BIOTECHNOLOGY
INDUSTRY ORGANIZATION

October 10, 2006

Dr. Susan Coller
Policy Analyst
Office of Public Health Emergency Preparedness
Department of Health and Human Services
330 Independence Avenue, SW
Room G640
Washington, DC 20201

Dear Dr. Coller,

The Biotechnology Industry Organization (BIO) appreciates the opportunity to provide comments to the Department of Health and Human Services (HHS) on the draft Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) Strategy for Chemical, Biological, Radiological, and Nuclear (CBRN) Threats. We applaud the Department's efforts and commitment to develop a strategy, as well as the efforts in the recent BioShield Stakeholders Workshop on September 25-26, 2006. We also applaud the recognition of the importance and need to clearly identify the government's medical countermeasure acquisition plans and to provide clarity and transparency to the processes by which those plans are determined and fulfilled. We provide the following comments for your consideration, and look forward to continued dialogue on the public-private partnerships for national preparedness.

Strategic Objective #1: Identify and Prioritize Current and Future Medical Countermeasure (MCM) Objectives

Implementation Plan and Identification of Needs:
We applaud the issuance of the draft Strategy and look forward to timely issuance of the final PHEMCE Strategy. Establishing guiding principles and strategies is important to assure transparency of government decision processes. We also encourage timely issuance of an Implementation Plan. In order for the biotechnology industry to fully engage in the development of countermeasures to enhance national preparedness, the Implementation Plan should provide a sufficient level of detail on: (1) the agents for which HHS intends to purchase medical countermeasures, (2) approximate and reliable estimates of the size of populations intended to be covered, (3) the extent to which pre-

exposure prophylaxis, diagnostics, post-exposure prophylaxis, and treatment countermeasures are targeted for procurement, (4) preferred product characteristics such as, but not limited to, route of administration (including self-administration vs. assisted administration), dosage form, shelf-life, storage and handling, packaging (including single-dose vs. multi-dose), and flexibility in manufacturing surge capacity. These preferred product characteristics should be expressed in quantitative ranges and estimates. Uncertainty in these specifications, or a significant change late in the procurement cycle, can have a profound impact on risk assessments, and ultimately the time and cost of development.

The preferred characteristics should be accompanied by an indication of the relative weight by which they will be considered in procurement decisions and a concept of the valuation that would accompany preferred characteristics. If there are preferences that manufacturing capacity be located domestically versus internationally, these preferences should also be identified with an indication of relative weight. Biotechnology product development is inherently a lengthy and risky process, and companies must make important strategic decisions early and throughout the development process regarding technologies and product characteristics to pursue. It is important that these decisions be informed by the best available information of the market, which in the case of biodefense products is nearly entirely dependent upon the government's articulation of needs.

We also suggest that HHS identify tentative product requirement needs in advance of formal material threat assessments by the Department of Homeland Security (DHS) when those assessments are not expected to be imminently available. It is recognized that the formal requirements processes of HHS are statutorily dependent upon material threat determinations by the Department of Homeland Security (DHS). However, due to the lengthy nature of product development and the need to make critical business decisions early in the development process, the availability of medical countermeasures for national preparedness could be accelerated by early identification of tentative requirements. These tentative requirements should not reduce the urgency for formal threat assessments and formal requirements assessments, but could serve as a valuable compass while those assessments are expeditiously executed.

Prudent and Timely Use of BioShield Funds

In order to achieve robust national preparedness, BIO encourages HHS, working with DHS, to expeditiously move forward with the identification of medical countermeasure requirements and subsequent procurement recommendations. In developing recommendations, the challenge of allocating limited resources toward the procurement of medical countermeasures is recognized, as is the need to assess opportunity costs in purchasing decisions. However, it is important that these challenges be appropriately balanced with recognition of the need for quick and robust preparedness as well as the inherent risk of medical product development for national preparedness.

