Testimony of

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Bioshield II: Responding to An Ever-Changing Threat

Thank you for providing me with the opportunity of testifying before you today on the issue of market incentives for encouraging development of countermeasures to respond to bioterrorism threats. I am testifying in my personal capacity, and the opinions I offer in this testimony are my own.

In my testimony, I will address the issue of intellectual property incentives that have been proposed for inclusion in BioShield II. In particular, I will be directing my testimony toward the questions of patent term restoration, a patent bonus concept, and data exclusivity proposals.

Earlier this year, the Congress started an important process of creating economic and other incentives to encourage industry to discover and develop new drugs and other technologies to respond to the threat of bioterror agents. It did this by setting up assured procurement opportunities, expedited and relaxed drug evaluation procedures, and other measures. Project Bioshield I is a well-designed effort and has enhanced incentives for the public and private sector to conduct research and development related to this important field of endeavor.

As many of the witnesses who testified on the original Bioshield legislation observed, the provision of an assured Federal Government purchasing authority and assured funding for research and development will only go so far in encouraging the development of new products. Additional measures are needed to encourage creation of an industry that will commit its own funding and take the risks necessary to bring innovative new products to market. And, as was previously observed, to be viable, the biodefense industry - and the markets from which it will obtain its capital - must view the opportunities in this field to be comparable to those in other fields of pharmaceutical industry. Thus, the environment in which this industry will exist must

have the same type of market incentives and certainties that exist in the biotechnology and pharmaceutical industry today.

A. Metrics for Success for a Biodefense Industry

A viable biodefense industry is one that engages in new product discovery and development motivated by the opportunity for market success, rather than through government support or indirect subsidies, standing alone. The factors that will be necessary for such an industry to evolve in the United States are the same as those that have proven necessary for our successful U.S. biopharmaceutical research and development environment. These factors can be summarized briefly as follows.

1. Assured Market Exclusivity for Successful Products

The biotechnology and pharmaceutical industries are extremely market-savvy, and the market is extremely savvy about these industries. What this means is that the market immediately rewards - and also severely punishes - those companies that stray from an essential formula for success. That formula requires the new venture to demonstrate not only that it has created an innovative new product or service, but that it will enjoy meaningful and assured market exclusivity for that new product or service.

Meaningful market exclusivity in these industries means that the innovator will face only technology competition, not price competition for a reasonable period after its product launches. In other words, the market assumes that the primary risk (if any) of competition during the market exclusivity period will come from different products that must be independently shown to be safe and effective ("technology" competition), and not from significantly lower cost copies of the same product ("price" competition). The consequences of earlier price competition are obvious - the sooner that price competition arrives, the smaller the overall return will be for the innovator and the investors that backed that innovator. And, of course, the smaller the possible return, the weaker the incentive will be to undertake the venture and fund it. In simple terms, unless companies can show that they have a decent chance of making a significant return on an investment, they will lose the fierce competition for capital.

Companies must also be able to convince savvy and skeptical investors that their market exclusivity will be relatively certain. In my experience, most companies and ventures tolerate a fair amount of risk of competition from other innovation in the biopharma field. This is in part because of the high failure rate in this industry, and in part the broad diversity in possible new products that can come out of basic research and development activities. Thus, while many examples exist where an innovator has faced competition from another innovative product within a year or two of the first product's market launch, it is more common that several years will pass after the first of a new class of products has been launched. Obviously, the longer the period of market exclusivity, the stronger the incentive for investing in research and development of new products. But, within the decision-making process of funding research and development toward a commercial product, this risk is accepted as a legitimate one that can be managed.

What is not tolerated by the investment community is risk that is unpredictable. For example, the prospect of political interventions in the market that operate to deprive a company of its market

exclusivity after that company has finally brought a product to market can be devastating to the industry. Similarly, a legal system that offers uncertain market exclusivity is very difficult to use to assure skeptical investors. Uncertainty in this respect means that a company that does the work to qualify for market exclusivity - either through patents, data or other market exclusivity - either is not granted that exclusivity, or is granted less exclusivity than anticipated.

2. Efficient Technology Transfer and Rights that Protect the Entire Venture

There is a diverse community of entities that contribute to the discovery and successful development of new pharmaceutical products. The members of this community include the public research community, including NIH and the university sector, small startup entities, the capital markets, and, critically, larger biotechnology and pharmaceutical companies. A close relationship among these entities is essential for the biotech and pharmaceutical - and correspondingly a future biodefense industry -to exist and succeed, and for new ideas to move from the lab bench to the market.

