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ONE HUNDRED THIRTEENTH CONGRESS

Congress of the United States

House of Representatives

COMMITTEE ON ENERGY AND COMMERCE
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MEMORANDUM

November 17, 2014

To: Subcommittee on Health Democratic Members and Staff

Fr: Committee on Energy and Commerce Democratic Staff

Re: Hearing on "Examining Medical Product Development in the Wake of the Ebola Epidemic"

On Wednesday, November 19, 2014, at 10:00 a.m. in room 2123 of the Rayburn House Office Building, the Subcommittee on Health will hold a hearing entitled "Examining Medical Product Development in the Wake of the Ebola Epidemic." According to the Republican hearing memo, this hearing will focus on medical product development, including treatments, vaccines and diagnostics, relating to the Ebola epidemic.

The Subcommittee on Oversight and Investigations held a hearing on the U.S. public health response to the Ebola outbreak on October 16, 2014 and will hold another hearing on this topic on November 18, 2014.

The following memo supplements information provided in the Republican memo circulated on November 17, 2014.

I. BACKGROUND ON EBOLA

Ebola hemorrhagic fever is a severe and often fatal illness caused by the Ebola virus. The disease has an onset time of two days to three weeks after exposure and results in fever, body pain, vomiting, reduced functioning of the liver and kidneys, and internal and external bleeding.[1] Ebola is transmitted only through direct contact with body fluids (blood, sweat, saliva, feces, and urine) of infected individuals and only during the time infected individuals are

[1] World Health Organization, *Ebola virus disease* (updated Sept. 2014) (online at www.who.int/mediacentre/factsheets/fs103/en/).

showing symptoms.[2] In comparison to other types of viruses, like measles or the flu, Ebola is not considered to be highly infectious; it is not spread through the air and proper infection control in hospitals can prevent its spread.[3]

As of November 12, 2014, the Centers for Disease Control and Prevention (CDC) reports that the ongoing Ebola outbreak in West Africa has infected 14,098 people (of whom 8,715 have been confirmed by laboratory tests) and killed 5,160.[4] These statistics likely underestimate the actual number of cases significantly.[5] These numbers include four Ebola cases diagnosed in the United States, two who were infected in West Africa and two nurses who became infected while caring for an Ebola patient in the United States who subsequently died. The other three recovered and have been released virus-free from the hospital.[6] An additional six patients who were diagnosed with Ebola in Africa have been brought to the US for treatment. Five recovered but the sixth, Dr. Martin Salia, who was flown in on Saturday, November 15th with an advanced case of Ebola after contracting it while treating patients in Sierra Leone, died Monday morning.[7]

II. EBOLA DIAGNOSTICS, DRUGS AND VACCINES

There is little private market for diagnostics, drugs or vaccines for infectious diseases and biological hazards like Ebola because the market is small and sporadic and because affected countries cannot afford to pay high prices. As a result, development of such products is entirely driven by government activity.

The DOD Defense Threat Reduction Agency (DTRA) and the National Institutes of Health's National Institute of Allergy and Infectious Diseases (NIAID) both fund treatment and vaccines for biological threats. Additionally, the Biomedical Advanced Research and Development Authority (BARDA) was established in 2005 within the Department of Health and Human Services' Office of the Assistant Secretary for Preparedness and Response (ASPR) to research and develop responses to bioterrorism and infectious diseases. BARDA funds development of drugs, assisting through the clinical trial phase and into drug production.[8]

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[2] Centers for Disease Control and Prevention, *Facts about Ebola* (Oct. 12, 2014) (online at www.cdc.gov/vhf/ebola/pdf/facts-about-ebola.pdf).

[3] *No, Seriously, How Contagious Is Ebola?*, NPR (Oct. 2, 2014) (online at www.npr.org/blogs/health/2014/10/02/352983774/no-seriously-how-contagious-is-ebola).

[4] Centers for Disease Control and Prevention, *2014 Ebola Outbreak in West Africa* (Oct. 10, 2014) (online at www.cdc.gov/vhf/ebola/outbreaks/2014-west-africa/index.html).

