioShield Act of 2004 provides expedited procedures for bioterrorism related procurement and awarding of research grants, making it easier for HHS to quickly commit funds to countermeasure projects. Project BioShield relaxes procedures under the Federal Acquisition Regulation for procuring property or services used in performing, administering or supporting biomedical countermeasure research and development. In addition, if the Secretary of HHS deems that there is a pressing need, Project BioShield authorizes the Secretary to use an expedited award process, rather than the normal peer review process, for grants, contracts and cooperative agreements related to biomedical countermeasure research and development activity.

Under Project BioShield, the Secretary of HHS, with the concurrence of the Secretary of the Department of Homeland Security and upon the approval of the President, can contract to purchase unapproved countermeasures for the SNS in specified circumstances. Congress is notified of a recommendation for a stockpile purchase after Presidential approval. Project BioShield specifies that a company supplying the countermeasure to the SNS is paid on delivery of a substantial portion of the countermeasure. To be eligible for purchase under these provisions, the Secretary of HHS must determine that there is sufficient and satisfactory clinical results or research data, including data, if available, from preclinical and clinical trials, to support a reasonable conclusion that the countermeasure will qualify for approval or licensing within eight years. Project BioShield also allows the Secretary of HHS to authorize the emergency use of medical products that have not yet been approved by the FDA. To exercise this authority, the Secretary of HHS must conclude that:

the agent for which the countermeasure is designed can cause serious or life-threatening disease;

the product may reasonably be believed to be effective in detecting, diagnosing, treating or preventing the disease;

the known and potential benefits of the product outweigh its known and potential risks; and

there is no adequate alternative to the product that is approved and available.

Although this provision permits the Secretary of HHS to circumvent the FDA approval process, its use would be limited to rare circumstances.

Safety Act

The Support Anti-Terrorism by Fostering Effective Technologies Act, or Safety Act, enacted by the U.S. Congress in 2002 creates product liability limitations for qualifying anti-terrorism technologies for claims arising from or related to an act of terrorism. In addition, the Safety Act provides a process by which an anti-terrorism technology may be certified as an approved product by the Department of Homeland Security and therefore entitled to a rebuttable presumption that the government contractor defense applies to sales of the product. The government contractor defense, under specified circumstances, extends the sovereign immunity of the United States to government contractors who manufacture a product for the government. Specifically, for the government contractor defense to apply, the government must approve reasonably precise specifications, the product must conform to those specifications and the supplier must warn the government about known dangers arising from the use of the product. Although sales of BioThrax are subject to the protections of the Safety Act, our product candidates may not qualify for the protections of the Safety Act or the government contractor defense.

Public Readiness and Emergency Preparedness Act

The Public Readiness and Emergency Preparedness Act, or PREP Act, enacted by Congress in 2005 provides immunity for manufacturers from all claims under state or federal law for loss arising out of the administration or use of a covered countermeasure. However, injured persons may still bring a suit for willful misconduct against the manufacturer under some circumstances. Covered countermeasures include security countermeasures and qualified pandemic or epidemic products, including products intended to diagnose or treat pandemic or epidemic disease, such as pandemic vaccines, as well as treatments intended to address conditions caused by such products. For these immunities to apply, the Secretary of HHS must issue a declaration in cases of public health emergency or credible risk of a future public health emergency. On February 1, 2007, the Secretary of HHS issued the first declaration under the PREP Act to protect countermeasures from liability that are necessary to prepare the nation for an avian influenza pandemic. We have applied for a PREP Act declaration for BioThrax in connection with our September 2007 BioThrax procurement contract with HHS. To date, the Secretary has not issued the declaration for BioThrax or for any of our product candidates.We cannot predict whether the PREP Act will provide protections for our products or product candidates in the future, whether Congress will fund the relevant compensation programs or if the necessary prerequisites for immunity would be triggered with respect to our product or product candidates.

Foreign Regulation

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we must obtain approval of a product by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. The actual time required to obtain clearance to market a product in a particular foreign jurisdiction may vary substantially, based upon the type, complexity and novelty of the pharmaceutical product candidate and the specific requirements of that jurisdiction. The requirements governing the conduct of clinical trials, marketing authorization, pricing and reimbursement vary from country to country.

In the European Union, our products are subject to extensive regulatory requirements. As in the United States, the marketing of medicinal products has for many years been subject to the granting of marketing authorizations by regulatory agencies. European Union member states require both regulatory clearance and a favorable ethics committee opinion prior to the commencement of a clinical trial, whatever its phase. Under European Union regulatory systems, we may submit marketing authorization applications either under a centralized or decentralized/mutual recognition procedure.