Of course, a continuing U.S. success story is the close partnership between the public sector research community and the commercially-focused biotechnology and pharmaceutical industries. This partnership has effectively moved scientific discoveries and advances from the lab into the stream of commerce. Each sector has its role to play in this partnership. The public research sector plays the critically important role in advancing basic science, and in identifying new drug candidates or platforms for drug discovery. The primary role of the private sector is the difficult task of translating advances in science into new products and services, and in taking the steps needed to bring these products to market.

The promise of market exclusivity that protects all members of the development venture is the glue that holds this environment together. Often, a compound discovered in the university lab becomes the basis of the ultimate product. Just as often, this is not the case, but the early work plays a significant role in identifying and developing the final product or service that does reach the market. Either way, the early patents that are awarded on these innovations - frequently to university researchers or small startup companies - become the patents that are relied upon to protect the products that eventually reach the market.

Efficient and effective technology transfer, through the Bayh-Dole Act and other mechanisms, is thus essential. Effective technology transfer means that the early stage developer can transfer intellectual property rights it has obtained that will protect its efforts, along with the work of a commercially-focused partner, and ultimately will enable the commercial partner to achieve market exclusivity in products that actually reach the market. Thus, efficient technology transfer enables a company to take in a promising candidate and begin the difficult process of developing these candidates into actual products and services.

In recent years, there has been a trend toward more partnerships between young biotechnology companies and established biotechnology or pharmaceutical manufacturers. Fewer and fewer companies are taking the highest risk path that starts with drug discovery and ends with the launch of a product. Instead, many biotech companies focus on early stage drug identification and development. Once the small biotech company has identified a promising lead, confirmed its potential and has secured strong intellectual property rights around it, it then seeks to partner

with a larger entity to take the lead in clinical development, manufacturing and marketing of the product. These partnerships efficiently leverage the ability of the small biotech company to efficiently conduct focused discovery and characterization work, up to the phase of pre-clinical animal investigations, or perhaps small scale human clinical investigations. The larger entity then takes on the more challenging, expensive and riskier phases of product development; namely, human clinical investigations, development of manufacturing process technology to scale up production to meet expected product demands, drug approval, product launch, domestic market development and foreign approval and marketing.

In recent years, the established pharmaceutical and biotechnology companies have also played a more prominent role in financing the development of these companies and products. Thus, while the early stage biotech company continues to depend primarily on venture capital or other private sources of capital, there is an earlier intervention by established biotechnology or pharmaceutical companies in the development of these companies and their products.

3. Effective and Assured Market Exclusivity is Essential

As noted above, the "glue" that holds these efforts together is the assurance of market exclusivity. There are several mechanisms by which market exclusivity is granted to pioneer drug developers, including patents, data exclusivity (along with pediatric exclusivity) and orphan drug protection.

(a) Patent Exclusivity

Patents give their owner the right to exclude others from making, using, selling, offering for sale or importing the patented technology for a specific period of time. Thus, the patent theoretically can be used to prevent competition in the sale of the products that are covered by the patent.

Importantly, patents do not "automatically" confer market exclusivity. Instead, they have to be enforced by the patent owner against the infringer through litigation in the Federal district courts. Patent litigation is notoriously unpredictable, risky and expensive. Moreover, given the fact that the most patents are sought many years before the identity of a final product is known, there are substantial risks that these early patents do not effectively cover the final product that is being marketed. And, because a patent can be properly granted only for inventions that have not been publicly disclosed, it is often only the innovators at the very beginning of the drug development process that can obtain patents that will cover the commercial product. Thus, universities, public research organizations and small start-up biotechnology companies often own the patents that cover the ultimate product, rather than the company that has done the clinical work and product development necessary to bring the product to market.

Certainly, one benefit of the U.S. environment is the Hatch-Waxman Act. This Act provides a way for pioneer manufacturers and generic producers to resolve disputes over patents before the generic product has been launched. Under the Hatch-Waxman Act, the generic producer must provide detailed reasons as to why they believe a patent listed for the drug is invalid or would not be infringed. If the producer does so, the patent owner can commence an action for infringement. Before a final resolution of that infringement litigation, the generic application will not be approved by the FDA (subject of course, to a 30 month limit on such a stay of approval). Thus,

under the Abbreviated New Drug Application procedure, the patent owner can intervene to prevent infringing products from entering the stream of commerce, and keep them from doing so until questions over the scope and validity of the patent are resolved.

(b) Data Exclusivity

The other primary form of market exclusivity for pharmaceuticals is data exclusivity. These rights give de facto market exclusivity for those companies that conduct the original clinical investigations of a drug to demonstrate the new drug is safe and effective. Companies that wish to market generic copies of a product without performing their own independent clinical investigations to prove the drug is safe and effective must wait for a certain number of years after the first or "pioneer" drug product has been approved. Under the U.S. system, five years of data exclusivity are provided for drug products containing an active ingredient that has not been previously approved, but only three years are provided for new indications or supplements to previously approved drug products.

(c) Pediatric Exclusivity

Companies that demonstrate that their drug product is safe and effective through clinical investigations in pediatric populations can obtain an additional six months of exclusivity for doing that clinical work. The pediatric exclusivity provisions have been an effective incentive for companies to undertake this work, which often results in very small populations of patients that benefit from the clinical work. Pediatric clinical investigations are very difficult to conduct, and the absence of significant pediatric patent populations ordinarily is a strong deterrent to seeking authorization to market products to pediatric patients.

(d) Orphan Drug Exclusivity

Orphan drug exclusivity is another form of market exclusivity mechanism for new drugs. Orphan drugs are those drugs that have limited patient populations (e.g., less than 200,000 with the particular indication). A company that demonstrates the safety and effectiveness of a new product to treat an orphan indication is given seven years of exclusivity for that product and that indication. Orphan drug exclusivity is broader in effect than data exclusivity; other versions of the same drugs for the same indication may not be approved for marketing prior to the expiration of seven years from the approval of the orphan drug. Thus, unlike data exclusivity, orphan drug exclusivity blocks approval of both generic versions (e.g., copies of the drug that do not include clinical data) as well as other drugs that are supported by independent clinical evidence of safety and effectiveness.

Each of these mechanisms for market exclusivity has played an important role in stimulating industry to develop and bring to market new drug products. The guarantee of market exclusivity has encouraged companies to pursue development of new products despite significant risk of failure, offer a significant return on investment. Special market exclusivity incentives - such as orphan drug or pediatric exclusivity -- have also proven to be very effective in overcoming economic obstacles that have deterred drug development efforts in these settings. For example, few orphan drugs were developed prior to enactment of the Orphan Drug Act. The reason is simple; drugs that have a very limited patient population inherently have a very limited capacity

to turn a profit, much less a strong profit. The orphan drug authority changed this economic equation, and has stimulated the development of more than 250 approvals for orphan indications. Similarly, pediatric exclusivity has proven to be an effective economic incentive for companies to take on the task of proving their drugs are safe and effective in pediatric populations. This indirect but strong incentive of an additional six months of market exclusivity has encouraged companies to take on this challenging task of conducting pediatric clinical investigations, with over 100 pediatric approvals since the legislation was enacted in 1998.

B. Market Incentives for Research and Development of Countermeasures for Bioterror Pathogens

As noted above, the Congress has created special market exclusivity mechanisms to encourage the private sector to develop new drugs in setting where ordinary market incentives have proven to not be effective. These special market exclusivity measures have been effective in stimulating the development of new products for orphan indications and for pediatric clinical investigations.

As in the case of orphan drugs and pediatric indications, the market does not provide a clear incentive for companies to develop countermeasures. The significant reasons for this can be summarized as follows:

- There is no assured or consistent market for these products. While there certainly will be products that have "dual use" capabilities, the non-countermeasure applications of these products are not assured. Moreover, the goal is to develop innovative new products that can respond to a variety of unknown challenges. It is unlikely that "off the shelf" products will meet these needs

- When a need arises for countermeasures, there could be severe demands for the volume of products. Depending on the scale of the need, immense stress could be placed on the ability of a manufacturer to make products available in sufficient quantities. This stress may cause the manufacturer to turn to other producers to meet product demand. Alternatively, it may cause the manufacturer to maintain artificially large stocks of products, despite the absence of market demand for those products.

- The primary purchaser is likely to be the Federal Government in an emergency setting. The private sector and capital markets remember the reaction of the Federal Government in response to the anthrax scare in 2002. The pressure put on the manufacturer of Cipro® to slash prices - primarily the implicit threat of procuring the drug from an alternate supplier - sent a clear message to the private sector that there is no guarantee of a market driven price for these types of products.

Certainly, Congress has taken an important step in addressing these problems through BioShield I. These steps have led a number of companies to initiate work on development of countermeasures for bioterror pathogens. However, this incentive structure is limited in its scope and power to induce the private sector to start development efforts for these types of products. Thus, to complement these efforts, more direct and powerful market incentives are needed to overcome these significant deterrents for industry. The provisions of the Lieberman-Hatch proposals (S.666) appear to be well-designed to address these market challenges.

