

Testimony of Dr. Eddie J. Davis,
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Before the
Subcommittee on Oversight & Investigations
of the
House Committee on Energy & Commerce
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Mr. Chairman, Ranking Member Barton and Members of the Subcommittee, my name is Eddie Joe Davis, Interim President of Texas A&M University at College Station. I have held this position since December 2006. The College Station campus is the largest of the 10 campuses that fall within the Texas A&M University System. I am appearing here today at the Subcommittee's request.

Texas A&M's College Station campus is home to approximately 38,000 undergraduate students at 10 colleges and approximately 7,000 graduate students. The University takes great pride in its reputation as a top tier research institution. I am here today to provide testimony regarding our select agent research laboratories. As you may be aware, these laboratories have recently been the subject of investigation by the Centers for Disease Control & Prevention or "CDC" and, as of June of this year, our select agent research work has been suspended pursuant to CDC's orders.

My comments today will first focus on some background information regarding the University's research program, internal compliance program and the select agent labs. I will then move on to the recent matters leading to the CDC's suspension of the University's

select agent research and our commitment to run a model program to which others compare themselves. Finally, I will provide observations regarding the application of recent federal regulations governing the possession and use of select agents in the laboratories that have emerged over the past few years.

I want to make it absolutely clear that Texas A&M University is, first and foremost, fully committed to both the safety and protection of our employees, students and community, and to following the guidelines and rules on safely and securely operating our laboratories that handle select biological agents and toxins. Only then, will we seek inspection and approval from the CDC to resume the research in these labs.

Texas A&M Select Agent Research and Compliance

Organizational Structure. The University's research organization falls under the Division of Research and Graduate Studies which carries out its mission through several internal units and a variety of external units and centers that are focused on important new fields of scientific inquiry. The work of the Division's units and centers spans the full range of scholarly endeavors and disciplines, securing Texas A&M University's place among the world's leading research institutions.

The Office of Research Compliance, which is a key unit of the University's Division of Research and Graduate Studies, is responsible for providing training and support to faculty, students and staff in regulatory requirements for scientific research. Through key committees and related programs and activities, the Office of Research Compliance develops, implements and oversees compliance with university policies and any applicable research requirements or regulations related to the following areas, among others:

- Research involving humans;

- Research involving animals; and
- Research involving hazardous materials, select agents or recombinant DNA.

Research projects involving infectious/biohazardous agents are subject to approval by the University's Institutional Biosafety Committee or "IBC." The IBC serves as the University's primary interface between the research institution, the Biological Safety Officer (BSO), and principal investigators (PIs) concerning lab review, security, safety, emergency plans, and other activities. In addition to the BSO, the University has also designated a responsible official or "RO" as required by the March 2005 federal regulations promulgated by the Department of Health & Human Services for select agents and toxins. The RO is the University's designated individual who has the authority and control to ensure compliance with the regulations governing our select agent labs.

We presently employ an RO and a BSO, but in an effort to assure full compliance and seamless communications, we will combine these responsibilities into a single person who will report directly to high-level University management. At present, we have an on-going nation-wide search for a new RO/BSO and we expect to have this position filled by the end of the month. With the promulgation of the select agents and toxins rule, the roles of the RO and BSO have evolved and taken on additional responsibilities, which require unique skill sets and experience.

Select Agent Research Laboratories. Texas A&M University has a long history of applied and basic research involving Shiga toxin-producing *E. coli*, *Brucella* and *Coxiella* species with the goal of advancing the understanding of mechanisms of infection and disease, gene function, and vaccine development. The research efforts of our investigators have resulted in a better understanding of mechanisms of infection, which have yielded significant and

relevant results with respect to immunogens for vaccine development, detection of the infectious agent and modes of delivery for achieving the highest probability for success in immunization against disease organisms. The collective contributions and over-arching theme of our research with Shiga toxin-producing *E. coli*, *Brucella* and *Coxiella* bacteria are in understanding host-pathogen interactions as the basis for prevention of disease. While these are zoonotic agents (*i.e.*, agents that are transferable from animals to humans) and prevalent in the surrounding environment, most of the research focuses on diseases in animals and the economic impact of the resulting animal losses, as well as development of better human and animal vaccines. The recognition of the bioweapons potential of these particular agents has only served to make the ongoing research at Texas A&M more relevant and important. The four BSL-3 research laboratories at the University that are registered with the CDC as handling select agents are led by principal investigators Dr. Garry Adams, Dr. Thomas Ficht, Dr. Jim Samuel and Dr. Vernon Tesch.