The centralized procedure provides for the grant of a single marketing authorization that is valid for all European Union member states. The centralized procedure is currently mandatory for products developed by means of a biotechnological process, including recombinant DNA technology, the controlled expression of genes coding for biologically active proteins and monoclonal antibody methods, and new chemical

entities for the treatment of acquired immune deficiency syndrome, cancer and neurodegenerative disorder or diabetes. Beginning in May 2008, the centralized procedure will be mandatory for products for the treatment of auto-immune diseases and other immune dysfunctions and viral diseases. The centralized process is optional for medicines that constitute a significant therapeutic, scientific or technical innovation or for which a centralized process is in the interest of patients.

The decentralized/mutual recognition procedures provide for mutual recognition of national approval decisions. Under these procedures, the holder of a national marketing authorization may submit an application to a member state of its choice (the reference member state, or RMS) and identify other member states in which it also wishes to seek approval (concerned member states, or CMS). The RMS reviews the application and circulates an assessment report to each CMS, which must then decide whether to accept the RMS determination. If a member state does not accept the RMS position, the disputed points are referred to the Committee for Medicinal Products for Human Use, or CHMP, within the European Medicines Agency, or EMEA. The CHMP adopts an opinion, which the European Commission uses as a basis for a decision that is binding on all member states.

Unlike the United States, the European Union member states do not have separate rules or review procedures for biologics and vaccines. Regulators apply broadly consistent principles and standards when reviewing applications, although they accept that the nature of the efficacy data supporting a vaccine application is likely to differ from the data that would support applications for the majority of therapeutic products. However, there are special procedures for some types of vaccine products. For example, influenza vaccines are subject to accelerated review and approval each year, following the release by the WHO, of the annual influenza strains. European Union member states have the discretion to require that marketing authorization holders submit samples of live vaccines or other immunological products for examination and formal batch release by a government control laboratory prior to release onto the market.

Orphan Drugs

Under the Orphan Drug Act, special incentives exist for sponsors to develop products for rare diseases or conditions, which are defined to include those diseases or conditions that affect fewer than 200,000 people in the United States. A vaccine also can receive these incentives if it is expected to be administered to fewer than 200,000 persons per year. Requests for orphan drug designation must be submitted prior to submission of an application for marketing authorization. Biologics may qualify for designation as an orphan drug.

Products designated as orphan drugs are eligible for special grant funding for research and development, FDA assistance with the review of clinical trial protocols, potential tax credits for research, reduced filing fees for marketing applications and a special seven-year period of market exclusivity after marketing approval. Orphan drug exclusivity prevents FDA approval of applications by others for the same drug or biologic intended for use for the designated orphan disease or condition. The FDA may approve a subsequent application from another person if the FDA determines that the application is for a different product or different use, or if the FDA determines that the subsequent product is clinically superior or that the holder of the initial orphan drug approval cannot assure the availability of sufficient quantities of the drug or biologic to meet the public s need. The FDA also may approve another application for the same drug or biologic that has orphan exclusivity but for a different use, in which case the competing drug or biologic could be prescribed by physicians outside its FDA approval for the orphan use notwithstanding the existence of orphan exclusivity. A grant of an orphan designation is not a guarantee that a product will be approved.

The European Union operates an equivalent system to encourage the development and marketing of medicinal products for rare diseases. Applications for orphan designations are submitted to the EMEA and reviewed by a Committee on Orphan Medicinal Products, or COMP, comprising representatives of the member states, patient groups and other persons. The final decision is made by the European Commission.

A product can be designated as an orphan drug if it is intended for either (i) a life-threatening or chronically debilitating condition affecting not more than 5 in 10,000 persons in the European Community when the application is made or a life-threatening, seriously debilitating; or (ii) a serious and chronic condition in the European Community for which, without incentives, it is unlikely that the marketing of the product in the European Community would generate sufficient return to justify the necessary investment. In either case, the applicant must also demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the European Community or, if such method exists, that the medicinal product will be of significant benefit to those affected by that condition. The COMP assesses the orphan status at both the time of first designation and also in parallel with the review of every marketing authorization application for an orphan medicine.

After a marketing authorization has been granted in the European Community for an orphan product, no similar product may be approved for a period of ten years. At the end of the fifth year, however, any member state can initiate proceedings to restrict that period to six years if it believes the criteria for orphan designation no longer apply, for example, because the prevalence of disease has increased or the manufacturer is earning an unreasonable profit. In addition, competitive products can be approved during the marketing exclusivity period if they are not similar to the original product or even if they are similar, are safer, more effective or otherwise clinically superior to it.