New risk agents and intelligence information will likely evolve over time. It is possible that the intelligence and risk assessment information upon which acquisitions are based may change after product procurement. Indeed, the very existence of effective medical

countermeasures against a particular agent could reduce the probability of malicious use of that agent. These factors make it infeasible to predetermine how the most efficient use of currently available reserve funds will be viewed in hindsight.

In light of the need for robust and expeditious preparedness and the infeasibility of complete accuracy in prediction of needs, we suggest that prudent use of BioShield funds, based on best available information on risk assessments and technology at a given point in time, be the overriding determinant in procurement recommendations. While opportunity costs are a reality to be considered, appropriate and prudent use of available funds that results in enhanced national preparedness should be both the goal in using currently available funds and the basis for any future requests for additional funding.

Procurement processes

Current authorities should be utilized to the fullest extent appropriate to lower the barriers to industry in contracting with HHS. Using simplified acquisition processes that are authorized under Project BioShield, where appropriate, could allow acquisition processes to be more consistent with standard commercial practices. For example, the requirement of submitting certified cost and pricing data can in some cases result in large administration burdens that create disincentives.

Once needs are identified, requests for information, requests for proposals, and contract awards should be developed and executed in a timely fashion. Significant delays between procurement process steps adversely affect the stability and predictability of the BioShield processes. This has the effect of dissuading investment in products needed for national preparedness and creates a disincentive for industry to engage in this area.

Additionally, to the extent authorized now or in the future, we encourage HHS to utilize milestone payments and advanced payments where appropriate. The receipt of any payment only upon delivery of product can present serious challenges to companies engaged in the long-term effort of medical countermeasure development. It is a common practice in standard biopharmaceutical development and marketing agreements for milestone payments to be provided upon successful completion of significant and agreed upon progress and to facilitate continued financial operation during the contractual time period. The receipt of payment only at the end of a project creates a disincentive and barrier to entry.

If strategies for vendor-managed inventory are contemplated, these should be carefully considered through dialogue with industry. In some cases these requirements may create a disincentive for industry participation, as they may be dissimilar to standard commercial practices of inventory management and create accounting and administrative burdens.

Opportunities to streamline and coordinate procurement processes and needs with other government stakeholders, including the Department of Defense, should be also incorporated into the Department's synchronization and coordination efforts. Separate

procurement processes can be costly and complicated for both industry and the government, whereas synergies can increase efficiencies.

Role of Research Tools, Diagnostics, and Surveillance Technologies

Research tools will be critical in developing technologies to identify and address enhanced, emerging, and advanced agents, and the development of these tools should be considered a priority. Additionally, diagnostics and surveillance technologies will be critical in detecting both current and future bioterrorism threats, as well as ensuring medical countermeasures of limited supply are most efficiently administered to those in need. Due to the specificity and sensitivity required for each targeted agent, many diagnostic technologies do not have a market to drive their development without government partnership and procurement, and similar to other biotechnology products, they require substantial time and resources for development. The funding and procurement of these technologies should be considered a high priority. Availability of these technologies in the mid-term time range will be predicated on appropriate development investments in the near-term time range. Accompanying reagents needed to fully employ the rapid use for targeted agents should also be considered for stockpiling. Additionally, in the area of diagnostic technologies, the potential addition of burdensome regulatory hurdles is a disincentive, especially for the development of products that will address future threats or current threats that have no market.

Currently Available, Next Generation, and Warm Base Manufacturing with Multiple Sources and Technologies.

We appreciate the long-term and comprehensive investment framework articulated in the draft strategy that considers both commercially available products and the continued and long-term investment in next generation products. A robust and stable market through public-private partnership is required to encourage and enable industry engagement. We are encouraged that the draft states the "PHEMCE Implementation Plan will address both currently available and next generation medical countermeasures and will regularly evaluate on a case-by-case basis strategies for long-term maintenance and/or replacement of medical countermeasures in the SNS. Currently available medical countermeasures will be considered for acquisition if they meet immediate, critical needs and may be effectively deployed under current preparedness plans. Investment to meet particular threats will not however be a singular event, but rather an ongoing process that synchronizes the lifecycle requirements of currently stockpiled medical countermeasures with on-going research and development efforts. This synchronization should ensure that, as current stockpiles age and decline, more appropriate, next generation products will be available for acquisition consideration."

The draft strategy also recognizes that the sophistication of threat agents across the CBRN spectrum will evolve over time, and that simultaneously the sophistication and availability of MCMs will evolve as technologies improve. The challenge in balancing these dimensions and opportunity costs is contemplated by "...[u]sing a more cost-effective and efficient approach, HHS might choose to fund fully the development of a needed MCM, take it through clinical trials and then purchase only a small stockpile and

principally rely on a finely honed, well-planned and exercised surge production capability to swiftly produce enough doses in a national crisis."

The complexity, cost, and regulatory considerations of biotechnology manufacturing facilities and production processes should be carefully considered in executing such an approach to ensure that both sunk investment costs and "warm-base" manufacturing costs are sufficiently addressed in contract terms. The ability of multiple manufacturers to mitigate supply risks should also be considered.

Biotechnology facilities must meet stringent regulatory requirements in their design, construction, validation, and maintenance, and their operation is often associated with high fixed costs. Additionally, regulatory requirements for processing can include maintaining personnel training and frequent equipment maintenance, and the timeline for some biotechnology product production is lengthy. These factors should be assessed in the valuation and viability of plans on a case-by-case basis in order to ensure that contracts will be adequate to incentivize industry and to inform its risk assessments in committing the time and costs of investment.

Recognizing the challenges of balancing the many dimensions of preparedness planning, we refer back to our suggestion above that the prudent use of funds, based on best available information at a given point in time, be the overriding determinant in acquisition planning, and that enhanced and continued national preparedness should be both the goal in using currently available funds and the basis for future requests for additional funding.

Concept of Operations

Concept of operations for medical countermeasures should include education and outreach to trauma centers, hospitals, and other establishments at which persons affected by an event may be presented. Education and outreach should also be extended to local authorities and first responders, as well as to entities and establishments (such as mass transit systems and large public gatherings), which if targeted could result in large populations requiring expedient medical attention. Including these elements in a concept of operations plan could increase awareness and understanding of the medical countermeasures by both medical professionals and the public, and ultimately enable the most efficient use of products.

Consideration should also be given to forward-deploying medical countermeasures where appropriate to ensure timely administration. For example, some threats may pose immediate life-threatening harm that requires expedient administration of medical countermeasures. In other cases, forward deployment may enable or improve efficient administration and maximize the number of persons who could benefit from countermeasures. Support for storage and maintenance costs to entities holding forward-deployed countermeasures should also be considered.

Additionally, because preparedness is dependent upon a strong public health infrastructure system, continual improvements to the nation's public health infrastructure should be considered in the concepts of operations. Enhancement of public health infrastructure, including detection, testing, vaccination and distribution infrastructure, is a necessary and complementary component to medical countermeasure development.

Strategic Objective #2: Build Balanced, Effective Programs Across all Phases of the PHEMCE

BIO has testified on the need for strong partnership throughout the development cycle of medical countermeasures and has urged strong support for such initiatives. We support partnering across the spectrum of product development, including advanced research and development. A coordinated effort that bridges the priorities of acquisition with both early and late stage development is needed to enable a strong public-private partnership. Proper funding and staffing of this function will be essential for its success.

The public/private partnership required for successful countermeasure development includes numerous government departments and agencies, each playing a key role in the process. The objectives and requirements of the various agencies must be aligned and coordinated with solicitation terms and must be part of the early dialogue. These activities include funding for early and late stage research and development, regulatory support, and contract management. For example, production and delivery of products are inherently affected by regulatory requirements. The expectations of regulators for licensure and emergency use authorization should be coordinated with the contract terms. Ambiguous, additional and unforeseen requirements that arise outside of contract terms magnify companies' financial risk. Strong and clear direction is required to coordinate the many agencies and objectives.

Strategic Objective #3: Increase Transparency and Predictability in the Nation's Civilian MCM Priorities

Dialogue with Industry

Transparency and predictability are essential to ensure a strong public-private partnership for national preparedness. This can be facilitated by the development of strategies and priorities through dialogue with industry. It is essential that industry and government have a shared understanding of objectives, and that purchase solicitations are developed in a framework that addresses the complexities of the biopharmaceutical industry and contain the appropriate level of specifications and delivery terms.

We support and appreciate the opportunity to provide comments to the draft strategy and the efforts devoted to the BioShield Stakeholders Workshop in September 2006. We also appreciate the efforts in developing the stakeholder Web portal, and look forward to assessing that tool and providing feedback on its utility.

We also urge the use of working groups and advisory boards, with industry membership, as vehicles to provide structured and formal dialogue. Committees and workgroups should extend dialogue to experts in academia and industry who may not be direct members of the committees or workgroups.

Regulatory Environment

BIO appreciates the recognition of the need to continue to streamline regulatory processes in the development of medical countermeasures. There has been significant progress in this area, including authorities for the approval of products using animal efficacy studies (the "Animal Rule") and Emergency Use Authorization. However, in order to fully realize the value of these authorities as mechanisms to enhance availability of medical countermeasures, further guidance on the application of these authorities is required.

For example, specific guidance on how the Animal Rule could apply to specific therapeutic areas is needed, including the development of animal models and the types of animal efficacy studies and human safety studies needed to enable approval through this authority. Additionally, specific guidance on the application of Emergency Use Authorization (EUA) to products is also required, including data submissions and potential and likely conditions and duration of use. It is recognized that because actual execution of EUA would require an assessment of an exigent emergency at hand, identifying criteria that may justify the application of EUA in advance of an emergency is challenging. However, because it is a very real possibility that medical countermeasures would be used under this authority, and because articulation of such criteria would provide an important and needed guide to the use of products, it is important that these guidance documents be developed expeditiously and with dialogue with industry.

Development and application of regulatory guidances and practices should be consistent throughout the centers in the Food and Drug Administration, and risks and benefits should be analyzed with recognition that products will be used in an emergency and in many cases may be the only medical intervention available.

Additionally, regulatory policy should be closely aligned with the PHEMCE strategy and Implementation Plan. New and burdensome regulatory hurdles, including in the area of diagnostics, present a disincentive especially for the development of products that will address future threats or current threats that have no market.

Among the strategies to develop and execute the above recommendations, a series of workshops dedicated to specific agents should be conducted to continue and foster in-depth dialogue with industry and increase understanding of the regulatory processes.

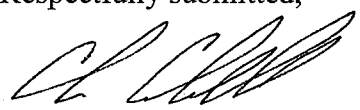
Strategic Objective #4: Develop, Recruit, and Support a World-class Workforce

BIO supports the recognition of the need for a highly qualified and accomplished government workforce in this public-private partnership for national preparedness. The

challenges and complex nature of countermeasure development, coupled with the urgent need to prepare, require that critical positions be staffed with expertise and understanding of the biopharmaceutical industry, including the functioning of both small and large companies. Mechanisms to identify experts through the use of fellowships, sabbaticals, internships, and exchange programs contemplated in the draft strategy are supported. In order to ensure the success of these efforts, HHS resources should be adequately available.

Thank you again for the opportunity to comment on this draft strategy. BIO appreciates the commitment of HHS in this matter and the progress that has been made in developing this draft strategy. We look forward to continuing to work with HHS on these important matters, including the forthcoming Implementation Plan. If there are any questions on these comments, please contact me at 202-962-9220 or ccolwell@bio.org.

Respectfully submitted,



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