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"Biodefense: Worldwide Threats and Countermeasure Efforts for the Department of Defense"

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Chairman Thornberry, Ranking Member Langevin, and members of the committee, thank you for the opportunity to be here today. I appreciate the opportunity to discuss government efforts and opportunities for collaboration to address our nation's biodefense priorities.

I am currently the Interim Executive Vice President and CEO of the Texas A&M Health Science Center and Principal Investigator for the Texas A&M Center for Innovation in Advanced Development and Manufacturing, a public-private partnership with the U.S. Department of Health and Human Services designed to enhance the nation's emergency preparedness against emerging infectious diseases.

My pathway to this position includes a career as an academic physician scientist, focusing on life threatening infectious diseases, particularly those diseases affecting adolescents and young adults. As a result of work in this field, I was invited to serve on one of DARPA's non-governmental science and technology assessment panels, the Defense Sciences Research Council (DSRC), which was responsible for developing concepts that could potentially lead to DARPA initiatives and "game-changing" capabilities benefitting national security. In this role, I chaired or co-chaired numerous intensive studies on chemical, biological, radiological, and nuclear (CBRN) security and countermeasures, decontamination, and warfighter performance under extreme conditions.

After five years on the DSRC, I was privileged to serve as Deputy Director, and then Director, of the Defense Sciences Office at DARPA, and honored to be the first medical doctor to become an office

director in the 50 year history of that agency. In my role as Director, working with a multidisciplinary team of the nation's finest scientists, physicians, and engineers, and with the budgetary opportunities provided to us by Congress, we developed and implemented an integrated platform of research initiatives, named Accelerating Critical Therapeutics (ACT), designed not only to provide new, highly effective medical countermeasure capabilities, but also to provide an unprecedented, flexible, adaptable, and rapid response to address and defeat the pervasive and growing threat of highly genetically modified or chimeric organisms for which the nation had no pre-existing vaccines, countermeasures, or technical approaches. Many DARPA programs begun at that time are now operational and have made an enormous impact on our public health preparedness and response.

One aspect of the portfolio that was extraordinarily challenging, even by DARPA standards, was the ability to develop low cost, highly flexible and adaptable manufacturing technologies capable of providing tens of millions of doses of vaccines or medical countermeasures (such as monoclonal antibodies or antidotes to chemical weapons) within weeks of notification. Such a capability did not exist in the civilian or military experience, and there were profound technical barriers to overcome. Among these barriers were traditional manufacturing facility architectures that were generally single use, and cost $1 billion or more. In addition, production platforms such as fertilized chicken eggs necessitated an enormous logistics tail, and therefore had very limited rapid response capabilities, even when heroic efforts were made by the U.S. Government and industry, as demonstrated in the 2009 H1N1 pandemic.

The concept of developing 21st century manufacturing capabilities had many champions, including DARPA and its technical assessment panels, leading academic groups such as the National Academy of Engineering and the University of Pittsburgh Medical Center, as well as many senior government officials including the President's Special Assistant for Biosecurity. Nonetheless, there was no obvious mechanism to test and implement these concepts, because there were no U.S. Government programs in place, and the concepts were far too innovative and high risk to be adopted by the commercial biopharmaceutical industry.

Implementation of 21st Century Manufacturing and Response at Texas A&M

The Texas A&M University System (TAMUS) is one of the largest systems of higher education in the nation, with a statewide network of 11 universities, seven state agencies, two service units and a comprehensive health science center. Led by Chancellor John Sharp, A&M System members educate more than 125,000 students and reach another 22 million people through service each year. With more than 28,000 faculty and staff, and a budget of approximately $3.8 billion annually, the A&M System has a physical presence in 250 of the state's 254 counties and a programmatic presence in every one. In 2011, externally funded research expenditures exceeded $780 million making it one of the premier research and development institutions globally.

In 2008, my assignment to DARPA was completed and I joined the Texas A&M System. Because the nation's security against CBRN threats was dependent on the development of highly flexible and adaptive manufacturing technologies, and to protect the U.S. commercial industry and tens of thousands of domestic jobs, we assembled a core team of scientists and engineers to fully leverage Texas A&M's robust resources and historical commitment to national service. Our mission was to perform the "proof of concept" breakthrough implementation of a flexible manufacturing facility that eventually could be the technological model for a national program.