None of our products or product candidates have been designated as orphan drugs.

Reimbursement and Pricing Controls

In many of the markets where we or our potential collaborators would commercialize a product following regulatory approval, the prices of pharmaceutical products are subject to direct price controls by law and to reimbursement programs with varying price control mechanisms.

In the United States, there is an increasing focus on drug and biologic pricing in recent years. There are currently no direct government price controls over private sector purchases in the United States. However, the Veterans Health Care Act establishes mandatory price discounts for certain federal purchasers, including the Veterans Administration, Department of Defense, and the Public Health Service; the discounts are based on prices charged to other customers.

Under the Medicaid program (a joint federal/state program that provides medical coverage to certain low income families and individuals), pharmaceutical manufacturers must pay prescribed rebates on specified drugs and biologics to enable them to be eligible for reimbursement. Vaccines are generally exempt from these rebate requirements and generally are not provided through Medicaid. Medicare (the federal program that provides medical coverage for the elderly and disabled) generally reimburses for physician-administered drugs and biologics on the basis of the product s average sales price, although the vaccines that are reimbursed under Part B (Influenza, Pneumococcal and Hepatitis B) are reimbursed based on average wholesale price. Outpatient drugs and other vaccines may be reimbursed under Medicare Part D. Part D is administered through private entities that attempt to negotiate price concessions from pharmaceutical manufacturers. Various states have adopted further mechanisms that seek to control drug and biologic prices, including by disfavoring higher priced products and by seeking supplemental rebates from manufacturers. Managed care has also become a potent force in the market place that increases downward pressure on the prices of pharmaceutical products.

Public and private health care payors control costs and influence drug and biologic pricing through a variety of mechanisms, including through negotiating discounts with the manufacturers and through the use of tiered formularies and other mechanisms that provide preferential access to particular products over others within a therapeutic class. Payors also set other criteria to govern the uses of a drug or biologic that will be deemed medically appropriate and therefore reimbursed or otherwise covered. In particular, many public and private health care payors limit reimbursement and coverage to the uses that are either approved by the FDA or that are supported by other appropriate evidence, such as published medical literature, and appear in a recognized compendium. Drug compendia are publications that summarize the available medical evidence for particular drug products and identify which uses are supported or not supported by the available evidence, whether or not such uses have been approved by the FDA.

Most non-pediatric commercial vaccines are purchased and paid for, or reimbursed by, managed care organizations, other private health plans or public insurers or paid for directly by patients. In the United States, pediatric vaccines are funded by a variety of federal entitlements and grants, as well as state appropriations. The CDC currently distributes pediatric grant funding on a discretionary basis under the Public Health Service Act. Federal and state governments purchase the majority of all pediatric vaccines produced in the United States, primarily through the Vaccines for Children Program implemented by the U.S. Congress in 1994. The Vaccines for Children Program is designed to help pay for vaccinations to disadvantaged children, including uninsured children, children on Medicaid and underinsured children who receive vaccinations at federally qualified health centers.

Different pricing and reimbursement schemes exist in other countries. In the European Community, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national health care systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. Other member states allow companies to fix their own prices for medicines, but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries cross-border imports from low-priced markets exert a commercial pressure on pricing within a country.

Regulations Regarding Government Contracting

Our status as a government contractor in the United States and elsewhere means that we are also subject to various statutes and regulations, including the Federal Acquisition Regulation, which governs the procurement of goods and services by agencies of the United States and other countries. These governing statutes and regulations can impose stricter penalties than those normally applicable to commercial contracts, such as criminal and civil damages liability and suspension and debarment from future government contracting. In addition, pursuant to various statutes and regulations, our government contracts can be subject to unilateral termination or modification by the government for convenience in the United States and elsewhere, detailed auditing requirements, statutorily controlled pricing, sourcing and subcontracting restrictions and statutorily mandated processes for adjudicating contract disputes.

Vaccine Injury Compensation Program

Because the cost of vaccine related litigation had reduced significantly the number of manufacturers willing to sell childhood vaccines, the U.S. Congress enacted the National Childhood Vaccine Injury Act in 1986. The Vaccine Injury Compensation Program established under the Vaccine Injury Act is a no-fault compensation program funded by an excise tax on each dose of a covered vaccine and is designed to streamline the process of seeking compensation for those injured by childhood vaccines. The Vaccine Injury Act requires all individuals injured by a vaccine to go through the compensation program before pursuing other remedies. Although claimants can reject decisions issued under the compensation program and pursue subsequent legal action through the courts, the Vaccine Injury Act determines the circumstances under which a manufacturer may be found liable in a civil action. The Vaccine Injury Act may not protect us if our products or product candidates cause injury.

