



PERSONNEL AND
READINESS

OFFICE OF THE UNDER SECRETARY OF DEFENSE
4000 DEFENSE PENTAGON
WASHINGTON, DC 20301-4000

29 DEC 2016

The Honorable Rodney P. Frelinghuysen
Chairman
Subcommittee on Defense
Committee on Appropriations
U.S. House of Representatives
Washington, DC 20515

2016 12 29 10 5

Dear Mr. Chairman:

The enclosed report is in response to Senate Report 114-63, pages 203-204, "Global Health," which accompanied H.R. 2685, the Department of Defense Appropriations Bill, 2016, and requested information on infectious-disease-related research, including funding, accomplishments, and goals.

This report includes information on activities sponsored by the Defense Health Program, the United States Army, the United States Navy, the Defense Advanced Research Program Agency, and United States Special Operations Command-sponsored activities for fiscal year (FY) 2015. The report provides a list of key areas of research associated with infectious diseases and related initiatives undertaken for FY 2015. The report documents progress in diagnostics development, wound infection prevention and management, and whole blood screening. It reports on work related to parasitic, viral, and bacterial diseases, as well as vector control and other initiatives. The data for this report were collected through the Armed Services Biomedical Research Evaluation and Management Community of Interest.

A similar letter is being sent to the other congressional defense Committees. Thank you for your interest in the health and well-being of our Service members, veterans, and their families.

Sincerely,

A handwritten signature in black ink, appearing to be "Peter Levine", written over a large, loopy scribble.

Peter Levine
Performing the Duties of the Under Secretary of
Defense for Personnel and Readiness

cc:
The Honorable Peter J. Visclosky
Ranking Member



PERSONNEL AND
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OFFICE OF THE UNDER SECRETARY OF DEFENSE
4000 DEFENSE PENTAGON
WASHINGTON, DC 20301-4000

The Honorable William M. "Mac" Thornberry
Chairman
Committee on Armed Services
U.S. House of Representatives
Washington, DC 20515

29 DEC 2016

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Peter Levine
Performing the Duties of the Under Secretary of
Defense for Personnel and Readiness

cc:
The Honorable Adam Smith
Ranking Member



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OFFICE OF THE UNDER SECRETARY OF DEFENSE

4000 DEFENSE PENTAGON
WASHINGTON, DC 20301-4000

The Honorable John McCain
Chairman
Committee on Armed Services
United States Senate
Washington, DC 20510

29 DEC 2016

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Performing the Duties of the Under Secretary of
Defense for Personnel and Readiness

cc:
The Honorable Jack Reed
Ranking Member



PERSONNEL AND
READINESS

OFFICE OF THE UNDER SECRETARY OF DEFENSE
4000 DEFENSE PENTAGON
WASHINGTON, DC 20301-4000

The Honorable Thad Cochran
Chairman
Subcommittee on Defense
Committee on Appropriations
United States Senate
Washington, DC 20510

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Performing the Duties of the Under Secretary of
Defense for Personnel and Readiness

cc:
The Honorable Richard J. Durbin
Vice Chairman

**REPORT TO THE CONGRESSIONAL DEFENSE COMMITTEES IN RESPONSE TO
SENATE REPORT 114-63, PAGES 203-204, WHICH ACCOMPANIED H.R. 2685, THE
DEPARTMENT OF DEFENSE APPROPRIATIONS BILL, 2016**

“GLOBAL HEALTH”



**SUBMITTED BY THE OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE
(HEALTH AFFAIRS)**

December 2016

The estimated cost of this report or study for the Department of Defense is
approximately \$3,100 in Fiscal Year 2016.
This includes \$2,600 in expenses and \$500 in DoD labor.
Generated on 2016Nov01: RefID: 8-E9DB4E6

Introduction

The following information is the final response to Senate Report 114-63, pages 203-204, which accompanied H.R. 2685, the Department of Defense (DoD) Appropriations Bill, 2016, concerning infectious-disease-related research. The Senate Report requested a report related to research on global health and infectious diseases for fiscal year (FY) 2015 similar to the report the Department submitted for FY 2011 through FY 2014. This report provides accomplishments and program funding for FY 2015 for each program within DoD currently involved in infectious-disease-related research.

