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**Testimony of
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Select Committee on Homeland Security**

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Hearing on “Bioshield: Countering the Bioterrorist Threat”

Mr. Chairman, members of the Select Committee, thank you for the invitation to appear before you today on behalf of Human Genome Sciences, Inc. My name is Dr. William Haseltine, and I am Chairman and Chief Executive Officer of Human Genome Sciences, which I founded in 1992. Prior to that, I was a professor at Dana-Farber Cancer Institute, Harvard Medical School and Harvard School of Public Health from 1976 to 1993.

Human Genome Sciences is a biopharmaceutical company located in Rockville, Maryland, that discovers, develops and manufactures gene-based drugs to treat and cure disease. Currently, we have eight drugs in clinical trials and a broad pipeline of preclinical compounds. These include novel human protein and antibody drugs discovered through our genomics-based research, as well as new, improved, long-acting versions of existing proteins created using our albumin fusion technology.

ABthrax™

The primary focus of Human Genome Sciences has *not* been the development of drugs to protect against attack by biological and chemical weapons. Nevertheless, just over seventeen months ago, we realized that our company had the technology and capability to develop an effective, near-term countermeasure against one of the nation's most immediate and serious bioterrorism threats – anthrax. As a company headquartered just outside Washington D.C., we witnessed first-hand the potentially devastating effects of the use of anthrax as a terrorist weapon in late 2001. Thus, using private funds, Human Genome Sciences developed a fully human monoclonal antibody drug – called ABthrax – that specifically binds to a key anthrax toxin, thereby preventing or treating the lethal effects of the bacteria.

The drug can be given prior to or after exposure; and it could be used alone or in conjunction with the current vaccine and antibiotics. We have shown, in animals, that ABthrax is effective against high doses of anthrax, and are now ready to begin manufacturing of this product and to initiate human safety trials. In order to move forward, however, we need a commitment from the federal government to purchase the drug. With proper funding, this product could be available for emergency use as early as the end of next year. A properly designed and implemented Bioshield would provide the mechanism for this to happen.

Anthrax infection is caused by a spore-forming bacterium, *Bacillus anthracis*, which multiplies in the body and produces lethal toxins. Most anthrax fatalities are caused by the irreversible effects of the anthrax toxins. Research has shown that protective antigen is the key facilitator in the progression of anthrax infection at the cellular level.¹ After protective antigen and the other anthrax toxins are produced by the bacteria, protective antigen binds to the anthrax toxin receptor on cell surfaces and forms a protein-receptor complex that makes it possible for the anthrax toxins to enter the cells. ABthrax blocks the binding of protective antigen to cell surfaces and prevents the anthrax toxins from entering and killing the cells.

¹ Inglesby TV, O'Toole T, Henderson DA, et al. Anthrax as a Biological Weapon, 2002: Updated recommendations for Management. JAMA May, 2002. 287(17): 2236-2252.

Currently, two options are available for the prevention or treatment of anthrax infections – a vaccine and antibiotics. Both are essential to dealing with anthrax, but both have limitations. The anthrax vaccine takes several weeks following the first doses before immunity is initially established. The vaccine also requires multiple injections over a period of eighteen months, in addition to annual boosters, to maintain its protective effect.² Antibiotics are effective in killing anthrax bacteria, but are not effective against the anthrax toxins once those toxins have been released into the blood. Antibiotics also may not be effective against antibiotic-resistant strains of anthrax.³

In ABthrax, Human Genome Sciences has discovered a third defense against anthrax infections. In contrast to the anthrax vaccine, a single dose of ABthrax confers protection immediately following the rapid achievement of appropriate blood levels of the antibody. In contrast to antibiotics, ABthrax is effective against the lethal toxins released by anthrax bacteria. It may also prevent and treat infections by antibiotic-resistant strains of anthrax.

Results from preclinical studies conducted to date demonstrate that a single dose of ABthrax administered prophylactically increases survival significantly in both rabbits and nonhuman primates exposed by inhaling many times the lethal dose of anthrax spores. In both models, we observed an absence of bacteria in the blood of all ABthrax-treated animals that survived. The rabbit and nonhuman primate models of inhalation anthrax are regarded as sufficient to demonstrate the efficacy of therapeutic and prophylactic agents in treating or preventing anthrax infection. A single dose of ABthrax also fully protected rats against a lethal challenge with the anthrax toxins. Full results of these studies will be

² The FDA-approved anthrax vaccine, known as Anthrax Vaccine Adsorbed (AVA), is only administered to persons at high risk of exposure, like U.S. military personnel, but it is not recommended for the general population. BioPort, Inc. Anthrax Vaccine Adsorbed (BIOTHRAX™) Product Insert. Jan. 31, 2002. An improved version of the vaccine is currently under development, but its efficacy and suitability for civilian use are unknown, and it is not projected to be available until 2005 at the earliest.