Hazardous Materials and Select Agents

Our development and manufacturing processes involve the use of hazardous materials, including chemicals, bacteria, viruses and radioactive materials, and produce waste products. Accordingly, we are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of these materials. In addition to complying with environmental and occupational health and safety laws, we must comply with special regulations relating to biosafety administered by the CDC, HHS and the DoD.

The Public Health Security and Bioterrorism Preparedness and Response Act and the Agricultural Protection Act require us to register with the CDC and the Department of Agriculture our possession, use or transfer of select biological agents or toxins that could pose a threat to public health and safety, to animal or plant health or to animal or plant products. This legislation requires increased safeguards and security measures for these select agents and toxins, including controlled access and the screening of entities and personnel, and establishes a comprehensive national database of registered entities.

In particular, this legislation and related regulations require that we:

- develop and implement biosafety, security and emergency response plans;
- restrict access to select agents and toxins;
- provide appropriate training to our employees for safety, security and emergency response;
- comply with strict requirements governing transfer of select agents and toxins;
- provide timely notice to the government of any theft, loss or release of a select agent or toxin; and
- maintain detailed records of information necessary to give a complete accounting of all activities related to select agents and toxins.

Other Regulations

In the United States and elsewhere, the research, manufacturing, distribution, sale and promotion of drug and biological products are potentially subject to regulation by various federal, state and local authorities in addition to the FDA, including the Centers for Medicare and Medicaid Services, other divisions of HHS, such as the Office of Inspector General, the U.S. Department of Justice and individual U.S. Attorney offices within the Department of Justice and state and local governments. For example, sales, marketing and scientific and educational grant programs must comply with the anti-kickback and fraud and abuse provisions of the Social Security Act, the False Claims Act, the privacy provisions of the Health Insurance Portability and Accountability Act and similar state laws. Pricing and rebate programs must comply with the Medicaid rebate requirements of the Omnibus Budget Reconciliation Act of 1990 and the Veterans Health Care Act of 1992. All of these activities are also potentially subject to federal and state consumer protection and unfair competition laws.

Outside the United States, advertising and promotion of medicinal products, along with associated commercial practices, are often subject to significant government regulation. We are subject to the Export Administration Regulations implemented by the Bureau of Industry and Security governing the export of BioThrax and technology for the development and use of pathogens and toxins in the development and manufacture of BioThrax and our product candidates. In connection with our international sales activity, we are also subject to export regulations and other sanctions imposed by the Office of Foreign Assets Control of the Department of the Treasury, the antiboycott provisions of the Export Administration Act and the Internal Revenue Code and the Foreign Corrupt Practices Act.

Personnel

As of December 31, 2007, we had 560 employees, including 170 employees engaged in product development, 244 employees engaged in manufacturing, 10 employees engaged in sales and marketing and 136 employees engaged in general and administrative activities. We believe that our future success will depend in part on our continued ability to attract, hire and retain qualified personnel. None of our employees is represented by a labor union or covered by collective bargaining agreements. We believe that our relations with our employees are good.

Available Information

We maintain a website at www.emergentbiosolutions.com. We make available, free of charge on our website, our annual report on Form 10- K, quarterly reports on Form 10-Q, current reports on Form 8-K and all amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, as soon as reasonably practicable after we electronically file those reports with, or furnish them to, the Securities and Exchange Commission, or SEC.

We also make available, free of charge on our website, the reports filed with the SEC by our executive officers, directors and 10% stockholders pursuant to Section 16 under the Exchange Act as soon as reasonably practicable after copies of those filings are provided to us by those persons. In addition, we intend to make available on our website all disclosures that are required by applicable law, the rules of the SEC or the New York Stock Exchange listing standards regarding any amendment to, or waive of, our code of business conduct and ethics. The information contained on, or that can be accessed through, our website is not a part of or incorporated by reference in this annual report on Form 10-K.

ITEM 1A. RISK FACTORS

Risks Related to Our Dependence on U.S. Government Contracts

We have derived substantially all of our revenue from sales of BioThrax under contracts with the DoD and HHS. If DoD and HHS demand for BioThrax is reduced, our business, financial condition and operating results could be materially harmed.