Dr. Adams is a Professor and Associate Dean for Research and Graduate Studies in the College of Veterinary Medicine. Dr. Adams' research involves studies of the genetic basis of natural disease resistance, molecular pathogenesis of intracellular bacterial pathogens, and the development of vaccines and diagnostic tests against zoonotic diseases. For almost two decades, he has been actively involved in improving the scientific basis of the two largest animal health regulatory issues in the U.S. – brucellosis and tuberculosis. Recently, he has been very active in developing and implementing biodefense and emerging diseases research initiatives.

Dr. Ficht is a professor in the Department of Veterinary Pathobiology at the University's College of Veterinary Medicine. Dr. Ficht's research involves *Brucella*, an animal

pathogen, which invades or persists in the phagosomal compartment of an animal's eucaryotic cells including professional phagocytes. His research explores host-agent interaction between monocyte-derived macrophages and *Brucella* with the aim of identifying the bacterial factors that subvert intracellular killing and the host factors responsible for protecting the host from infection.

Both Dr. Samuel and Dr. Tesch are Associate Professors in the Department of Microbial and Molecular Pathogenesis in the College of Medicine at the Texas A&M University System Health Science Center. Dr. Samuel's research involves identifying recombinant vaccine strategies to elicit protective immunity to the obligate intracellular bacterial pathogen, *Coxiella burnetii*, the etiologic agent of Q fever and a bioterror agent. Dr. Tesch's research involves a family of bacterial toxins called Shiga toxins known to cause disease in humans. Shiga toxins are produced by *Shigella dysenteriae* and *E. coli*. These microorganisms have been in the news lately, as the ingestion of undercooked hamburgers or other foods contaminated with Shiga toxin-producing *E. coli* may lead to widespread outbreaks of bloody diarrhea. A fraction of patients, mostly children, go on to develop life-threatening complications involving acute renal failure and neurological abnormalities.

Texas A&M University has been conducting research involving the propagation of *Brucella* since the late 1970's and has performed research using BSL-3 facilities since the mid 1990s. Research in the other BSL-3 laboratories has similarly been on-going for some time. In addition to the four research laboratories, two BSL-3 diagnostic laboratories are operated by the Texas Veterinary Medical Diagnostic Lab ("TVMDL") located at the College Station campus. From its inception, the TVMDL has occasionally received tissue or blood samples

from animals which contain biological agents and toxins (e.g., rabies, *e-coli*, and *Brucella*) and, therefore, it must be equipped to handle these samples in a high containment laboratory.

CDC's Investigation of Texas A&M's Select Agent Research Labs

I now would like to turn our attention to the reported exposure of a University lab worker to the select agent *Brucella* and the resulting CDC investigation of the University's select agent labs. I will first address the details of the exposure and follow that up with comments regarding the CDC's investigations earlier this year.

2006 Brucella Exposure. In February 2006, a post-doctoral research associate in Dr. Thomas Ficht's lab was conducting an experiment involving brucellosis using a Madison Chamber. A "Madison Chamber" is an aerosol infection chamber that is used to infect test animals with various pathogens. The use of the chamber for this experiment was loaned to Dr. Ficht's research associate by another researcher at the University's Health and Science Center, who used the chamber for tuberculosis research. A Ph.D. research assistant involved in the tuberculosis research which uses the Madison chamber was present during the burcellosis experiment conducted by Dr. Ficht's research associate. The research assistant is proficient in the operation of the Madison Chamber from her use in research concerning tuberculosis. At the time of the experiment, she was present in Dr. Ficht's lab to observe the proper use of the chamber by the research associate who was working with *Brucella*. After the experiment had concluded and the test animals removed, she cleaned the chamber as she would if the pathogen had been tuberculosis.

About 2 months later, the research assistant notified Dr. Ficht that she was ill with flu-like symptoms and inquired as to whether or not anyone else was ill. On that same day, Dr. Ficht had all other lab employees who were present during the experiment in February

tested and notified the BSO. Within the next two weeks, the research assistant was diagnosed with Brucellosis and, through blood testing, it was confirmed that no other employees had contracted it. The research assistant's positive test for *Brucella* was entered into the public health database by the Brazos County Health Department, which was automatically transmitted to the Texas Department of Health and CDC. The research assistant returned to work, was given follow up blood testing and has continued to be monitored pursuant to the institution's occupational health program.

In October 2006, the University received a request for public documents involving incident reports for risk group 2 and higher pathogens from Mr. Edward Hammond of the Sunshine Project, one of the witnesses at today's hearing. In November 2006, the University produced a document showing that there had been a single incident relating to brucellosis. The University continued to inquire internally as to whether there were any additional documents. In April 2007, additional documents were identified regarding the *Brucella* exposure. At that time, the University immediately notified CDC and provided the documents to Mr. Hammond.

CDC's 2007 Investigation. Following the notification to CDC, the University received a notice of suspension of select agent research in Dr. Ficht's lab. Inspectors from CDC then visited the University to follow-up on the notification of exposure and conducted an inspection of the University's four BSL-3 laboratories. A few weeks later, the University submitted information to CDC regarding elevated titers for Q fever – a term of measurement of antibodies in the blood – for three employees who worked in Dr. Jim Samuel's lab. Although it was not clear whether notification was required for these elevated titers, the University elected to report these levels to CDC out of an abundance of caution.

While these elevated titers were cause for concern, none of the individuals became ill.

Following this disclosure by the University, the CDC issued an order suspending all select agent research at the University. The University immediately complied.

On July 23, 2007, an 18-member team from the CDC conducted a comprehensive site review of the University's select agent research activities which ultimately led to the CDC's August 31st site visit report. Though the CDC's report acknowledged the efforts of the University in curing the deficiencies noted by the CDC inspectors, we acknowledge that several additional steps need to be accomplished in order to be re-certified for select agent research. Our number one goal is to ensure that our laboratories are operated in a safe and secure manner, in compliance with all applicable laws and regulations.

We are using CDC's August 31st site report as our roadmap to full compliance. In fact, we have already begun to take corrective action to cure many of the deficiencies cited in the report and have engaged outside experts – some of who were recommended by the CDC – to assist in this process. This will continue full speed ahead. Only after we have satisfied ourselves in the areas of biosafety, security, training, recordkeeping and incident response, we will ask the CDC to allow us to re-start the laboratories. We desire to get back to the important business of vaccine research, with the CDC as our partner, as soon as possible.

March 2005 CDC Regulations Could Use Some Clarification

I would now like to turn our attention to the Select Agent and Toxins regulations that were promulgated in March 2005. These regulations are found at 42 C.F.R. § 73.1 *et seq.* and were developed pursuant to the Public Health Security and Bioterrorism Preparedness and Response Act of 2002. These federal regulations pertain specifically to the possession,

use and transfer of select agents and toxins and I will refer to them as the “SAT Regulations.”

Like many labs in the U.S. handling select agents and toxins, we have grappled with compliance with these regulations. Over the past two and one-half years since their promulgation, several areas have emerged which we believe need further clarification or improvement. I address a few of these areas below:

1. **Definitions** – perhaps the most challenging aspect of the SAT Regulations pertain to definitional interpretations of key terms. The possession, use and transfer of select agents and toxins in biomedical laboratories is a highly complex scientific endeavor. Added to that is the need to operate the laboratories in a safe and secure manner. Given these complexities, the application of definitional terms in the regulations can take on different meanings given different operating scenarios. Terms that are broadly defined can take on different meanings to different people, which can result in differential application and enforcement of the regulations. The following terms in the SAT Regulations have led to a good deal of confusion:
 - a. “Access” to select agents or toxins. 42 C.F.R. § 73.10(a) restricts access to select agents and toxins to only those individuals that have been approved by the HHS Secretary or Administrator, following a security risk assessment by the Attorney General. Whether someone has access or not depends on “if the individual *has possession* of a select agent or toxin (e.g., ability to carry, use, or manipulate) or the *ability to gain possession* of a select agent or toxin.” 42 C.F.R. § 73.10(b) (emphasis added). While the former condition (“...has possession...”) is straightforward, it is the latter condition that creates the

bulk of the confusion (“...has...the ability to gain possession...”). For example, does someone who has not been pre-approved and observes an experiment in a select agent lab have the ability to gain possession of the select agent? Or, if the select agent or toxin is in an animal that is locked in cage within the lab, does that change the analysis? Presently, the definition of access to select agents or toxins is interpreted to be extremely broad. Some degree of reason needs to be applied to the rule in order to facilitate good laboratory practices and the advancement of scientific research. The effect of the broad application of the definition is that any person who enters a SAT lab could arguably have access to the select agent and, therefore, must be pre-approved.