With the enthusiastic support of Texas Governor Rick Perry, the Texas A&M Regents, and Chancellors McKinney and Sharp, and with a $50 million investment from Texas Emerging Technology Fund, our team aimed to design, develop, build, and operate a facility and associated program that would demonstrate: 1) highly flexible, adaptable, mobile manufacturing architectures and platforms, 2) an unprecedented response capability against emerging and intentional threats, and 3) a capital cost at least 80% less than the current state of the art. We named the project the National Center for Therapeutics Manufacturing (NCTM). The NCTM is now the core facility and primary site for developing and manufacturing Medical Countermeasures and Vaccines against CBRN threats for the Texas A&M Center for Innovation. A full description of the NCTM is provided below.

Overview of the Department of Health and Human Services Texas A&M Center For Innovation in Advanced Development and Manufacturing (CIADM)

The Texas A&M CIADM is the most highly funded of three national centers competitively awarded by the Department of Health and Human Services in June 2012, and is the only Center led by an academic institution. It is founded on an initial $285.6 million public-private partnership, consisting of approximately $176 million committed investment by the HHS, and $109 million supplied as cost share by academic, commercial, and State of Texas stakeholders and collaborators. The Center is designed to enhance the nation's preparedness and response against emerging infectious diseases, including pandemic influenza, and chemical, biological, radiological and nuclear threats. The Center will perform advanced research, facilitate development, ensure domestic manufacturing capacity, enable product FDA approval and mentor the next generation of public health professionals through education, training and outreach. The initial $285.6 million contract, over a five-and-one-half year base period, will result in the establishment of ***all capabilities*** required by the U.S. Government. In addition, there is a total potential contract duration of 25 years, including an additional >$2.4 billion in readiness and task order options that can be exercised at the discretion of the U.S. Government.

The Center leverages over $200 million in prior investments by the Texas A&M University System and the State of Texas in facilities and programs dedicated to advanced development and manufacturing of biopharmaceuticals. The specific high level objectives of the Center are the following:

- Provide the strategic national vaccine response to pandemic influenza, defined as 50 million vaccine doses delivered to the U.S. Government within four months, with initial doses available in 12 weeks;
- Research, develop, and manufacture vaccines and medical countermeasures to chemical, biological, radiological, and nuclear (CBRN) threats as requested by HHS; and
- Train the U.S. national workforce in biopharmaceutical manufacturing, animal model development, biosecurity-related clinical trials, and regulatory approval processes.

Subcontractors and Collaborators

Texas A&M has assembled a multidisciplinary team of subcontractors with expertise that spans the spectrum of disciplines needed to achieve the objectives, including process development, flexible manufacturing, preclinical testing (including BSL3 and BSL4 capacity), clinical trials, quality assurance/control, and regulatory affairs. Key subcontractors include:

- GlaxoSmithKline Vaccines (GSK): The world's largest vaccine developer with 30+ vaccines marketed worldwide, 11 licensed by the FDA, and 1.4 billion doses distributed annually. GSK is providing the cell based pandemic influenza vaccine candidate, as well as their proprietary adjuvant technology, to TAMUS in order to meet the nation's pandemic influenza vaccine surge requirements.

- Kalon Biotherapeutics (Kalon): The commercial development and manufacturing organization (CDMO) founded and owned by Texas A&M and the State of Texas, which provides core process development and manufacturing services for CBRN vaccines and medical countermeasures. Kalon is also GSK's development partner for its cell-based pandemic and seasonal influenza vaccines. Kalon staff includes former leaders from the global biopharmaceutical industry including Sanofi-Pasteur, Novartis, and Medimmune. These experienced professionals are already being supplemented by recent graduates from the Center's workforce development program.

- Other CIADM Partners include Lovelace Biomedical and Environmental Research Institute (non-profit research organization that conducts pre-clinical CBRN studies including nerve agents), UTMB-Galveston National Laboratory, Lonza (global pharmaceutical services company), Caliber Biotherapeutics (plant made vaccines and biopharmaceuticals), the Sabin Vaccine Institute at the Baylor College of Medicine (non-profit vaccine development institute), Sartorius (leading global bioprocess technology provider), and multiple Texas A&M System Components including the Texas A&M Institute for Preclinical Studies, the Texas A&M Engineering Experiment Station, Texas A&M University, and the Texas A&M Veterinary Diagnostic Laboratory.

- Collaborations: In addition to the above established partnerships, TAMUS has new collaborations with multiple entities focused on specific aspects of the CIADM, or related product development. Among these collaborations are confidential global pharmaceutical corporations, biotechnology companies, adult stem cell and cell therapeutics companies, the MD Anderson Cancer Center, and the University of Texas in Austin.