We have derived and expect for the foreseeable future to continue to derive substantially all of our revenue from sales of BioThrax, our FDA-approved anthrax vaccine and only marketed product. In 2006 and 2007, we derived substantially all of our revenue from our BioThrax contracts with the DoD and HHS. In October 2007, the White House issued a Presidential Directive that outlines the U.S. government s objective to enhance coordination and cooperation among federal agencies with respect to countermeasure procurement and stockpile management. Also in October 2007, the U.S. Government Accountability Office, or GAO, issued a report that was critical of HHS for lacking an effective strategy to minimize waste in the SNS, citing concerns of large amounts of BioThrax that will become unusable each year due to shelf life expiration. We believe that the DoD has a continued commitment to procure BioThrax for its active immunization program, but that in the future the DoD will likely procure additional doses of BioThrax to satisfy ongoing requirements for its active immunization program directly from HHS and not from us. It is possible that these purchases by DoD from HHS will not result in any additional purchases by HHS from us. Our existing and prior contracts with the DoD and HHS do not necessarily increase the likelihood that we will secure future comparable contracts with the U.S. government. HHS has issued an RFP for grants to develop and procure a recombinant protective antigen based anthrax vaccine. If we apply for the grant, we may not win the award. The development of our recombinant protective antigen product candidate could be harmed. Additionally, procurement by HHS of a recombinant protective antigen based anthrax vaccine could reduce demand for BioThrax. The success of our business and our operating results for the foreseeable future are substantially dependent on the price per dose, the number of doses and the timing of deliveries for BioThrax sales to the U.S. government.

Our business may be harmed as a result of the government contracting process, which is a competitive bidding process that involves risks not present in the commercial contracting process.

We expect that a significant portion of the business that we will seek in the near future will be under government contracts or subcontracts awarded through competitive bidding. Competitive bidding for government contracts presents a number of risks that are not typically present in the commercial contracting process, including:

- the need to devote substantial time and attention of management and key employees to the preparation of bids and proposals for contracts that may not be awarded to us;
- the need to accurately estimate the resources and cost structure that will be required to perform any contract that we might be awarded; and
- the expenses that we might incur and the delays that we might suffer if our competitors protest or challenge contract awards made to us pursuant to competitive bidding, and the risk that any such protest or challenge could result in the resubmission of bids based on modified specifications, or in termination, reduction or modification of the awarded contract.

The U.S. government may choose to award future contracts for the supply of anthrax vaccines and other biodefense product candidates that we are developing to our competitors instead of to us. If we are unable to win particular contracts, we may not be able to operate in the market for products that are provided under those contracts for a number of years. For example, if any other company is successful in developing a next generation anthrax vaccine, U.S. government customers may purchase only the next generation vaccine and not BioThrax. If we are unable to consistently win new contract awards over an extended period, or if we fail to anticipate all of the costs and resources that will be required to secure such contract awards, our growth strategy and our business, financial condition, and operating results could be materially adversely affected.

Our U.S. government contracts for BioThrax require ongoing funding decisions by the government. The failure to fund one or more of these contracts could cause our financial condition and operating results to suffer materially.

Our principal customer for BioThrax is the U.S. government. In addition, we anticipate that the U.S. government will be the principal customer for any other biodefense products that we successfully develop. Over its lifetime, a U.S. government program may be implemented through the award of many different individual contracts and subcontracts. The funding of some government programs is subject to Congressional appropriations, generally made on a fiscal year basis even though a program may continue for several years. Our government customers are subject to stringent budgetary constraints and political considerations. If levels of government expenditures and authorizations for biodefense decrease or shift to programs in areas where we do not offer products or are not developing product candidates, our business, revenues and operating results may suffer.

The success of our business with the U.S. government depends on our compliance with additional regulations and obligations under our U.S. government contracts.

Our business with the U.S. government is subject to specific procurement regulations and a variety of other legal compliance obligations. These obligations include those related to:

procurement integrity;

export control;

government security regulations;

employment practices;

protection of the environment;

accuracy of records and the recording of costs; and

foreign corrupt practices.

In addition, before awarding us any future contracts, the U.S. government could require that we respond satisfactorily to a request to substantiate our commercial viability and industrial capabilities. Compliance with these obligations increases our performance and compliance costs. Failure to comply with these regulations and requirements could lead to suspension or debarment, for cause, from government contracting or subcontracting for a period of time. The termination of a government contract or relationship as a result of our failure to satisfy any of these obligations would have a negative impact on our operations and harm our reputation and ability to procure other government contracts in the future.