[5] *No One Knows Exactly How Bad West Africa's Ebola Epidemic Is*, Vox (Oct. 9, 2014) (online at www.vox.com/2014/10/6/6889037/reporting-ebola-epidemic-virus-outbreak).

[6] Centers for Disease Control and Prevention, *Cases of Ebola Diagnosed in the United States* (Nov. 8, 2014) (online at http://www.cdc.gov/vhf/ebola/outbreaks/2014-west-africa/united-states-imported-case.html).

[7] *Ebola patient Dr. Martin Salia dies in Omaha,* CBS News (Nov. 17, 2014) (online at http://www.cbsnews.com/news/ebola-patient-dr-martin-salia-dies-in-omaha/).

[8] Office of the Assistant Secretary for Preparedness and Response, *BARDA Unveils Path Forward in the BARDA Strategic Plan 2011-2016* (Aug. 19, 2013) (online at www.phe.gov/about/barda/Pages/2011barda-stratplan.aspx).

CDC works with ASPR to develop federal response plans, guidance, and communications and to interact with state and local entities to deploy and distribute medical countermeasures. CDC also works with the Food and Drug Administration (FDA), in efforts to monitor safety and performance of deployed countermeasures.[9] The Public Health Emergency Medical Countermeasures Enterprise (PHEMCE), also part of ASPR, coordinates these various federal agencies on chemical, biological, radiological, and nuclear threats and infectious disease preparedness.[10]

A. Diagnostics

Currently, testing for Ebola requires sending a blood sample to a lab that can do a specialized test to determine whether the Ebola virus is present.[11] While the testing itself may only take several hours, getting the sample to the lab and getting the results back can take days, depending on where the patient is located.[12] Diagnostic tests that could be used at the point of care and that could provide an answer in minutes would have enormous benefit. Such tests would greatly enhance efforts to contain transmission by allowing rapid separation, quarantine and treatment of those with Ebola. Additionally, such tests would facilitate the rebuilding of the healthcare systems in West African countries in which hospitals and clinics have closed because of fears that any patient coming for routine care, whether it be for delivering a baby or treatment for malaria, might also have Ebola.

Under section 564 of the Federal Food, Drug, and Cosmetic Act (FDCA), the FDA Commissioner may issue an Emergency Use Authorization (EUA) to allow unapproved medical products or unapproved uses of approved medical products to be used in an emergency to diagnose, treat, or prevent serious or life-threatening diseases or conditions caused by threat agents when there are no adequate, approved, and available alternatives.[13] FDA has issued six EUAs to date for experimental diagnostics to detect Ebola infection.[14]

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[9] Office of the Assistant Secretary of Preparedness and Response, *PHEMCE Mission Components* (June 20, 2012) (online at www.phe.gov/Preparedness/mcm/phemce/Pages/mission.aspx).

[10] Office of the Assistant Secretary of Preparedness and Response, *Public Health Emergency Medical Countermeasures Enterprise* (May 30, 2013) (online at www.phe.gov/Preparedness/mcm/phemce/Pages/default.aspx).

[11] *How Hospitals Test for Ebola*, Newsweek (October 3, 2014) (online at http://www.newsweek.com/how-hospitals-test-ebola-274898).

[12] Researchers Seek Crucial Tool: A Fast, Finger-Prick Ebola Test. New York Times (Nov. 4, 2014) (online at http://www.nytimes.com/2014/11/05/business/ebola-researchers-rush-to-find-a-fast-diagnostic-test.html?action=click&contentCollection=US%20Open&region=Article&module=Promotron).

[13] FDA Emergency Preparedness and Response, (online at http://www.fda.gov/emergencypreparedness/counterterrorism/medicalcountermeasures/mcmlegalregulatoryandpolicyframework/ucm182568.htm).

[14] *Id.*

B. Drugs

There are no medicines that have been shown to be effective in treating patients with Ebola. However, there are a number of drugs that have been shown to be effective against the Ebola virus in the test tube or in animal studies.[15] These include:

(i.) Favipiravir, which is approved in Japan to treat the flu and has been shown to work against Ebola in mice studies. It appears to be safe for use, based on its use to treat flu patients.[16]

(ii.) Brincidofovir, which has been shown to work against Ebola virus in the lab but has not been tested in animals. It has been used in the U.S. on two Ebola patients, one of whom, Ashoka Mukpo, lived and the other, Thomas Duncan, who died.[17] It has completed phase II studies, and appears to be safe for use.

(iii.) ZMapp, which has been shown to work in monkeys. It has been used in several health workers who survived, though it is not known if ZMapp had a role in their recovery due to the lack of clinical trials.[18]

(iv.) Tekmira Ebola, which also has been shown to work in monkeys.[19]

Blood plasma from people who have recovered from Ebola infection has also been used in a number of Ebola patients, in the hope that it contains protective antibodies against the virus. While it has been used in several health workers who subsequently survived, it is not known whether the plasma contributed to their recovery because clinical trials have not been conducted using this technique.[20]

MSF will be conducting three clinical trials in outbreak centers in Africa, looking at the safety and effectiveness of: (1) Favipiravir in Guinea; (2) blood plasma also in Guinea; and (3) Brincidofovir, in an African country to be determined.[21] MSF has asked the manufacturers of

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[15] *Trials of Two Antivirals to Treat Ebola Patients to Start Next Month*, Wall Street Journal (Nov. 13, 2014) (online at http://online.wsj.com/articles/researchers-to-start-studies-of-two-antivirals-in-ebola-patients-in-december-1415833226**)**.

[16] *Treating Ebola: The Hunt for a Drug*, New York Times (Oct. 23, 2014) (available online at http://www.nytimes.com/interactive/2014/10/23/world/africa/ebola-drugs.html)

[17] *Id*.

[18] *Id.*

[19] *Id*.

[20] *Id.*

[21] *Id*. Medecins Sans Frontieres, *First trials for Ebola treatments to start at MSF sites in December* (Nov. 13, 2014) (online at http://www.msf.org/article/first-trials-ebola-treatments-start-msf-sites-december).

these drugs to scale up production, so that if they are found to work, they can immediately be used to treat patients. There are no tests starting on ZMapp or Tekmira Ebola because there isn't enough of the drug currently available to conduct the trials.[22]

FDA and NIAID are also planning to conduct a clinical trial that would begin in the United States, assuming there are more Ebola patients treated here in the future, and then move to Africa. Unlike the MSF trials, the US trial would have a placebo controlled arm, that is, some patients would not be given any experimental drug, but only standard supportive care such as replacing fluids and medicines to fight off other infections.[23]

C. Vaccines

There currently are two candidate vaccines available for phase 1 pre-licensure clinical trials. One is "cAd3-ZEBOV," developed by GlaxoSmithKline in collaboration with NIAID. It uses a chimpanzee-derived adenovirus vector with an Ebola virus gene inserted. The other is VSV-EBOV, developed by researchers at the Public Health Agency of Canada, and licensed to NewLink Genetics Corp, based in Ames, Iowa. The vaccine uses an attenuated or weakened vesicular stomatitis virus, a pathogen found in livestock with one of its genes replaced by an Ebola virus gene.[24]

NIH is currently conducting clinical trials on both of these candidates, looking at safety, their ability to generate an immune system response in healthy adults, and appropriate dosage.[25] NIH began the trial of cAd3-ZEBOV in early September, and the trial of VSV-EBOV in October. The Canadian Institutes of Health Research and the Public Health Agency of Canada also just began recruiting healthy volunteers for a clinical trial of VSV-EBOV in Halifax, Canada.[26] Once dosages are determined for each candidate vaccine, WHO and others will begin work to initiate trials in sites of Ebola infection in West Africa.[27]

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[22] *3 Potential Ebola Therapies To Be Tested; Liberia Lifts Emergency*, NPR The Two-Way (Nov. 13, 2013) (online at http://www.npr.org/blogs/thetwo-way/2014/11/13/363741032/3-new-ebola-therapies-will-be-tested-liberia-lifts-emergency?).