Biomanufacturing Infrastructure

The CIADM is leveraging pre-existing process development and manufacturing infrastructure at Texas A&M, but will also design, construct, and validate additional core facilities to supplement existing infrastructure. Among the key Center facilities now in design and/or construction are the following:

- National Center for Therapeutics Manufacturing (NCTM)
  Status: Operational and undergoing expansion and enhancement. All retrofit and upgrade activities are scheduled for completion by March 2014.

  The NCTM is a revolutionary, first-in-class, multi-product, multi-technology, 150,000 sq. ft. biopharmaceutical development and manufacturing facility. A key feature of the NCTM is the use of Modular Clear Rooms (MCRs), which are newly-developed, standalone, modular, **mobile**, self-contained and fault-tolerant biopharmaceutical clean rooms. The initial MCR concept was funded by the Department of Defense through DARPA and ARO. Through the NCTM project, TAMUS has developed, implemented, and validated novel bioprocess architectures that provide solutions for the commercial industry and the U.S. Government.

  These solutions include: the ability to accommodate multiple (up to six) simultaneous products up to the 1000 liter (L) scale in support of Phase I through Phase III clinical trials, as well as commercial manufacturing; flexibility to fundamentally rearrange, in near real-time, entire unit processes and clean room suites without disruption of simultaneous ongoing operations; the ability to surge multi-fold on a single product, within 24 hours, as needed to support biosecurity or commercial clinical needs. The NCTM also maintains limited fill and

finish capabilities primarily in support of clinical trials.

The NCTM is being expanded, enhanced, and outfitted for large scale operations via the CIADM contract, including the provision of an additional eight MCRs.

- Pandemic Influenza Vaccine Facility (PIF)

  Status: Design development completed; construction and initial facility commissioning are scheduled for completion by the 3rd quarter of 2015.

  The PIF will be a new, stand-alone, 100,000 sq. ft. facility designed to supply bulk antigen to meet the U.S. Government requirements for 50 million doses of pandemic influenza vaccine within four months, with the first doses supplied in twelve weeks. The PIF emphasizes the use of flexible, single use technologies, made possible by the highly advanced cell based production system from GSK. Within seven years, it is expected that the PIF will have no ongoing readiness costs charged to the U.S. Government, because it will also function as the licensed manufacturing facility for GSK's cell based seasonal influenza vaccine for North America. When not supplying commercial or pandemic influenza vaccines, the PIF is available for production of other CBRN countermeasures, particularly monoclonal antibodies and therapeutic proteins. The PIF will be operated by Kalon in partnership with GSK.

- Live Virus Vaccine Facility (LVVF)

  Status: Completed advanced schematic design, scheduled for completion of construction and commissioning by the 3rd quarter of 2015.

  The LVVF will be a new, stand-alone facility, adjacent to and synergistic with the PIF, dedicated to the process development and manufacture of live virus vaccines including products that require BSL-3 level biosafety. The LVVF will primarily focus on vaccines and countermeasures for biothreat agents, but also on commercial vaccines that utilize similar technologies. Live virus vaccines are emerging as a major platform technology for a variety of civilian diseases, including cancer. The current concept calls for an approximately 70,000 sq. ft. facility utilizing a combination of fixed modular, and mobile modular (MCRs), and the ability to more than triple its initial capacity as demand for live virus vaccines increases in

the next decade. To reduce capital and operational costs, the LVVF will leverage core infrastructure, such as power and utilities, from the adjacent PIF.

- Fill and Finish Facility

  Status: In phase of defining a program of requirements.

  This facility, to be located within the United States, will provide comprehensive large scale fill and finish capabilities for the CIADM as well as other government and commercial customers. The primary objective is to supply the CIADM with capability for fill and finish of live virus vaccines, to the level of two million vials per year. We also expect the facility to maintain additional capabilities including lyophilization for both viral and non-viral based vaccines. The operational partner for this program is currently under evaluation and selection by Texas A&M leadership team in collaboration with HHS.

- Process Development Facility (PD Facility)

  Status: In concept design, scheduled for completion in early 2015.

  To expand on current PD capabilities, the CIADM will build a flexible PD capability designed to support a full range of manufacturing platforms and products, from microbial to insect cell and mammalian systems, and products ranging from personalized protein and DNA vaccines, to monoclonal antibodies and therapeutic proteins.

- Caliber Biotherapeutics Facility

  Status: Completed and operational.

  Developed and built through a consortium comprised of Texas A&M and G-CON, LLC, and funded by the DARPA Blue Angel Program, the CIADM has partnered with Caliber Biotherapeutics to make available Caliber's plant-made pharmaceutical facility for HHS task orders, including vaccines and monoclonal antibodies. The facility has the capability to produce up to 20 kg of purified protein per month through its highly automated, *Nicotiana benthamiana*, plant-based production system; we consider this program to be the most responsive, secure, and capable plant-made vaccine program currently available worldwide.

Workforce Training

The Texas A&M Engineering Experiment Station (TEES) and TEES subcontractors {(Baylor College of Medicine, Blinn College, and Texas A&M Engineering Extension Service (TEEX)}, are already providing comprehensive workforce training in all aspects of process development and biopharmaceutical manufacturing at the technical certificate level through post-graduate, professional training.

TEES has already performed a workforce needs assessment, established an advisory committee that includes multiple industry partners, developed preliminary curricula, begun training courses, and implemented an internship program with CIADM pharmaceutical partners. As an option to the US Government which may be exercised in the future, TEES and subcontractors will also provide training in preclinical models, including BSL-3 and BSL-4 procedures, as well as diagnostics and regulatory science.

The workforce training program builds on a pre-existing program initiated by TEES under the sponsorship of the Texas Workforce Commission. TEES has also begun an innovative STEM summer initiative for high school students, primarily from historically underserved groups, aimed at developing a diverse, highly qualified work force. TEES completed is second summer program in 2013, all self-funded by TEES, with remarkable successes in generating both strong interests as well as life-changing experiences for underserved students. It is hoped that the federal government will support such efforts aimed at underserved STEM education, and expand these programs nationally, to assure a future workforce that is both diverse and capable.

Department of Defense Opportunities

As a leading academic institution with a history of dedicated national service, TAMUS is highly motivated to leverage its capabilities to support the Department of Defense (DoD) requirements for CBRN vaccine and medical countermeasure development, manufacturing, licensure, and delivery to warfighters. In addition to pre-existing capabilities at TAMUS and its subcontractors, at least 50% of CIADM capabilities will also be available for non-HHS projects. As such, TAMUS has been independently monitoring and submitting proposals to DoD through open solicitations, including two

recent Requests for Information (RFI) seeking capabilities for the development and manufacturing of vaccines and therapeutics of interest to the DoD.

Of particular interest to TAMUS is the exploration of partnerships within the LVVF and NCTM, as well as the Process Development facility, all of which could develop and manufacture DoD products for the stockpile, special immunization programs, as well as provide the basis for emergency response to "unknown unknowns" including genetically modified or chimeric organisms. The available Texas A&M capacity, which is already funded by HHS, would not only dramatically reduce operational risks, but would also substantially reduce DoD capital expenditures and operational costs. It is important to note that the HHS capacity is meant to serve 300 million civilians, so the addition of capacity for DoD personnel, staff and families could be easily accommodated. Moreover, the great majority of vaccines and countermeasures will be identical to those developed for civilians.

There are several models for partnership that would provide priority for DoD needs over commercial or academic projects. Among these of high interest to TAMUS is a "civil reserve air fleet, or CRAF, model" in which the DoD reserves space with priority for an annual fee which can be applied to DoD task orders.

By leveraging nearly $500 million in Texas, Texas A&M, and DHHS investments, we believe that the DoD could achieve its mission at low risk, minimal initial capital outlay, and easily sustained operational costs. Our preliminary estimates suggest that by utilizing the pre-existing and already funded capacity provided by HHS, the DoD can guarantee all the availability required, with substantially less risk, for *ten years,* at approximately half of the initial facility costs budgeted for a dedicated DoD facility. This would free up substantial resources that could be reallocated to provide additional vaccines, countermeasures, and capabilities to our warfighters. Furthermore, the co-location of HHS and DoD programs would enhance cooperation, reduce duplication, and increase the likelihood for enhanced quality and responsiveness.

In conclusion, I believe the federal government's current investment in biodefense and CBRN countermeasures, primarily through HHS, should be a focus for collaboration, risk reduction, and cost effectiveness for the DoD. Through the three recently awarded Centers for Innovation in Advanced Development and Manufacturing (ADM) , the nation now has the capacity to develop,

manufacture, and stockpile a wide array of medical countermeasures arising from diverse platforms. Better coordination and collaboration among the DoD, HHS, and these public-private partnerships would maximize the use of limited resources and provide a more efficient and productive return on the government's overall investment in this critical area of national security.