On September 25, 2007, we entered into an agreement with HHS to supply 18.75 million doses of BioThrax to HHS for placement into the SNS for a firm fixed price of $400 million. If we receive FDA approval of an application to extend the expiry dating of BioThrax from three years to four years, HHS has agreed to adjust the price per dose under the agreement, with an aggregate value of such price increase of approximately $34 million. The regulatory approval process is complex and uncertain, and there is no guarantee that we will receive approval of four-year expiry dating. If we do not receive FDA approval of four-year expiry dating during the term of the agreement, we will not be entitled to receive the $34 million related to the increased price per dose.

The pricing under our fixed price government contracts is based on estimates of the time, resources and expenses required to deliver the specified doses of BioThrax. If our estimates are not accurate, we may not be able to earn an adequate return under these contracts.

Our existing and prior contracts for the supply of BioThrax with the DoD and HHS have been fixed price contracts. We expect that our future contracts with the U.S. government for BioThrax as well as biodefense product candidates that we successfully develop also may be fixed price contracts. Under a fixed price contract, we are required to deliver our products at a fixed price regardless of the actual costs we incur and to absorb any costs in excess of the fixed price. Estimating costs that are related to performance in accordance with contract specifications is difficult. Our failure to anticipate technical problems, estimate costs accurately or control costs during performance of a fixed price contract could reduce the profitability of a fixed price contract or cause a loss.

Unfavorable provisions in government contracts may harm our business, financial condition and operating results.

Government contracts customarily contain provisions that give the government substantial rights and remedies, many of which are not typically found in commercial contracts, including provisions that allow the government to:

terminate existing contracts, in whole or in part, for any reason or no reason;

unilaterally reduce or modify contracts or subcontracts;

cancel multi-year contracts and related orders if funds for contract performance for any subsequent year become unavailable;

decline to exercise an option to renew a contract;

exercise an option to purchase only the minimum amount specified in a contract;

decline to exercise an option to purchase the maximum amount specified in a contract;

claim rights to products, including intellectual property, developed under the contract;

take actions that result in a longer development timeline than expected;

direct the course of a development program in a manner not chosen by the government contractor;

suspend or debar the contractor from doing business with the government or a specific government agency;

pursue criminal or civil remedies under the False Claims Act and False Statements Act; and

control or prohibit the export of products.

Generally, government contracts, including our HHS contract for BioThrax, contain provisions permitting unilateral termination or modification, in whole or in part, at the government s convenience. Under general principles of government contracting law, if the government terminates a contract for convenience, the terminated company may recover only its incurred or committed costs, settlement expenses and profit on work completed prior to the termination. If the government terminates a contract for default, the defaulting company is entitled to recover costs incurred and associated profits on accepted items only and may be liable for excess costs incurred by the government in procuring undelivered items from another source. One or more of our government contracts could be terminated under these circumstances. Some government contracts grant the government the right to use, for or on behalf of the U.S. government, any technologies developed by the contractor under the government contract. If we were to develop technology under a contract with such a provision, we might not be able to prohibit third parties, including our competitors, from using that technology in providing products and services to the government.

Ongoing legal proceedings or any future similar lawsuits could limit future purchases of BioThrax by the U.S. government.

The results of ongoing or future legal proceedings could reduce demand for BioThrax by the U.S. government. For example, in 2003, a group of unnamed military personnel filed a lawsuit seeking to enjoin the DoD from administering BioThrax on a mandatory basis without informed consent of the recipient or a Presidential waiver, and, in 2004, a federal court issued the requested injunction. In 2005, the FDA issued an order affirming the BioThrax license, and, as a result, an appellate court ruled in February 2006 that the injunction was dissolved. In October 2006, the DoD announced that it was resuming a mandatory vaccination program for BioThrax for designated military personnel and emergency DoD civilian personnel and contractors. In December 2006, the same counsel who brought the prior lawsuit filed a new lawsuit contending that the FDA's 2005 final order should be set aside and that BioThrax is not properly approved for use in the DoD s vaccination program. In February 2008, the federal court in which that case was pending dismissed the action, concluding that FDA did not make a clear error of judgment in reaffirming the safety and efficacy of BioThrax.

Although we are not a party to the lawsuits challenging the DoD s mandatory use of the vaccine, if a court were to again enjoin the DoD's use of BioThrax on a mandatory basis, the amount of future purchases of BioThrax by the U.S. government could be affected. Furthermore, contractual indemnification provisions and statutory liability protections may not fully protect us from all related liabilities, and statutory liability protections could be revoked or amended to reduce the scope of liability protection. In addition, lawsuits brought directly against us by third parties, even if not successful, require us to spend time and money defending the related litigation.

Risks Related to Our Financial Position and Need for Additional Financing

We may not maintain profitability in future periods or on a consistent basis.

