Infectious Diseases

UNCLASSIFIED

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Panel Members

- COL Nelson Michael (Moderator)
- COL Michael Kozar – Government Lead
- Dr. Sanjay Gurunathan – Sanofi-Pasteur
- Dr. William Ripley Ballou – GSK
- Dr. Joe Larsen – Deputy Director, BARDA
- Dr. Lou Jasper – USAMMDA

Military Infectious Diseases Research Program

Mission

To conduct for the Department of Defense, a focused and responsive world class infectious diseases research and development program leading to fielding of effective, improved means of protection and treatment to maintain maximal global operational capability with minimal morbidity and mortality

- Force Health Protection
- Naturally occurring, known, predictable threats
- Requirements driven

Mission and Functions

Plan, coordinate and oversee a DOD Science and Technology (S&T) program that develops effective and improved countermeasures to minimize the impact of naturally occurring endemic infectious diseases upon the warfighter.

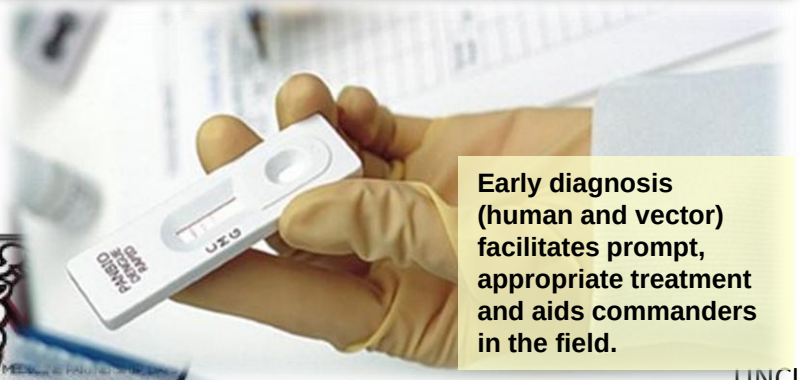
Prevention

- Infectious diseases adversely impact military operations. Vaccines are the long-term solution.

Treatment

New drugs are continually required to overcome evolving drug resistance.

Diagnostics



Early diagnosis (human and vector) facilitates prompt, appropriate treatment and aids commanders in the field.

Insect Vector Control

Most militarily relevant infectious diseases are transmitted by biting insects and other arthropods.

What Makes the MIDRP Unique?

- **Focused on FDA/EPA approved products for adult indications**
  - **Enhance global health security**
  - **Enhance stability operations**
- **USAMRMC organized like a pharmaceutical company**
  - **Product development oriented organizational structure and processes**
  - **Decision Gate System integrates best industry business practices**
  - **Historical success of vaccines/therapeutics**
- **Core research program embedded in Military labs with uniformed researchers**
  - **Discipline and mission focus**
  - **Global research platform – Host nation partners**
  - **Unique overseas clinical trial sites**

Infectious Diseases Countermeasure Development Strategy

	Prevention	Field Interventions	Long Term Treatment/ Management
Points of Use	• Pre Exposure/Pre-Deployment	• Deployed in the Field	• MTF/Definitive Care
Capability Need	• Provide Immunity Before Exposure	• Reduce Risk of Exposure to Pathogens • Reduce Risk of Illness (LDD) • Identify Agents	• Reduce Exposure to Nosocomial Pathogens • Identify Agents of Wound Infections • Optimize Wound Infection Management
Research Solutions	• Understand Epidemiology, Pathophysiology, and Immunity • Develop and Test Candidate Products	• New Drugs • Vector Control Products • Blood Screening Tools • Human Diagnostics – Vector Detection	• New Drugs and Biologics • Diagnostics • Environmental Decontamination Products • Bio-Marker Discovery
Products	• Malaria Vaccine • Dengue Vaccine • ETEC Vaccine • HIV Vaccine • HFRS Vaccine	• Improved Bed Net • Tafenoquine • IV Artesunate • Non-DEET Repellants • Topical Paromomycin • Leishmania Rapid Diagnostic Device	• Anti-Microbial Human Skin Substitute • Sideromycins - Antibacterial Delivery Systems • Arbekacin • MDRO Real-time Diagnostics

