"Science of Zika: The DNA of an Epidemic"

HEARING BEFORE THE

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TESTIMONY
OF
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Good morning Mr. Chairman and distinguished committee members. Thank you for convening this hearing and inviting me to address this very important emerging public health threat. My name is Steve Presley, I am a medical entomologist and a Professor of environmental toxicology at The Institute of Environmental and Human Health, and I serve as the Director of the Biological Threat Research Laboratory at Texas Tech University. I have almost 30 years of experience working with zoonotic and vector-borne infectious diseases. A significant portion of that time was as an active duty entomologist in the United States Navy conducting related vector-borne disease operations and research work in Africa, Asia and South America. My current research and teaching activities are focused on gaining a better understanding of the occurrence, transmission and maintenance dynamics, and developing strategies to control or otherwise protect humans and livestock from biological threats in the environment, including arthropod-borne diseases of animals and those that are transmissible to humans (i.e., zoonoses).

As you may be aware from previous testimony, Zika fever is a rapidly emerging mosquito-vectored and sexually-transmitted disease caused by a *Flavivirus*; the same genus as the viruses that cause other mosquito-vectored diseases such as dengue fever, St. Louis encephalitis, West Nile fever and yellow fever. Zika virus, like Chikungunya virus, dengue virus and yellow fever virus, is transmitted to humans through the bite of *Aedes aegypti*, the yellow fever mosquito, and *Aedes albopictus*, the Asian tiger mosquito - which is considered to be the most invasive mosquito species in the world. The biology and behavior of these mosquito species differs significantly from the principle vector species that transmit West Nile virus and other arboviruses in the United States, and these differences pose unique challenges to public health agencies necessary for surveying and controlling them in urban and suburban areas.

In the next few minutes I will address the three specific points requested by this committee, to include: ***(1) A description of the process to screen and test for the Zika virus in the U.S., and in particular Texas; (2) An explanation of my participation in the preparation efforts to prevent and control the spread of Zika virus in Texas and the challenges unique to the Aedes aegypti mosquito and Zika virus; and (3) A description of the public health education efforts currently underway regarding Zika virus including how to prevent its spread, and challenges facing such efforts.***

Effective protection of people from mosquito-transmitted Zika virus presents numerous public health and vector control challenges from many different perspectives. Beyond the very tragic and devastating Zika virus-related cases of microcephaly in infants and Guillain-Barre syndrome, Zika virus infection in otherwise healthy adults typically results in less than severe illness, with only about 20% of infected individuals presenting with symptoms. The other 80% of infected individuals may have very mild or no symptoms at all. So, theoretically, a mosquito taking a blood meal from an unaware, asymptomatic but viremic and infectious individual could become infected with the virus, incubate it, and transmit it to other people – thus being the initial steps in establishing local transmission in an area in which no Zika virus cases were previously reported.

The extrinsic factors associated with *Ae. aegypti* and *Ae. albopictus* and the establishment, maintenance and transmission of Zika virus in an area differ significantly from mosquitoes that transmit West Nile virus and St. Louis encephalitis virus. The mosquito vectors of Zika virus are predominantly daytime biters that prefer to be in our houses and office buildings. They are container breeders, laying their eggs in water reservoirs of flower pots, vases, bird baths, toys, and any discarded debris that may collect water, be it artificial or natural like tree-holes or leaf axils. They prefer to rest in shaded cool areas during the heat of the day, in the house under or behind furniture, or outdoors under the eaves of houses and buildings or in vegetation. These aspects of the vector's biology and behavior offer very difficult challenges to the development of effective vector surveillance and control strategies, and implementation of such operations.

Screening and Testing for Zika Virus

The Biological Threat Research Laboratory at Texas Tech University is a component of the U.S. Centers for Disease Control and Prevention (CDC) Laboratory Response Network for biological threat diagnostics, and is a Clinical Laboratory Improvements Amendment Program (CLIA)-certified human diagnostics testing facility. Within that capacity we are a Texas Department of State Health Services reference laboratory for testing human clinical samples from our region of Texas for the presence of Zika virus and other high-consequence infectious disease pathogens. Human sample diagnostic testing for Zika virus is limited to qualified laboratories designated by the CDC, and is accomplished using a specific CDC protocol allowed under the Food and Drug Administration's emergency use authorization. The *Trioplex Real-time (TaqMan) RT-PCR Assay* detects and differentiates RNA extracted from dengue, Chikungunya and Zika viruses in both serum and cerebrospinal fluid, and detects Zika virus RNA in urine and amniotic fluid. A reverse transcription step produces complementary DNA (cDNA) from RNA present in the sample. The protocol allows multiplex testing and is designed to facilitate simultaneous testing for the presence of these viruses from a single sample. The assay is intended for use with specimens collected from individuals meeting specific Zika virus clinical criteria (e.g., clinical signs and symptoms associated with Zika virus infection) and/or Zika virus epidemiological criteria (e.g., history of residence in or travel to a geographic region with active Zika virus transmission at the time of travel, or other epidemiologic criteria for which Zika virus testing may be indicated as part of a public health investigation).

