Outside Witness Testimony
Senate Appropriations Committee Hearing on the U.S. Government Response to the Ebola Outbreak

Dr. Stewart Schneller on behalf of Auburn University
November 12, 2014

Chairman Mikulski and Vice Chairman Shelby,

Thank you for the opportunity to present testimony today in regards to the current Ebola virus epidemic and the President's proposed emergency spending to address the domestic and international concerns it has raised. My name is Dr. Stewart Schneller, Professor of Chemistry and Biochemistry at Auburn University, in the Vice Chairman's home state of Alabama. I provide this testimony on behalf of myself and on behalf of Auburn University. I hope to provide the Committee and the decision makers within the Administration with some background on research being conducted at Auburn, and with thoughts on how our nation's approach to deadly viruses such as Ebola can be improved through drug research and research infrastructure improvement and development.

Infectious diseases have plagued humans since the dawn of civilization. These pathogens fall into various categories: bacteria, parasites, fungi, and viruses. I will focus my testimony on viruses. Rarely a month goes by that the medical community isn't reporting the appearance of a new or re-emerging viral threat to the wellbeing of a local population with the likelihood that people and/or insect or animal vectors will spread this infection to other locales. Placing this in a historical perspective shows that mankind has had to coexist with and combat infectious agents for centuries. However, the distribution of such agents has been increased by recent circumstances, including: social globalization, increased microbial mutation rate, environmental alteration caused by urbanization, famine and poverty accompanying increasing populations, interspecies crossover of infectious diseases, immunomodulation in individuals, threat of bioterrorism, etc.

Within the category of viruses are filoviruses, which include Ebola and Marburg. Both are classified as viral hemorrhagic fever viruses, and are life-threatening. Until the current devastating outbreak of Ebola in West Africa, the seriousness of this virus was limited by its containment in smaller population centers in Central Africa. As a result, there was no unified effort towards having treatment regimens available, which in turn means that there are no current methods for confronting the present situation.

The research underway in the Schneller laboratory at Auburn University is focused on seeking drug candidates for the viruses in the emerging or re-emerging disease categories for which no suitable therapy (including vaccination) currently exists.

Viruses require host cells for replication and, in turn, survival. In this process, the invading virus commandeers the host cell's metabolic "pantry" for most of its essential replicative steps. While depending extensively on the host cell for survival, viruses do generate a sizable number of enzymes and proteins specific to their own development (rather than depending exclusively on those of the host cell). This latter unique characteristic forms the basis for selective drug design to affect viral replication. Of particular interest to Auburn University is the processing of messenger RNA (mRNA), which is the link between viral genetic information and viral progeny formation.

About 10 years ago, the Schneller research team began a program of drug discovery aimed towards viruses that moderate immune responses. Ebola is one of those. The plan has been to develop a drug (or drugs) that would prevent Ebola from carrying out its immune-debilitating process.

From a team of undergraduate and graduate students and postdoctoral research associates guided by trial (success) and error (failure), a compound has arisen with significant anti-Ebola effects whose mechanism of action, as designed, may be to interfere with immune modulation caused by Ebola. This can be viewed as the first step towards a potential anti-Ebola drug. This effect has been identified as the result of an Ebola-orchestrated protein (a biological worker) designated VP35 (VP standing for viral protein). Preventing VP35 from carrying out this immune antagonism offers a unique means to Ebola drug design and discovery and is the focus of the program at Auburn. In that latter regard, agents have been uncovered with anti-Ebola activity whose mechanism of effect is designed to inhibit VP35.

To achieve that goal, extensive studies are now planned at the National Institutes of Health (which coordinated the initial viral screen) to determine the likelihood of moving this sample along to in-depth analyses in animals before any consideration could possibly be given for humans. Thus, the new discovery is too recent to be considered for the current Ebola presence in West Africa. For now, it is likely that the Ebola outbreak will be contained, but the virus will not be eradicated. Thus, we must be prepared with tools more powerful than containment for control of the next Ebola outbreak. A drug will be at the forefront in the search to greatly reduce the mortality rate for this vicious disease.

Auburn University has always and continues to support the concept of a broad-based approach to addressing emerging concerns, both in the field of diseases and disease response and also more broadly across research and development as a whole. We applaud this Committee for its longstanding support of research and development at our nation's research universities and the continued focus on maintaining the United States as the leader in innovation and discovery.

Since the WHO declared the West Africa Ebola outbreak an epidemic in early summer, an expedited effort has been made towards potential vaccine candidates. Auburn supports the proposed funding of the NIH and FDA to make every effort to find any number of drugs and treatment protocols that will greatly reduce the deadly nature of Ebola and its apparent newfound virulence and ability to spread quickly through new areas.

In supporting this funding request, I would raise two specific issues that I believe are important for the Committee to hear and consider. First, I am concerned that the current focus of funding, and quite possibly the focus of any additional funds, is limiting in its area of opportunity.

Currently, vaccines and laboratory-developed antibody applications are receiving the most scrutiny. There is no focused traditional (that is, pill/capsule) drug therapy for Ebola infection to complement those procedures, other than evaluating drug candidates that are either in existence for treating viral infections unrelated to Ebola or have not been rationally designed to consider blocking Ebola's ability to compromise the immune response.

It should be noted that traditional drugs can be given after infections and that there are limitations with vaccines and antibody regimens. For example, they require low temperature storage to remain stable; thus impacting their value in regions of the world where electricity is at best unreliable, and often nonexistent. These approaches also require numerous trained individuals to confidently

administer the requisite injections. Furthermore, viruses (including Ebola) are constantly mutating. In turn, ongoing regular upgrading of the vaccines is required.

Finally, by the nature of their preparation, there can be serious side effects from a vaccine (mild infection) and the physiological characteristics of individuals being vaccinated may be such that they do not respond successfully to vaccination (for example, immunosuppressed individuals). While I am not asking the Administration or this Committee to ignore the potential of vaccines and/or antibody regimens, I do believe equitable time, effort, and funding should be dedicated to antivirals like the one under development at Auburn University. While a rifle shot approach to research can be useful, I believe in a situation like the one we have today, where many viable approaches to prevention, treatment, and containment exist, we must look at them all and dedicate ourselves to solving the problem however possible and as quickly as possible.

Second, while any increase in funding to research drugs and treatments for viruses like Ebola are welcomed, I must point out the need for a greater level of capacity in our research laboratory system, specifically development and access to labs that have the Biosafety Level 4 or BSL4 designation. When researching exotic and dangerous diseases like Ebola, researchers become restrained and limited if they cannot gain access to BSL4 labs where they can move their research forward through actual interaction with the virus. While I understand the President's request does not address this need in additional capacity, I would ask that the Committee take it under consideration, either as a part of this funding bill or in future bills.

Thank you for this opportunity, and I hope you have found the information provided in my testimony useful.

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