We commenced operations in 1998, and the FDA approved the manufacture of BioThrax at our renovated facilities in Lansing in December 2001. Although we were profitable for each of the last five fiscal years, we have not been profitable for every quarter during that time. Our profitability is substantially dependent on revenues from BioThrax product sales. Revenues from BioThrax product sales have fluctuated significantly in recent quarters, and we expect that they will continue to fluctuate significantly from quarter to quarter based on the timing of our fulfilling orders from the U.S. government. We may not be able to achieve consistent profitability on a quarterly basis or sustain or increase profitability on an annual basis.

Our indebtedness may limit cash flow available to invest in the ongoing needs of our business.

As of December 31, 2007, we had $57.9 million principal amount of debt outstanding and remaining borrowing availability of $3.2 million under our revolving line of credit. We may seek to raise substantial external debt financing to provide additional financial flexibility. Our leverage could have significant adverse consequences, including:

requiring us to dedicate a substantial portion of any cash flow from operations to the payment of interest on, and principal of, our debt, which will reduce the amounts available to fund working capital, capital expenditures, product development efforts and other general corporate purposes;
increasing the amount of interest that we have to pay on debt with variable interest rates if market rates of interest increase;

increasing our vulnerability to general adverse economic and industry conditions;

limiting our flexibility in planning for, or reacting to, changes in our business and the industry in which we compete; and

placing us at a competitive disadvantage compared to our competitors that have less debt.

We may not have sufficient funds or may be unable to arrange for additional financing to pay the amounts due under our existing debt. In addition, a failure to comply with the covenants under our existing debt instruments could result in an event of default under those instruments. In the event of an acceleration of amounts due under our debt instruments as a result of an event of default, we may not have sufficient funds or may be unable to arrange for additional financing to repay our indebtedness or to make any accelerated payments, and the lenders could seek to enforce security interests in the collateral securing such indebtedness. The covenants under our existing debt instruments and the pledge of our existing assets as collateral limit our ability to obtain additional debt financing.

We expect to require additional funding and may be unable to raise capital when needed, which would harm our business, financial condition and operating results.

We expect our development expenses to increase in connection with our ongoing activities, particularly as we conduct additional and later stage clinical trials for our product candidates. We also expect our commercialization expenses to increase in the future as we seek to broaden the market for BioThrax and if we receive marketing approval for additional products. We also are committed to substantial capital expenditures in connection with our facility expansion in Lansing and may undertake additional facility projects in the future.

As of December 31, 2007, we had $105.7 million of cash and cash equivalents. Our future capital requirements will depend on many factors, including:

the level and timing of BioThrax product sales and cost of product sales;

the timing of, and the costs involved in, completion of validation and qualification activities related to our new manufacturing facility in Lansing, Michigan and the build out of our manufacturing facilities in Frederick, Maryland;
the scope, progress, results and costs of our preclinical and clinical development activities;

the costs, timing and outcome of regulatory review of our product candidates;

the number of, and development requirements for, other product candidates that we may pursue;

the costs of commercialization activities, including product marketing, sales and distribution;

the costs involved in preparing, filing, prosecuting, maintaining and enforcing patent claims and other patent-related costs, including litigation costs and the results of such litigation;
the extent to which we acquire or invest in businesses, products and technologies;

our ability to obtain development funding from government entities and non-government and philanthropic organizations; and

our ability to establish and maintain collaborations, such as our collaboration with Sanofi Pasteur.

Our committed external sources of funds consist of the remaining borrowing availability under our revolving line of credit with Fifth Third Bank, development funding under our collaboration agreement with Sanofi Pasteur, funding from NIAID and BARDA, including for studies related to our anthrax immune globulin therapeutic product candidate. To the extent our capital resources are insufficient to meet our future capital requirements, we will need to finance our cash needs through public or private equity offerings, debt financings or corporate

collaboration and licensing arrangements, which we may not be able to obtain when needed or on attractive terms, which would force us to delay, reduce the scope of or eliminate our research and development programs or reduce our planned commercialization efforts.

Our ability to borrow additional amounts under our loan agreements is subject to our satisfaction of specified conditions. Additional equity or debt financing, grants, or corporate collaboration and licensing arrangements may not be available on acceptable terms, if at all. If we raise additional funds by issuing equity securities, our stockholders may experience dilution. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

Any debt financing or additional equity that we raise may contain terms, such as liquidation and other preferences that are not favorable to us or our stockholders. If we raise additional funds through collaboration and licensing arrangements with third parties, it may be necessary to relinquish valuable rights to our technologies or product candidates or grant licenses on terms that may not be favorable to us.