[23] *U.S. Will Test Multiple Ebola Drugs in Clinical Trials*, Bloomberg News (Nov. 6, 2013) (online at http://www.bloomberg.com/news/2014-11-05/u-s-will-test-multiple-ebola-drugs-in-clinical-trials.html).

[24] World Health Organization, *Experimental Ebola vaccines*, (Oct. 1, 2014) (available online at http://www.who.int/mediacentre/news/ebola/01-october-2014/en/).

[25] NIH, *NIH begins early human clinical trial of VSV Ebola vaccine* (Oct. 22, 2014) (online at http://www.nih.gov/news/health/oct2014/niaid-22.htm).
Ebola Vaccine, Ready for Test, Sat on the Shelf, New York Times (Oct. 23, 2014) (online at http://www.nytimes.com/2014/10/24/health/without-lucrative-market-potential-ebola-vaccine-was-shelved-for-years.html?_r=0).

[26] *Ebola vaccine clinical trial to begin in Halifax*, CBC News, (Nov. 14, 2014) (available online at http://www.cbc.ca/news/canada/nova-scotia/ebola-vaccine-clinical-trial-to-begin-in-halifax-1.2835412).

[27] World Health Organization, *Experimental Ebola vaccines*, (Oct. 1, 2014) (available online at http://www.who.int/mediacentre/news/ebola/01-october-2014/en/index1.html).

III. FUNDING FOR EBOLA RESPONSE

In September 2014, Congress passed a Continuing Appropriations Resolution (H.J. Res. 124) that provided $88 million (the full amount requested by the Obama Administration) in additional funds to respond to the Ebola crisis in West Africa: $58 million to accelerate countermeasure and product advanced research and development and $30 million to support the CDC's response efforts in West Africa.[28]

The Department of Defense in September 2014 also requested that it be allowed to transfer $1 billion between accounts to pay for the deployment of military resources in West Africa, a transfer that requires the consent of the Chair and Ranking Member of the House and Senate Appropriations and Armed Services Committees. On October 10, the Committees approved up to $750 million in funding for Ebola response to move forward.[29]

On November 5, 2014, the Administration requested $4.64 billion for the immediate US response to the Ebola outbreak and a $1.54 billion contingency fund that could quickly provide additional resources as the situation progresses. This emergency funding would strengthen public health systems in the United States, contain and mitigate the Ebola outbreak in West Africa, accelerate the procurement and testing of vaccines and therapeutics, and strengthen global health security.[30]

The request includes $25 million for FDA to support the development, review, regulation, and post-market surveillance of Ebola therapeutics and vaccines; $238 million for NIH to fund advanced clinical trials for Ebola therapeutics and vaccines, as well pre-clinical testing of new vaccines, therapeutics, and diagnostics; $157 million for BARDA to manufacture the therapeutics and vaccines needed for clinical trials; and $112 million for the Defense Advanced Research Projects Agency within DOD to develop technologies to address Ebola. Additionally, potential uses of the contingency fund could include a campaign to vaccinate the health care workers treating Ebola patients, if a vaccine is proven safe and effective.[31]

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[28] Office of Management and Budget, *OMB Director Shaun Donovan on the Passage of HJ Res 124, Continuing Resolution, 2015* (Sept. 18, 2014) (online at www.whitehouse.gov/blog/2014/09/18/omb-director-shaun-donovan-passage-hj-res-124-continuing-resolution-2015).

[29] *$750 Million in Ebola Funding Approved*, Politico (Oct. 10, 2014) (online at www.politico.com//story/2014/10/us-ebola-funding-111774.html).

[30] White House, *FACT SHEET: Emergency Funding Request to Enhance the U.S. Government's Response to Ebola at Home and Abroad* (Nov. 5, 2014) (online at www.whitehouse.gov/the-press-office/2014/11/05/fact-sheet-emergency-funding-request-enhance-us-government-s-response-eb).

[31] *Id.*

IV. WITNESSES

Rear Admiral Stephen Redd, M.D.
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