- b. “Routine cleaning, maintenance, repairs, or other activities not related to select agents or toxins” 42 C.F.R. § 73.11(d)(2) provides for certain exceptions to the rule requiring that individuals entering a SAT lab be pre-approved. The exception in (d)(2) specifies that an individual who conducts routine cleaning, maintenance, repairs, or other activities may gain access to the lab so long as (1) his or her activity is “not related to select agents or toxins” and (2) he or she is accompanied by an approved individual. The exception is often confused with the requirement set forth in § 73.10(b) as described above. Furthermore, it is unclear what is meant by an activity that is “not related to select agents or toxins.” Does the maintenance or repair of a vent hood that is used for the handling of select agents or toxins fall within

this exception? It could be argued that any activity within a select agent or toxin laboratory is “related” to the agent or toxin handled in that laboratory.

- c. “Occupational exposure or release” of a selection agent or toxin. 42 C.F.R. § 73.19(b) specifies the notification requirements in the event of a release of a select agent or toxin. The trigger for the notification is based upon whether there is an “occupational exposure or release of a select agent or toxin outside the primary barriers of the biocontainment area.” The SAT Regulations do not define the terms “occupational exposure” or “release,” leaving both the regulator and the regulated without clear direction as to what is expected. In terms of select agents and toxins, there is little guidance as to what constitutes an occupational exposure (*e.g.*, mode of the exposure or acceptable limits or levels?).
- d. “Restricted experiments.” 42 C.F.R. § 73.13(a) establishes a requirement that an individual or entity may not conduct certain “restricted experiments” unless approved by the HHS Secretary. Subsection (b) sets forth two types of restricted experiments – experiments using recombinant DNA that involve the deliberate transfer of a drug resistance trait to select agents and experiments that involve the deliberate formation of recombinant DNA containing genes for the biosynthesis of select agents. While there are likely strong public policy reasons for restricting these types of experiments (based upon the ultimate end use) without express approval from HHS, these two types of restricted experiments are very broadly defined and may

unintentionally limit legitimate experiments involving similar approaches but result in completely different outcomes (and end uses).

2. Authorization of Access to Select Agents and Toxins – another area of confusion involves the authorization of an individual’s access to a select agent or toxin. 42 C.F.R. § 73.10(a) states that “[a]n individual or entity...may not provide an individual access to a select agent or toxin, and an individual may not access a select agent or toxin, unless the individual is approved by the HHS Secretary or Administrator, following a security risk assessment Attorney General.” The confusion arises as to whether the authorization of an individual is (a) as to a specific select agent, wherever that select agent might be handled, OR (b) as to a specific select agent handled at a specific location. If the latter interpretation is correct, the authorization requirement becomes a bureaucratic paperwork mess. For example, a research scientist and his/her staff who work with *Rickettsia prowasekii* (a select agent) may, from time to time, visit the labs of or work with other research scientists who handle the same agent. Requiring that scientist and his/her staff who are already authorized to access this select agent at their home lab to obtain authorization anytime they visit another lab or location where the select agent is handled serves no purpose, nor does it achieve any public policy. The regulation should be clarified such that the authorization applies to the specific agent in question, not the specific agent and location. The focus of the authorization should be, first, on the individual (which is why there is a security risk assessment on the individual) and, second, on the handling of the select agent.

Closing Remarks

In closing, I want to express my appreciation to the CDC for providing a comprehensive review of the steps necessary to rebuild the compliance model for our select agent and toxin research program at Texas A&M. As I mentioned previously, we are using it as our road map to full compliance.

The University has made significant progress in implementing corrective actions that cure the deficiencies noted by CDC in its findings and has brought in outside experts, including several recommended to us by CDC, who have aided us greatly in the process. Our efforts will continue at full speed ahead until we have satisfied the CDC and ourselves. Our goal is for the University's select agent labs to be the model to which others compare themselves.