Risks Related to Manufacturing and Manufacturing Facilities

We have initiated a manufacturing facility expansion program. Delays in completing and receiving regulatory approvals for these manufacturing facility projects could limit our potential revenues and growth.

We are spending significant amounts for the validation and qualification activities for our new 50,000 square foot manufacturing facility on our Lansing, Michigan campus, which has been designed and constructed to enable us to manufacture BioThrax on a large scale for our existing and potential future customers. This new facility is a large scale manufacturing plant that we can use to produce multiple vaccine products, subject to complying with appropriate change-over procedures.

We also own two buildings in Frederick, Maryland that are available to address our future manufacturing requirements and have initiated initial engineering design and preliminary utility build out for these facilities. The completion of the Lansing facility and, if we proceed, the build out of the Frederick facilities, will involve substantial expenditures and likely require external sources of funds. Any delays in the validation and qualification activities may adversely affect our ability to manufacture our commercial product candidates for clinical trials or commercial sale.

We anticipate that we will initiate large scale manufacturing of BioThrax at the new Lansing facility in 2008. Our plans assume that the FDA will not require us to complete a human bridging trial demonstrating that BioThrax manufactured at our new facility is bioequivalent to BioThrax manufactured at our existing facility. We currently expect to rely on non-clinical studies for these purposes. However, the FDA has not approved our plan to rely on non-clinical studies without conducting a human bridging trial and may not do so. If the FDA requires us to conduct a human bridging trial, the initiation of large scale manufacturing of BioThrax at our new Lansing facility will be delayed and we will incur additional unanticipated costs.

Constructing and preparing a facility for commercial vaccine manufacturing is a significant project. For example, constructing the new Lansing facility with increased manufacturing capacity requires that we scale-up both fermentation and downstream processing compared to the levels employed at our existing production facility. These projects may result in unanticipated delays and cost more than expected due to a number of factors, including regulatory requirements. The FDA must approve our new manufacturing facilities before they can be used to commercially manufacture our products. For example, we are required to show that the product we manufacture in our new Lansing facility is comparable to BioThrax manufactured at our existing facility, which, as discussed above, may require additional clinical studies.

The costs and time required to comply with the FDA s current Good Manufacturing Practice, or cGMP, regulations, or similar regulatory requirements for sales of our products outside the United States, may be significant. If validation and qualification activities of our new facility in Lansing are delayed, we may not be able to manufacture sufficient quantities of BioThrax to allow us to increase sales of BioThrax to the U.S. government and other customers, which would limit our opportunities for growth. Cost overruns associated with constructing either our Lansing or Frederick facilities could require us to raise additional funds from external sources. We may not be able to do so on favorable terms or at all.

BioThrax and our immunobiotic product candidates are complex to manufacture, especially on a large scale commercial basis, which could cause us to delay product launches or experience shortages of products.

BioThrax and all our product candidates are biologics. Manufacturing biologic products, especially in large quantities, is complex. The products must be made consistently and in compliance with a clearly defined manufacturing process. Accordingly, it is essential to be able to validate and control the manufacturing process to assure that it is reproducible. Slight deviations anywhere in the manufacturing process, including obtaining materials, filling, labeling, packaging, storage and shipping and quality control and testing, some of which we experience from time to time, may result in lot failures, delay in the release of lots, product recalls or spoilage. We will not be able to sell any lots that fail to satisfy release testing specifications.

FDA approval is required for the release of each lot. We must provide the FDA with the results of potency testing before lots are released for sale. We have one mechanism for conducting this potency testing that is reliant on a unique animal strain for which we have no redundancy. In developing redundancy, we may face significant regulatory hurdles. In the event of a problem with this strain, if we have not developed redundancy, we would not be able to provide the FDA with required potency testing.

In addition, BioThrax must be maintained at a prescribed temperature range during shipping, and variations from that temperature range could result in loss of product and could adversely affect profitability. Delays, lot failures, and shipping deviations or spoilage could cause us to fail to satisfy customer orders or contractual commitments, lead to a termination of one or more of our contracts, lead to delays in our clinical trials or result in litigation or regulatory action against us, any of which could be costly to us and otherwise harm our business.

Disruption at, damage to or destruction of our manufacturing facilities could impede our ability to manufacture BioThrax, which would harm our business, financial condition and operating results.

We currently rely on our manufacturing facilities at a single location in Lansing for the production of BioThrax. Any interruption in manufacturing operations at this location could result in our inability to satisfy the product demands of our customers. A number of factors could cause interruptions, including: