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Response

"Examining the Public Health Response to the Ebola Outbreak"

Before the House Committee on Energy and Commerce

Subcommittee on Oversight and Investigations

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Burgess

1. Can you describe what impact the Ebola outbreak has had on BARDA's advanced research and development budget?

Response: The Biomedical Advanced Research Development Authority (BARDA) redirected $24.9 million of its Fiscal Year (FY) 2014 advanced research and development (ARD) funding in September 2014 to support the development and manufacturing of the Ebola monoclonal antibody therapeutic candidate, ZMapp, for Phase 1-2 clinical trials. As a result, funding of select activities in BARDA's broad spectrum antimicrobials and radiological and nuclear therapeutics portfolio was shifted to FY 2015. Since rapid acceleration of the development and manufacturing of other Ebola vaccine and therapeutic candidates was needed to address the escalating United States Government response to the evolving Ebola epidemic, BARDA requested additional funding for Ebola medical countermeasure (MCM) advanced development and manufacturing in the FY 2015 Continuing Resolution ($58 million) and the President's emergency funding request ($157 million).

2. Have you had to shift funding to Ebola projects from other previously planned programs?
a. if so, how costly will it be to start them up again?

Response: In FY 2014, BARDA had originally planned to expend $8 million in MCM research and development for viral hemorrhagic diseases. To meet the $24.9 million level necessary to support the first contract for ZMapp development and manufacturing in September 2014, BARDA delayed spending on planned actions to support antibiotic and radiation therapeutic candidate-development projects until FY 2015. Given the urgency and increasingly rapid spread of the Ebola virus in West Africa, BARDA shifted $17 million in FY 2014 to support the development of ZMapp.

In the absence of funds ($157 million) for Ebola MCM development and manufacturing that BARDA asked for in the President's emergency funding request, BARDA has determined that

reprogramming FY 2015 funds away from ongoing CBRN MCM activities would have an exceedingly detrimental effect on those projects. Companies developing these CBRN MCMs could abandon these MCM candidates and move resources onto the development of more lucrative and stably-funded commercial product candidates. Not only would BARDA potentially lose these MCM candidates in the pipeline, but earlier investments that BARDA and the National Institute of Allergy and Infectious Diseases (NIAID) had previously made would be lost as well. BARDA would have to start over with new companies and repeat these same investments. Additionally, some clinical trials are already underway and would need to be stopped, which would not only harm the product development (loss of valuable data to move products to the next level of development), but it would also be unethical to treat the study participants in this manner. For example, the projects below are planned for funding in FY 2015 and build upon approximately $177 million in prior investments. Shifting funds would jeopardize those prior investments as discussed above.

Existing BARDA Projects requiring FY 2015 Funding	
Threat Area	**Description of Projects**
Anthrax	Development of lyophilized formulation of Raxibacumab (anthrax antitoxin)
Broad Spectrum Antimicrobials	pediatric clinical trials, novel antimicrobials
Radiation/Nuclear	clinical studies for treatment of radiation effects; nonclinical trials and manufacturing of pediatric radiation treatment

3. Have development projects against other threats-like smallpox and anthrax- been shut down as a result?

Response: To date, no BARDA medical countermeasure development projects have been shut down to support Ebola response activities, though staff and resources have been stretched to accommodate the increased workload.

4. What additional funds do you need to develop Ebola countermeasures?

Response: The Office of the Assistant Secretary for Preparedness and Response (ASPR)/BARDA needs additional funding ($157 million) for the Ebola response to continue supporting the accelerated development of promising vaccine, therapeutic, and antibody candidates that may

be used in the current Ebola epidemic in West Africa. The successful development of MCMs against Ebola could be instrumental in protecting health care workers, decreasing the mortality rate of people infected with Ebola, and ultimately halting the spread of the disease. Furthermore, these MCMs and corresponding manufacturing capabilities will be key to not only resolving the current Ebola epidemic, but extremely important to helping address the medical consequences of future Ebola outbreaks.

This request will fund BARDA's support of promising Ebola vaccine and therapeutic candidates. These candidates were previously supported during early development by NIAID and/or the Department of Defense's Defense Threat Reduction Agency (DoD/DTRA) and can now be transitioned to BARDA for advanced development and manufacturing as part of ASPR's response to the current Ebola epidemic. Building on development activities funded during FY2014 and during the FY2015 Continuing Resolution, the request will support the following (see **Table 1**):

- Advanced development and manufacturing of Ebola monoclonal antibodies produced in tobacco plants (ZMapp) and CHO mammalian cells for Phase 2/3 clinical trials for efficacy in affected West African countries in 2015 and scaling up manufacturing from pilot scale to commercial scale;

- Advanced development of other Ebola therapeutic candidates (small molecule antiviral drug therapeutic candidates) for Phase 2 clinical trials in affected West African countries in 2015;

- Advanced development of Ebola vaccine candidates (adenovirus and MVA-vectored vaccines) for Phase 2 clinical trials to evaluate efficacy in affected West African countries in 2015, including freeze-dried formulation development for field administration, and scaling up manufacturing from pilot scale to commercial scale; and,

- Fill-finish manufacturing of Ebola vaccine and therapeutic candidates for clinical trials in 2015, using BARDA's Fill-Finish Manufacturing Network.

The request will also subsequently support Phase 2/3 clinical trials to evaluate the safety and efficacy of these Ebola vaccine and therapeutic candidates in affected West African countries and, if the resulting data are sufficiently encouraging, submissions for Food and Drug Administration (FDA) approval.

Table 1. BARDA FY2014-2015 budgets for Ebola medical countermeasure development and manufacturing activities (in million dollars)

BARDA Ebola MCM Activity	FY 2014	FY2015			FY14-15
	Sept	CR Anomaly	Supplemental	FY 2015 Total	2-Yr Total
Therapeutics	24.9	1.5	141.0	142.5	**167.4**
Ebola antibody product development (ZMapp & CHO cell mAbs)	24.9	1.5	116.0		
Ebola small molecule antiviral drug therapeutic candidate development			25.0		
Vaccines		53.5	15.0	68.5	**68.5**
rVSVΔG EBOV (Newlink Genetics/Merck)		30.5			
cAd3 EBOV (GSK)		17.0			
AdVac/MVA EBOV (J&J/BN)			15.0		
rVSVN4CT1 EBOV (Profectus)		6.0			
Other Activities		3.0	1.0	4.0	**4.0**
Ebola MCM Fill finish manufacturing	0	3.0	1.0		
Total	**24.9**	**58.0**	**157.0**	**215.0**	**239.9**
Note: FY 2015 CR anomaly provides $58 million for Ebola.					
THIS TABLE DOES NOT CONTAIN FUNDING REQUESTS FOR COMMERCIAL SCALE MANUFACTURING OF VACCINES FOR MASSIVE VACCINATION CAMPAIGNS.					

The President submitted a request to Congress in October 2014 for Ebola Supplemental Appropriations ($6.2 B) to address domestic and international responses to the current Ebola epidemic.

The present Ebola epidemic is similar to other biothreats, as they are caused by infectious agents and are considered bioterrorism threats. Unlike smallpox or anthrax, where the former was eradicated in the 1970s and the latter occurs infrequently from handling contaminated hides (among other means), Ebola still persists with outbreaks in Africa over the past forty years and now as an emerging epidemic in West Africa.

Lujan

1.Can each of you discuss if budget cuts have had any impact on our response to the Ebola outbreak in West Africa or impacted the handling of the cases here in the United States?

Response: To date, no BARDA medical countermeasure development projects have been shut down to support Ebola response activities, though staff and resources have been stretched to accommodate the increased workload.

In FY 2014, BARDA had originally planned to expend $8 million in MCM research and development for viral hemorrhagic diseases. To meet the $24.9 million level necessary to support the first contract for ZMapp development and manufacturing in September 2014, BARDA delayed spending on planned actions to support antibiotic and radiation therapeutic candidate-development projects until FY 2015. Given the urgency and increasingly rapid spread of the Ebola virus in West Africa, BARDA shifted $17 million in FY 2014 to support the development of ZMapp.

In the absence of funds ($157 million) for Ebola MCM development and manufacturing that BARDA asked for in the President's emergency funding request, BARDA has determined that reprogramming FY 2015 funds away from ongoing CBRN MCM activities would have an exceedingly detrimental effect on those projects. Companies developing these CBRN MCMs could abandon these MCM candidates and move resources onto the development of more lucrative and stably-funded commercial product candidates. Not only would BARDA potentially lose these MCM candidates in the pipeline, but earlier investments that BARDA and the National Institute of Allergy and Infectious Diseases (NIAID) had previously made would be lost as well. BARDA would have to start over with new companies and repeat these same investments. Additionally, some clinical trials are already underway and would need to be stopped, which would not only harm the product development (loss of valuable data to move products to the next level of development), but it would also be unethical to treat the study participants in this manner. For example, the projects below are planned for funding in FY 2015 and build upon approximately $177 million in prior investments. Shifting funds would jeopardize those prior investments as discussed above.

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Green

1. Dr. Robinson, can you please tell us which US agency or agencies are responsible for the development of vaccines and therapies to treat Ebola? Do you think sufficient resources are available to successfully develop these needed products?

Response: ASPR/BARDA and the National Institutes of Health (NIH)/NIAID are the Department of Health and Human Services agencies that hold primary responsibility for the development of Ebola vaccines and therapies. The Centers for Disease Control and Prevention (CDC) and the Department of Defense also play important roles in Ebola vaccine and therapy development. Specifically, BARDA is responsible for the advanced development and manufacturing of the Ebola vaccine and therapeutic candidates for clinical trials and possible large scale administration campaigns.

At this point, the Administration has submitted an emergency funding request $6.1 billion to augment FY 2015 available funds to meet the additional development and manufacturing needs of these medical countermeasures for response in West Africa.

2. As we know, the development of a medical countermeasure for a biological threat agent can take a decade or more, and a billion dollars, to develop. Ebola will be no different. The US government research program on Ebola countermeasures goes back a decade. But the level of financial priority and urgency on getting these countermeasures developed and stockpiled was insufficient to prepare us for the situation we currently face. Most would agree we are only aggressively pressing forward into clinical trials now because of the gravity of the situation. Approximately how much funding do you think is needed to invest in development of Ebola vaccines and drugs to give us the best chance of developing one new vaccine and one new therapy?

Response: In addition to budget requests from NIAID and CDC for Ebola vaccine and therapeutic development and clinical trials, BARDA seeks $157 million in funding through the President's emergency funding request to further the advanced development and manufacturing of at least four Ebola vaccine candidates, two or three Ebola monoclonal antibody therapeutic candidates, and at least two Ebola small molecule antiviral drug candidates for clinical trials in West Africa that will determine whether these candidates work, are safe, and to ensure that these Ebola product candidates can be made at commercial scale if mass administration campaigns are needed in 2015.