Additionally the Biological Threat Research Laboratory includes an academic research capability for the collection, processing and testing of environmental samples, including samples or specimens from wildlife and arthropods. Of particular relevance to my testimony today, our research team was the first to detect West Nile virus in mosquito populations in western Texas during 2003, and we have since that time worked directly with local and regional public health agencies to collect and screen mosquitoes from the area for West Nile virus, St. Louis encephalitis virus, and other pathogens. We are prepared to collect and screen *Ae. aegypti* and *Ae. albopictus* mosquito populations for Zika virus, should an active case occur in our region.

Participation in Preparation Efforts to Prevent and Control Zika Virus in Texas, and Challenges Unique to the Vector Mosquitoes

In late February of this year, through coordination by the Texas Department of State Health Services, an Entomology Consultation Group was formed to focus on developing strategies and identifying resources needed for the surveillance and effective control of the mosquito vectors of Zika virus across Texas. The consultation group is composed of medical entomologists and public health professionals that are actively engaged in mosquito and infectious disease research or public health education, and represent both academia and local, regional and state public health agencies. We convene by teleconference as necessary to discuss the most up-to-date information being published about the mosquito vectors and geographic spread of the Zika virus, various appropriate personal protection and individual homeowner resources available for effective mosquito control, as well as educational materials and resources being made accessible to the general public relative to the Zika virus threat.

Specific actions that are underway by the Texas Entomology Consultation Group include a county-specific field surveillance project to determine the presence of *Ae. aegypti* and *Ae. albopictus* throughout the state, development of jurisdiction-specific projects to identify the occurrence and degree of resistance to commonly used insecticides in populations of potential Zika virus vectors, and the development and promulgation of public education resources to heighten awareness and provide guidance for personal protection from exposure to Zika virus.

Presence of Ae. aegypti and Ae. albopictus Across Texas

Currently 66% (168 of 254) of Texas counties have no records documenting the occurrence of *Ae. aegypti* and *Ae. albopictus* over the past decade, and more than 200 counties have not conducted mosquito surveillance during the last two years. Many of these counties are sparsely populated and only have rural small towns and communities with very limited, or lack any type of vector control resources. In coordination with local county leadership, we are organizing and fielding teams of entomologists and public health technicians to survey and update distribution maps for *Ae. aegypti* and *Ae. albopictus* in as many of the 168 counties as possible in order to determine areas potentially at risk for local transmission of Zika, chikungunya, and dengue viruses. Currently teams of entomologists from across Texas are collaborating to conduct the various county surveys, with specimen rearing and identification being performed at Texas Department of State Health Services, Baylor University, Texas A&M University, Texas Tech University, University of Texas-El Paso, and University of Texas-Rio Grande Valley.

Pesticide Resistance in Ae. aegypti and Ae. albopictus Adult Populations

There is much discussion based on both anecdotal and empirical reports regarding the resistance of *Ae. aegypti* and *Ae. albopictus* populations to many of the most commonly used classes and formulations of public health insecticides throughout the regions where the mosquitoes occur. In discussions with research entomologists and vector control professionals from various states, *Ae. aegypti* and *Ae. albopictus* populations from Florida, Louisiana and Texas exhibit some degree of insecticide resistance. Insecticide resistance in a vector population is initially detected and characterized by using some sort of bioassay to determine whether a particular insecticide is efficacious at a given time. Ideally, this fundamental question should be answered before a particular insecticide is acquired for vector control operations.

As a component of the Texas Entomology Consultation Group, we are actively engaged in logistical planning and identifying sources of funding to determine the occurrence and degree of insecticide resistance in *Ae. aegypti* and *Ae. albopictus* populations from throughout Texas. Initial plans are to collect eggs of these mosquitoes from various jurisdictions, rear the eggs to adults, and then utilize the CDC bottle bioassay protocol to screen female mosquitoes to determine populations that may be resistant to insecticides that are most commonly used in that specific jurisdiction. The CDC bottle bioassay is designed to help determine if a particular formulation of an insecticide is able to control a vector at a specific location at a given time.