³ Bioengineered strains of anthrax that are resistant to multiple antibiotics, including Ciprofloxacin, have already been produced both domestically and overseas, and can be readily made using ordinary laboratory procedures. Friedlander A.M. Anthrax: clinical features, pathogenesis, and potential biological warfare threat. In: Remington J.S., Schwartz M.N., eds. Current clinical topics in infectious diseases. Vol. 20. Malden, Mass.: Blackwell Science, 2000:335-49. Brook et al. In vitro resistance of *Bacillus anthracis* Sterne to doxycycline, macrolides, and quinolones. *Intl. J. Antimicrob. Agents.* 2001; 18:559-562.

disclosed in upcoming scientific meetings and publications as appropriate; they have already been shared with key government scientists.

Based on our preclinical results to date, we believe that ABthrax has the potential to be used both prophylactically and therapeutically. For example, ABthrax may be used to protect rescuers entering a contaminated building, soldiers in an infected environment, or exposed individuals after an attack. In addition, post-exposure treatment may lessen the natural progression of anthrax infection and increase survival. Human Genome Sciences plans to file an Investigational New Drug application in the near future, seeking clearance from the U.S. Food and Drug Administration (FDA) to begin clinical trials to evaluate the safety, tolerability, and pharmacology of ABthrax in healthy adults.

Project Bioshield

Many companies have the capability and are willing to develop new products to protect against attack by biological and chemical weapons or other dangerous pathogens. A few firms, such as Human Genome Sciences, have already done so. The primary challenge we all face is the absence of a commercial market for such drugs. In most cases, the only viable market is the federal government and, potentially, our foreign allies.

Project Bioshield, which aims to harness public and private resources in an innovative effort to develop defenses against bioterror, could potentially create such a market. While the Department of Health and Human Services currently has the authority to purchase and stockpile drugs such as ABthrax, the specific framework created by Project Bioshield would clarify and enhance that authority. Indeed, overlapping jurisdictions between HHS and the Department of Homeland Security have complicated the picture, at least temporarily. A defined and transparent process – with a clear path between threat evaluation, scientific validation and product procurement – will go a long way toward giving companies the assurance they need to develop innovative new products to protect the public from chemical or biological attacks.

With respect to Project Bioshield, I would urge to Select Committee to consider three broad points:

First, in order to be as effective as possible, the program must be flexible. President Bush recently stated that, “Project Bioshield will give our scientific leaders greater authority and flexibility in decisions that may affect our security.”⁴ The vast differences between biological pathogens is mirrored by the diversity of potential treatments. For example, traditional small-molecule drugs, such as Ciprofloxacin, are manufactured from simple chemical building blocks or extracted from natural sources. In contrast, biologics such as ABthrax are manufactured in genetically engineered living organisms (bacteria or mammalian cells) and require a process that is more expensive, complex, and time consuming. The process of transitioning from an early-stage process to large-scale manufacture often can take anywhere from 12 to 16 months to complete. Thus, a “one size fits all” procurement model will ultimately discourage the development of certain countermeasures.⁵ Project Bioshield should provide not only for procurement of products that have already been developed, but also for late-stage development of promising drugs.

Second, Project Bioshield should be an equal partnership between the federal government and those companies willing to commit their expertise and resources to defeat weapons of bioterror. As Secretary Tommy Thompson stated before the Select Committee’s Subcommittee on Emergency Preparedness and Response:

“[Project Bioshield] must be a public and private partnership. The pathway from idea to final product is complex. The best scientific approach to identifying the best drug and

⁴ Remarks by President George W. Bush on the Bioshield Initiative (Feb. 3, 2003), *at* <http://www.whitehouse.gov/news/releases/2003/02/20030203-13.html>.