The information below includes information from the Defense Health Program, the United States Army, the United States Navy, the Defense Advanced Research Program Agency (DARPA), and the United States Special Operations Command (USSOCOM)-sponsored activities for FY 2015.

Fiscal Year 2015 Department of Defense Accomplishments by Component

Defense Health Program Accomplishments

Diagnostics Development

Developed assays for detecting malaria, dengue, chikungunya and leptospirosis on Next Generation Diagnostic Systems platform.

Wound Infection Prevention and Management

1. Developed an automated digital microscopy device that can identify the bacteria and determine if it is resistant to antibiotics within 6 hours – a process that normally takes more than 48 hours. Pivotal clinical studies are underway to support the Food and Drug Administration (FDA) clearance. By providing same-day diagnostic information, clinicians will be able to immediately identify the appropriate therapeutics necessary to treat infections and improve clinical outcomes.
2. Conducted studies to better understand the host immune response to *Staphylococcus aureus* nasal colonization and skin and soft-tissue infection among high-risk military trainees. Knowledge gained from these studies will help develop better prevention and treatment options.
3. A phase II study at University of Pennsylvania in collaboration with Microbion Corporation, to evaluate the efficacy and safety of the use of BisEDT to treat postoperative infections following surgical stabilization of open fractures of the lower extremity received FDA qualifying infectious disease product destination.
4. A study at the Denver Health Medical Center in collaboration with the Denver VA Medical Center and Accer18 Technology for developing a diagnostic capability using advanced microscopy and bacterial culturing techniques. The researchers are developing

the capability to identify bacteria and determine drug resistance profiles within six hours of receiving the specimen.

5. Developed clinical practice guidelines for the recognition and comprehensive management of invasive fungal infections in war wounds.
6. Conducted skin and soft tissue staphylococcal infection studies in military basic trainees to develop better prevention and treatment options.

Antimicrobial Countermeasures

1. Developed a human skin substitute with antibiotic properties to facilitate healing of traumatic combat wounds. Investigational new drugs (IND) application was submitted in Q2 of 2015.
2. Developed new topical treatment based on nano-emulsion formulations that have anti-microbial activity against a broad range of pathogens including antibiotic resistant strains infecting traumatic wounds; validations studies are ongoing.

Rapid Screening of Fresh Whole Blood

Continued development of the Rapid Transfusion Transmitted Disease Diagnostic product that will serve as one of the products developed to improve the safety of emergency blood collections. This product will improve the use of more timely and accurate rapid donor blood screening by having FDA approved clinical diagnostic devices used during emergency blood drives. Multiplexed HIV, Hepatitis B (Surface Antigen) and HCV test will reduce the time and expense of performing rapid donor screening.

Army Core 6.1 – 6.3 Accomplishments

Parasitic Diseases

1. Identified E140, a novel *Plasmodium yoelii* antigen that protects against malaria in 71 percent of mice alone or 93 percent in combination with Falstatin, UIS3, and CSP antigens.
2. Completed IND enabling pre-good laboratory practice (GLP) studies to advance self-assembling nanoparticle vaccine to GLP toxicology testing and initial manufacture for human trials.
3. In collaboration with PATH-MVI and GlaxoSmithKline (GSK), achieved 87 percent efficacy against controlled human malaria infection with delayed fractional dosing of RTS,S malaria vaccine-efforts to assess durability ongoing.
4. Achieved 92 percent efficacy against controlled human malaria infection challenge using irradiation attenuated sporozoite vaccine developed by Sanaria.
5. To identify molecular target of program leading triazine chemical series, induced a fourfold increase in 50 percent inhibitory concentrations in a Dd2 parasite line .

Completed rodent and primate testing of three lead triazine candidates to enable initiation of regulated studies necessary to advance a candidate to human trials.

6. Triazine pre-IND package submitted to FDA. Selected for study an agency approved Exploratory IND approach to down select lead candidate among three compounds selected for study.
7. Joint effort between Walter Reed Army Institute of Research (WRAIR) and Uniformed Services University of the Health Sciences scientists is determining extent of low metabolizer phenotype for cytochrome P450 2D6 (CYP2D6) in active duty military population to guide better use of primaquine-like drugs for treatment of relapsing malarias.

Viral Diseases

1. Conducted comparative cell-mediated immune assessments for GSK, Sanofi, Takeda and in-house program dengue vaccines using common assay platforms.
2. Conducted initial assessments of humanized immune system engrafted DRAG mouse model capable of infection and disease manifestations by human dengue viruses.
3. Conducted first human infections with controlled human dengue infection model; Dengue 1 challenge virus strain.
4. Engaged Takeda, Inc. in preparation for Phase 3 dengue vaccine trial in SE Asia.
5. Newly developed versions of the Crimean Congo hemorrhagic fever DNA Vaccine was evaluated in hamsters. Immunogenicity showed promise with further evaluation planned.
6. Lethal disease models for Hantavirus Pulmonary Syndrome were developed against Andes virus in hamsters and Sin Nombre virus in immunosuppressed hamsters.
7. Clinical trial (Phase 2a) with the Hemorrhagic fever with Renal Syndrome DNA vaccine delivered by muscle electroporation continuing; more than 100 subjects (7 of 8 vaccination groups) have been vaccinated at least once and the final group (group 8) is planned.

Bacterial Diseases

1. *Shigella* live-attenuated vaccine candidates for four different serotypes have been engineered and are ready for testing in animal models.
2. A third generation *Shigella* subunit vaccine candidate has been manufactured using Current Good Manufacturing Practice (cGMP) methods and is ready for testing in animal models.

3. For *Campylobacter*, the multiplex PCR-capsule typing system has been expanded from 14 capsule types to 35 types. This typing method was successfully applied to a collection of 996 clinical isolates from Thailand, Cambodia, and Nepal with a 98 percent success rate.
4. Completed two Phase I clinical trials for vaccine candidates to prevent disease caused by *Shigella*, one Phase 2b clinical trial for a prototype vaccine candidate to prevent disease caused by Enterotoxigenic *Escherichia coli* (ETEC) and a Phase I clinical trial of a vaccine candidate to prevent disease caused by *Campylobacter*.
5. Conduct research in the development of novel therapeutics for the treatment of multiple drug resistance (MDR) infections, and the characterization of genetic mechanisms of antimicrobial resistance by various groups at the WRAIR and Naval Medical Research Center in Silver Spring, MD.
6. Viruses that infect and kill bacteria (bacteriophages) have shown promise in the treatment of a mouse wound infection model with *A. baumannii*. Development in a proof-of-principle 5-member phage cocktail that is highly effective against MDR *A. baumannii* infections.

Diagnostics and Vector Control

1. Developing a companion Rapid Diagnostic Test for predicting severe Dengue infection using an Interleukin IL-10 prototype.
2. Patented the world's first *in vitro* sporozoite production system that no longer requires live mosquitoes (initiated patent application process). System will advance and expedite malaria vaccine and drug testing efforts throughout the world.
3. Conducted eight controlled human malaria infections to evaluate malaria vaccine candidates that led to the identification of the best malaria vaccine candidates thus far, RTSS PfSPZ.
4. Immunized 12 volunteers with more than 1,000 radiation attenuated malaria infected mosquito bites in the largest study of this kind ever conducted with human volunteers, which provided significant insight into correlates of protection for attenuated sporozoite vaccines.
5. Completed the Chikungunya Arthropod Vector Rapid Detection Device development and laboratory evaluation, now commercially available for purchase to provide field surveillance capability of Chikungunya disease in mosquito vectors that informs vector control operations and reduces incidence of disease. Field testing in Thailand is planned in 2016.
6. Outside Continental United States (OCONUS) field labs are well connected with collaborators and field sites with capability to use semi-field cages to test new vector collection tools, mosquito attractants, spatial repellent products and to study important

mosquito behaviors. Field tested five different insect vector surveillance systems at sites in Peru, Ghana, Liberia, and Thailand to help develop DoD next generation flying insect trap and attractants for use in disease surveillance programs.

7. New civilian National Research Council fellow entomologist hired in Kenya, working on spatial repellents.
8. VectorMap now more productive than ever, produced eight regional vector risk assessment profiles for key diseases and vectors in important area of responsibilities across the globe.
9. Carbon Dioxide Generator testing in Thailand resulted in progress through Milestone B. Carbon dioxide capability dramatically improves vector trapping for all arthropod vector surveillance programs, providing specimens for identification, pathogen detection and risk calculation to inform vector control programs and reduce incidence of diseases.
10. New mosquito ID Keys for Culex of West Africa, Central, and East Africa.
11. New online keys and tutorials for mosquito and sand fly identification.

Army Core 6.4-6.5 Accomplishments

Rapid Tests for Transfusion Transmitted Diseases

Effort terminated in 2015, due to poor performance in the pivotal clinical trial.

Topical Antileishmanial Drug (Paromomycin Alone)

The New World Pivotal Phase 3 Study in Panama was completed in March 2016.

Combined Camouflage Face Paint

No 2015 actions.

Dengue Tetravalent Vaccine

No 2015 actions.

Adenovirus Vaccine

In 2015, began a contract to support PaxVax, Inc. for research and early development of Modernized Production Adenovirus Vaccine.

New Standard Military Insect Repellent

No 2015 actions.

Antimalarial Drug, Artesunate Intravenous

1. For 2015, maintained the DoD's emergency treatment IND for OCONUS treatment facilities ensuring that Service Members and beneficiaries can receive the same standard of care as within the U.S.
2. In 2015 completed more than half of the NDA regulatory dossier writing and preparation of the common technical document.

Leishmania Rapid Diagnostic Device

No 2015 actions.

Next Generation Malaria Prophylaxis (Tafenoquine)

1. In 2015, successfully negotiated a License Agreement with the Army's development partner.
2. In 2015, successfully acquired approval from GSK for a cross reference to its IND and received access to GSK's manufacturer for the production of 100mg Tafenoquine tablets.
3. In 2015, initiated writing of the NDA regulatory dossier and preparation of the common technical document for FDA and Therapeutic Goods Administration submissions.

Next Generation Diagnostic System (NGDS)

1. In 2015, a delivery Order for development of Infectious Disease Panel for use on the NGDS platform awarded to BioFire Defense. Successful completion of this effort will culminate in an FDA licensed *In-vitro* Diagnostic for multiple pathogens to include Dengue, Malaria, Chikungunya and Leptospirosis.
2. In 2015, partnered with National Institutes of Health to expand the breadth of disease coverage on the Infectious Disease Panel to include an additional ten pathogens.

Q Fever Vaccine

No 2015 actions.

Regional HIV Vaccine

1. Initiated, fully enrolled and vaccinated all participants in a randomized, double blind evaluation of late boost strategies for HIV-Uninfected participants in the HIV Vaccine efficacy trial with live recombinant ALVAC-HIV priming with AIDSVAX B/E boosting in HIV-Uninfected Thai adults.
2. Initiated a randomized, double blind evaluation of ALVAC-HIV (VCP1521) Priming and Multiple boosting strategies with and without AIDSVAX B/E in HIV-Uninfected Thai adults. This project will finish in FY 2016, with sample and data analysis completion in FY 2017.

3. Initiated and fully enrolled a double blind, randomized, placebo controlled clinical vaccine trial of AIDSVAX B/E protein boost vaccine. This study will finish in FY16 with sample and data analysis completion in FY 2017.

Carbon Dioxide Generator

1. Completed surveillance testing in Thailand in November 2014.
2. Achieved successful Milestone B in April 2015.
3. Completed operational testing and all but one surveillance test for Milestone C in April 2015.

Improved Dual-Insecticide Impregnated Bed Net

1. Obtained Environmental Protection Agency registration in December 2014.
2. Received National Stock Number assignment for the bed net from the Armed Forces Pest Management Board in April 2015.
3. Developed a rain fly for the improved dual-insecticide impregnated bed net in June 2015.

Navy Accomplishments

Malaria vaccine Engineering and Manufacturing Development

1. Augmented clinical trial efforts to test the safety and efficacy of a militarily relevant and promising malaria vaccine candidate.
2. Initiated validation of GMP support for malaria vaccine production scale up.

ETEC Vaccine Engineering and Manufacturing Development

Continued an intradermal vaccine efficacy study in an experimental challenge model of ETEC and completed analysis of third ETEC clinical study cohort.

BioSurveillance Information Service System Development

Transitioned a centralized bio-surveillance data repository that uses both open and DoD health surveillance data to Joint Program Executive Office for Chemical and Biological Defense (JPEO-CBD) BioSurveillance Portal to provide a more robust picture of overall disease and medically related threats in an area.

DARPA Infectious Diseases Program Accomplishments

Diagnostic and Medical Countermeasure Platforms against Infectious Diseases

1. Transitioned environmental biothreat multiplex detection assay to Joint Program Executive Office for Chemical and Biological Defense (JPEO-CBD).

2. Achieved protective serum concentrations over a clinically relevant duration using gene-encoded anti-infective monoclonal antibodies against dengue and *Pseudomonas* in animal models.
3. Demonstrated delivery and efficacy of gene constructs encoding an anti-infective antibody resulting in protection against *Pseudomonas* and chikungunya in small animal models.
4. Developed a viral removal filter that was fielded after regulatory approval and used to successfully treat an Ebola patient in Germany.

Supplemental Funding for Ebola Response

Completed an Ebola DNA vaccine Phase 1 trial and observed no clinical adverse events.

USSOCOM Accomplishments

Mobile Analytics Platform (MAP)

1. Recently begun the Febrile Illness assay panels development under the MAP project with DARPA. The vendor, Ibis has identified and tested primer and probe pairs for all of the pathogens outlined in the statement of work.
2. An America Febrile Illness assay comprising Zika virus, four serotypes of Dengue virus, Chikungunya virus, the four major species of Malarial parasite, *Leptospira*, and *Yersinia Pestis*.
3. An Africa Febrile Illness assay comprising the four primary species of Ebolavirus (Zaire, Sudan, Bundibugyo and Cote d'Ivoire), Lassa viruses, the four major species of Malarial parasite, and Crimean Congo Hemorrhagic Fever virus.

Funding Overview of Department of Defense Infectious Disease Research

Activities

Program Element	Project	FY 2015 (K)
<i>Defense Health Program</i>		
6.1	GDF - Basic Operational Medical Research Sciences	\$1,360
6.2	GDF - Applied Biomedical Technology	\$3,520
6.3	GDF - Medical Technology Development	\$3,495
6.4	GDF - Medical Products Support and Advanced Concept Development	\$8,433
6.5	GDF-Medical Products and Support System Development	\$1,253
6.2	Military HIV Research Program	\$ 7,175
6.3	Military HIV Research Program	\$5,773
<i>Army Core (6.1-6.3)</i>		
6.1	SCI BS/MED RSH INF DIS	\$11,005
6.2	DOD MED DEF AG INF DIS	\$17,745
6.2	HIV EXPLORATORY RSCH	\$ -
6.3	IND BASE ID VACC&DRUG	\$18,274
6.3	MED PROTECT AGNST HIV	\$ -
6.3	MILITARY HIV INITIATIVES (CA)	\$ 6,790
6.4	DOD DRUG & VACC AD	\$ -
6.4	MIL HIV VAC&DRUG DEV	\$ -
6.5	MIL HIV VAC&DRUG DEV	\$ -
6.5	INFEC DIS DRUG/VACC ED	\$ -
<i>Army Core Advanced Development</i>		
6.2	GDF - Applied Biomedical Technology	\$ -
6.3	GDF - Medical Technology Development	\$ -
6.3	DoD Drug & Vacc AD	\$6,888
6.4	Infec Dis Drug/Vacc ED	\$12,510
6.3	MIL HIV Vacc & Drug Dev	\$550
6.4	MIL HIV Vacc & Drug Dev	\$3,900
6.3	Field Medical Systems Advanced Development	\$7,595
6.4	Field Medical Systems Engineering Development	\$23,037
<i>Defense Advanced Research Program Agency</i>		
6.1	Transformative Sciences	\$ -
6.1	Basic Operational Medical Science	\$ 48.43
6.2	Biologically Based Materials and Devices	\$ -
6.2	Biomedical Technology	\$55.39
6.2	Ebola Response and Preparedness Congressional Add	\$45.00
<i>Navy</i>		
6.5	Infectious Diseases Drugs and Vaccines Engineering Development and Surveillance System Development	\$3,495
<i>United States Special Operations Command</i>		
6.4	Blood Donor Pathogen Kit	\$0
6.4	Mobile Analysis Platform	\$986
6.4	Smart Phone POC Diagnostic	\$214

Conclusion

As shown in this report, the Department has made progress in many infectious-disease research areas, such as parasitic, viral, and bacterial disease identification and testing, wound infection prevention and management, and many others. The continued goal of DoD is to conduct a focused and responsive infectious-diseases research and development program leading to fielding effective and improved means of protection and treatment necessary to maintain maximal global operational capability with minimal morbidity and mortality.