1. Full Patent Term Extension Authority

An important part of the Hatch-Waxman Act is its authority for a patent owner to extend the term of a patent to compensate for periods of time while a drug is in the regulatory review process. Under 35 U.S.C. §156, however, several limits are placed on the duration and nature of the extension. For example, the patent during its "extended" period can only be enforced against drugs the same drug product (within certain limits). The effective period of the patent (i.e., the period from the date the drug is approved until the patent expires) cannot exceed 14 years, and any individual extension cannot exceed five years. The way the present extension is calculated also gives only partial credit for phase I and II clinical investigations.

Section 5(c)(1) of Lieberman-Hatch would create a patent term extension authority that is not subject to these arguably arbitrary limits. Unlike present §156, the period of extension that will be available corresponds to the full period of regulatory review - including phase I activities -and is not capped by the 14 year effective term and 5 year individual extension limitations. This is important, as it may be possible to get a countermeasure approved on a faster track than the ordinary path a pharmaceutical product. In the absence of this new basis for calculating the extension authority, an otherwise deserving countermeasure patent might not qualify for a meaningful patent term adjustment.

2. Patent Bonus

An innovative feature of Lieberman-Hatch is its "patent bonus" provision. We note that there are many design options possible for creating such a bonus system. Under §5(d)(1), an entity that develops a countermeasure will be given the right to extend the term of one patent it owns, regardless of whether the product is the countermeasure.

The patent bonus appears to be limited in several key respects.

- Only an unexpired patent can be extended; it cannot operate to take revive expired patents or take generic products off the market.

- The patent bonus is only awarded once the company has successfully developed its new countermeasure, and fully met all procurement requirements and Government-specified product needs.

- A company that attempts to develop a countermeasure and ultimately fails will not get a patent bonus.

- Measures are included that prohibit marketing of a patent bonus - including the prohibition against acquisition for the purpose solely of obtaining the patent bonus and patent ownership requirements. These measures will effectively prevent improper use of the patent bonus.

- The only entities that appear capable of benefiting from the bonus are small businesses with less than $750M in revenue.

- The patent that is to benefit from the bonus authority must have been issued before the countermeasure marketing authority was granted.

These measures, along with other aspects of the legislation will ensure that the patent bonus is not abused.

The patent bonus appears to be an indirect but powerful incentive for companies to undertake countermeasure development notwithstanding the lack of commercial potential of such products. It is analogous to the pediatric extension authority, in that it awards an extension of market exclusivity for any indication for the drug product, in exchange for the sponsor successfully undertaking development of the countermeasure. To be successful, the patent bonus must (i) be assured, and (ii) encourage companies to shift existing resources to develop new countermeasures. An obligation that seeks to require a company to devote profits from products that have been given a patent bonus will not induce the pre-development activities that this patent bonus is designed to do. Moreover, the more "strings" that are attached to the patent bonus - particularly with how those strings limit future research and development activities of the company - the less effective the patent incentive will be. The experience of industry is that funding and incentives that come with strings attached that limit the commercial discretion of companies typically fail to win the confidence of companies and their investors.

3. Extended Data Exclusivity and Orphan Drug Exclusivity Periods

The third incentive in Lieberman-Hatch is an extension of data and orphan drug exclusivity periods for new countermeasures.

The legislation would extend the duration of new chemical entity (NCE) countermeasures and new indications/supplements/etc from the 5 and 3 year periods up to a 10 year period. Patent challenges that now are possible in the 4th year from product approval for NCE drugs and at any time after approval for non-NCE drugs may be made at nine years from product approval. Also, if the countermeasure qualifies as an orphan drug candidate, it also can obtain up to ten years (instead of seven) of orphan drug exclusivity.

The extended data exclusivity and orphan drug act periods are justified given the lack of certainty in when these countermeasure products might be needed. A data exclusivity period that pushes out the expiration of data exclusivity protection will be far more valuable to the industry than the 3 or 5 year options available (and which might expire before the commercial product actual is put on the market).

C. Conclusions

Product development against known diseases and disorders is immensely challenging and unpredictable. The industries that have undertaken the business of finding new products to treat these known diseases do so based on the availability of strong market exclusivity protections for their products. They understand that market demand for their products, coupled with strong market exclusivity through patents, data protection and other measures creates the possibility of a high return on investment. The incentives plainly work - experiences from the Orphan Drug Act

and pediatric exclusivity show that strong economic incentives can effectively overcome market-based impediments to product development.

By contrast, the threats of future bioterrorism are unknown and cannot be easily predicted. Even more pronounced market exclusivity measures will be necessary to encourage the private sector to enter and stay in this market, and to successfully develop countermeasures. The measures outlined in Lieberman-Hatch seem well-designed to achieve the goal of having companies stay active in the biodefense industry so that they can respond quickly when new threats materialize.

Thank you for your time and consideration of my views.