⁵ Current versions of the Project Bioshield authorizing legislation do not grant the Department of Health and Human Services the authority to engage in “other transactions” for R&D and prototype development, thereby limiting the agency’s ability to engage in collaborative R&D arrangements. In contrast, the Department of Defense has such “other transactions” authority to make acquisitions through transactions other than contracts, grants or cooperative agreements, allowing the military to reap the benefits of research and development being done by non-defense contractors for commercial applications. The Department of Homeland Security was recently granted similar authority through the Homeland Security Act of 2002. See Pub. L. No. 107-296, 116 Stat. 2135, § 831 (2002).

vaccine candidates must be based on laboratory studies. Testing must be performed in appropriate animal models to document safety and appropriate protective or treatment response, and to help determine dosing. Human studies must be carefully initiated to assure the basic safety of the product, and then appropriate dosing and response must be determined based on measurements of levels of drug or antibody predicted to have a protective effect. Steps must be taken to assure that the materials used to make the product and the final product itself can be manufactured safely, free of contaminants, and with reproducible and predictable purity, potency, and composition. Careful trials in humans, or where not possible, animal models, must be performed to show that the product is safe and effective for the types of populations who might receive it and against the methods of infection or exposure that could be encountered. All of these steps require careful planning, experience, and ongoing management and scientific evaluation. Costs to develop and manufacture high quality biological products and perform and evaluate the needed animal and human studies are high. Grants and contract mechanisms may not always be sufficient or attract the most experienced manufacturers. Manufacturing capacity for biological products, particularly for vaccines, is not substantial. For all these reasons, the best possible support and public-private partnerships and teamwork are essential.”⁶

A critical element of such a partnership is the mutual willingness to take and share measured risks. Thus, provisions in the Bioshield legislation that allocate unfairly contract risk in a manner inconsistent with current federal procurement policy and practice could have a chilling effect on collaboration with the private sector.⁷ In particular, Bioshield should provide for early funding of products in order to fairly allocate the risk between the parties.

Similarly, in the absence of a commercial market for drugs such as ABthrax, a permanent and secure source of funding is vital to encourage private investment in the development of medical countermeasures. Pharmaceuticals – and biologic drugs in particular – have enormous development

⁶ Statement by HHS Secretary Tommy G. Thompson on Project Bioshield before the Committee on Energy and Commerce Subcommittee on Health and Committee on Homeland Security Subcommittee on Emergency Preparedness and Response (Mar. 27, 2003), at <http://www.hhs.gov/asl/testify/t030327.html>.

⁷ Current versions of the Project Bioshield authorizing legislation would preclude payment under a contract until delivery is made of a “substantial portion” of the product. In contrast, existing procurement laws and regulations provide for a variety of payment procedures that are negotiated by the parties based on the unique requirements and risks of each contract. Similarly, the Bioshield legislation permits the termination of a contract if a reasonable quantity of the product is not delivered within 3 years. In such a case, the contractor is not entitled to any payment.

costs that can only be recouped well into the procurement phase. Without guaranteed funding, companies will face substantial risk in developing these products and will likely choose instead to pursue more commercially viable projects. The President's proposal for the creation of a permanent indefinite funding authority will stimulate innovation, spur private investment, and enable the government to purchase novel therapies without delay.

This brings me to my final point: Timing is critical. Agencies responsible for administering Project Bioshield should take a proactive approach to identifying, evaluating and procuring effective drugs. I applaud the Select Committee for acting expeditiously in considering the Bioshield legislation and the Administration for making its enactment and implementation a priority. Near-term delays in evaluating and securing the production of viable countermeasures can disproportionately prolong the procurement such drugs. In the case of ABthrax, Human Genome Sciences is ready to move the drug into production, which will require significant investment to secure a manufacturing facility and perfect the manufacturing process. Due to the demand for such specialized facilities, a delay of months now could postpone delivery of the drug by over a year. We are also ready to begin clinical safety trials in humans, having already demonstrated the drug's efficacy.⁸ To date, ABthrax has been developed entirely with private funds, but in order to move forward the company needs a commitment from the federal government to develop, manufacture and purchase the drug. With sufficient government support, Human Genome Sciences can begin producing significant quantities of ABthrax by the end of next year.

Thank you again for this opportunity to testify and I look forward to answering your questions.

⁸ Under the Bioterrorism Act of 2002, the FDA specified the evidence required to demonstrate the efficacy of new drug and biological products used to counter biological agents, when traditional efficacy studies in humans are not feasible. Public Health Security And Bioterrorism Preparedness And Response Act Of 2002: Section 123. <http://www.fda.gov/oc/bioterrorism/PL107-188.html>. According to the guidelines set forth in the Act, successful studies in relevant animal models will be considered sufficient to establish efficacy for licensure and marketing approval. ABthrax is effective in preventing anthrax infection in two relevant models, rabbits and nonhuman primates. According to the guidelines, human clinical trials will be required to establish safety, tolerability, and pharmacology, but not efficacy.