The CDC bottle bioassay relies on time mortality data, which are measures of the time it takes an insecticide to penetrate an insect mosquito, traverse its intervening tissues, get to the target site, and act on that site. Anything that prevents or delays the compound from killing insects contributes to resistance. Information derived from the bottle bioassay may provide initial evidence that an insecticide is losing its effectiveness. The diagnostic dose is the amount of insecticide that kills 100% of susceptible insects within a given period of time. The expected time for the insecticide to achieve this objective is called the diagnostic time. Insecticide resistance is assumed to be present if a significant portion of the test population survives the diagnostic dose at the diagnostic time. The diagnostic dose and the diagnostic time should be defined for each insecticide, each region, and each vector species that is monitored. Major advantages of the CDC bottle bioassay protocol are that different concentrations of a specific insecticide may be evaluated, and the technique is simple, rapid, and relatively economical.

<u>Public Health Education Efforts Regarding Zika Virus to Prevent Its Spread, and Challenges to the Efforts</u>

Currently the scientists working with the Texas Entomology Consultation Group are very aggressively drafting content and developing approaches to make Zika virus prevention information available to the public through various on-line and social network technologies. These educational resources are primarily focused on providing "do-it-yourself" information to homeowners and other property owners regarding how best to eliminate, or at least reduce, mosquitoes on their property. This guidance emphasizes the fact that the first and most important action for mosquito control, particularly for *Ae. aegypti* and *Ae. albopictus*, is to find and eliminate mosquito breeding sites from in and around homes. In one Texas-based study, approximately one-quarter of residents who called their local health department about mosquito problems were unknowingly allowing mosquitoes to breed in their own backyards. Information detailing how best to search for and drain or treat breeding sites is provided, including a listing of several mosquito control options and a review of commercially available larvacides, adulticides and repellents that can be used by property owners.

The homeowner guidance provides a relatively detailed assessment of the safety (both human health and environmental impact) and effectiveness of various off-the-shelf pesticide products and application equipment. Pesticide application equipment options now available off-the-shelf to homeowners include thermal foggers, residual sprayers such as aerosol sprays, pump-type garden-sprayers, hose end-sprayers, and mister systems. Information is also provided regarding other non-insecticide control approaches such as "bug-zapper" electrocution devices and vacuum traps baited with carbon dioxide and other lures. These traps are designed to attract mosquitoes that are seeking a blood meal by looking for traces of carbon dioxide, which is normally exhaled by people and other animals and is a natural attractant.

From a national perspective, information regarding Zika virus is most certainly abundant and readily available. For example, on the 18th of May I executed a *Google* search for the words "Zika virus" and had more than 91 million results. Fortunately at the top of the listing of results appeared the *Centers for Disease Control Zika Virus* page (www.cdc.gov/zika), which provides extensive information targeted to a wide audience, including: pregnant women and those planning to become pregnant, health care providers, travelers, parents, mosquito control professionals, state public health laboratories and departments, law and policymakers, and people at risk due to their occupation.

The *Citizen Science Invasive Mosquito Project* (www.citizenscience.us/imp/resources.php) is a "grass roots" effort coordinated through the U.S. Department of Agriculture aimed at monitoring invasive container-inhabiting mosquito species to determine where the invasive and native mosquito species occur throughout the country as a means of identifying at-risk human and animal populations. The project provides students, teachers, and anyone interested the opportunity to collect real data and contribute to a national mosquito species distribution study, and raises awareness of diseases that can be transmitted by mosquitoes.

The American Mosquito Control Association is currently in the process of developing guidelines specifically geared towards the control of *Ae. aegypti* and *Ae. albopictus* by government public health agencies and commercial entities. The guidelines will emphasize urban mosquito control and the paradigm shift in control practices that must be considered due to differences in the biology and behavior of floodwater/salt marsh mosquitoes and container-breeding mosquitoes.

As I detailed above, there are various and numerous public health educational efforts currently being undertaken in response to the significant threat of local transmission of the Zika virus within the continental United States. It is reported as of 11 May 2016 by the CDC that there have been 503 patients tested positive for Zika virus infection throughout the United States, with only six (6) states having not reported positive cases (i.e., Alaska, Idaho, North Dakota, South Dakota, Wisconsin, and Wyoming). All of these Zika virus infections have been attributed to travel-associated exposures, whether directly or through sexual contact with an infective partner, with no local transmission confirmed. Conversely, there have only been three (3) travel-associated cases and 798 locally acquired Zika virus infections reported in the United States Territories of American Samoa, Puerto Rico and the U.S. Virgin Islands, as of 11 May 2016. I believe that this very significant difference between locally acquired and travel-associated infections is due to seasonal and climatic differences between tropical and subtropical areas. In other words, in most regions of the United States *Ae. aegypti* and *Ae. albopictus* seasonal activity is just now on the rise. Therefore I believe it is essential that all efforts be made to stay ahead of peak mosquito activity in areas of the country where the potential mosquito vectors occur by enhancing and implementing very robust and comprehensive public health education programs at the local, regional and state levels immediately, as well as enhance public health-directed vector surveillance and control capacity.

Other Zika virus Related Projects

In addition to the Public Health Emergency Preparedness and Laboratory Response Network efforts, and various wildlife and zoonotic disease research projects that we are engaged in, my research lab group at Texas Tech University is collaborating directly with two private entities conducting work specific to the development of information resources that are directly applicable to preventing the spread of Zika virus. Those collaborations are with *COR Medical Technologies, Inc.* (26305 Countryside Drive, Spicewood, Texas 78669; www.cormedicaltechnologies.com/landing.aspx) and *Biomeme, Inc.* (20 N 3rd St., Philadelphia, PA 19106 biomeme@biomeme.com), and are in the final planning stages. *COR Medical Technologies* operates the largest medical relational database in the world, and provides extensive reference resources for all known disease manifestations. The *COR* capability is designed as a comprehensive digital outcome support system for health care professionals and patients, with content and technology specifically designed for mobile use on *Apple* and *Android* devices, and with PC and MAC versions also intrinsic to the system. As of December, 2015, registrants utilizing *COR* services are located in all states in the United States of America and Canada, as well as in 47 other countries. In its current configuration *COR* is devoted primarily to diagnosis, surveillance, and reporting of acute, high risk medical disorders, including infections, toxins, cardiovascular diseases, and other life-threatening conditions.

Biomeme, Inc. has developed a smartphone-based DNA detection platform that is field deployable and does not require laboratory facilities. The *Biomeme* device is a real-time PCR thermocycler that attaches to an *iPhone SE* and enables one to perform gold-standard DNA analysis using sample preparation kits to isolate RNA/DNA from an environmental sample, add the sample to a specific test cartridge, and put it into the thermocycler. The *Biomeme* sample preparation system takes only 1-2 minutes and eliminates the need for common lab equipment such as pipettes, centrifuges and vortex machines, and fits on the end of a syringe to bind and clean DNA as you pipette up and down from reagent to reagent. Within 40-45 minutes an individual can determine the presence or absence of a series of specific molecular targets from a sample. PCR test results can be automatically tagged with GPS location and other metadata, and then synced to *Biomeme's* web portal for access by remote users and easy integration into public health and mosquito surveillance databases. The web portal is HIPAA-compliant and includes an API enabling external databases to easily share data.

Through my ongoing collaboration with *COR Medical Technologies* a collaborative research relationship with *Biomeme* has developed in which we are planning to conduct field trials in areas of Florida, Puerto Rico, and Central and South America to validate the accuracy of the *Biomeme* system for detecting Zika virus in *Ae. aegypti* and *Ae. albopictus*, as well as in other clinical samples such as blood, saliva, sputum, urine. Follow-on efforts may include validation of the system's effectiveness in testing for dengue virus and Chikungunya virus as well.

Conclusion

Historically in Texas, epidemics of dengue fever, malaria and yellow fever were relatively common. Less than 100 years ago, during 1922 and 1923, there were approximately 48,000 cases of malaria and 42,000 cases of dengue fever in Texas, respectively. There are numerous examples, both historic and contemporary, of outbreaks and epidemics of vector-borne diseases such as bubonic plague and St. Louis encephalitis. This rapidly evolving Zika virus threat in Texas and throughout the continental United States is just the most recent example of an emerging or resurgent arthropod-borne infectious disease to threaten the public health. I believe there is a common realization made apparent each time such a public health threat occurs, that being regardless of how modern medical and scientific technologies advance, protecting the public health from vector-borne disease threats requires both basic and applied understanding of the arthropod vector's biology, behavior and vulnerabilities.