Investment Strategy

Tier 1 - High user need, High operational risk

Disease
Malaria (all types)
Diarrhea - bacterial
Dengue fever
Chikungunya/Onyong-nyong, Ross River Fever
Norovirus
Mers-CoV and other Emerging Inf. Diseases
MDR Bacteria
Ebola hemorrhagic fever/Marburg
Influenza

Active MIDRP Effort

Vaccine, prophylactic or treatment available

Select Agents

Strong National/ Global Effort

Tier 2 - Medium user need, Medium operational risk

Disease
HIV/AIDS
Leishmaniasis - cutaneous and mucosal -visceral
Hantavirus hemorrhagic fever with renal syndrome/pulmonary syndrome
Adenovirus
Leptospirosis
Schistosomiasis
Typhoid/paratyphoid fever
Meningococcal meningitis
Rabies
Crimean-Congo hemorrhagic fever
Q fever
Lassa fever
Rift Valley fever
Melioidosis
Tuberculosis w/MDR included
West Nile fever

Conduct of Chemical And Biological Defense Program

50 U.S.C. § 1522 (d)(2) "Funding requests for the program may not be included in the budget accounts of the military departments.

Laboratories

USAMRIID
Ft. Detrick, MD

U.S. Army Medical Research Institute of Infectious Diseases

WRAIR
Forest Glen, MD

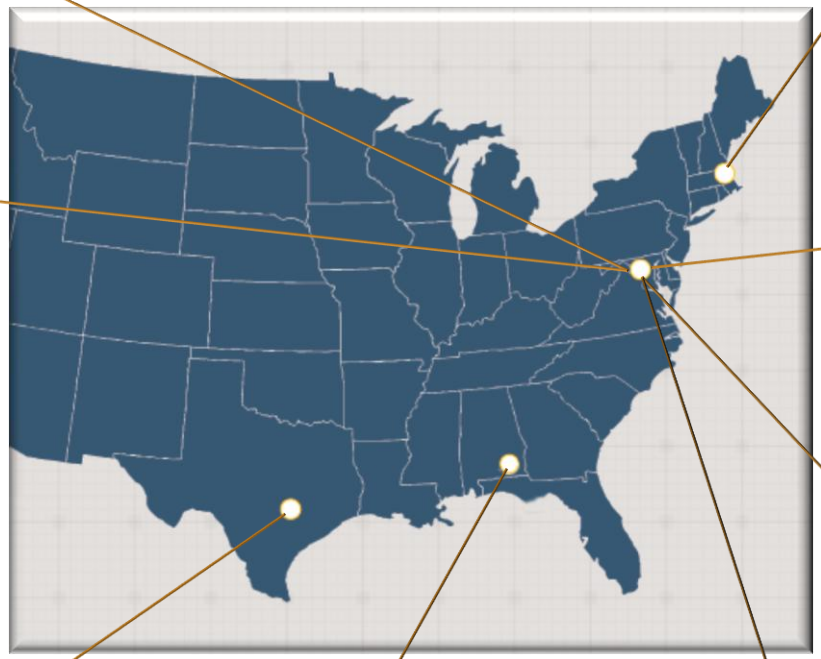
Walter Reed Army Institute of Research

- Armed Forces Research Institute for Medical Sciences (AFRIMS),Thailand, Asia
- U.S. Army Medical Research Division, JBLM
- U.S. Army Research Division, Kenya, Africa
- U.S. Army Medical Research Division, Georgia. Europe

USAISR
Ft. Sam Houston, TX

U.S. Army Institute of Surgical Research

- U.S. Army Dental and Trauma Research Detachment (USADTRD), Ft. Sam Houston, TX
- U.S. Army Medical Research Detachment (USAMRD), Ft. Sam Houston, TX



USAARL
Ft. Rucker, AL

U.S. Army Aeromedical Research Laboratory

USARIEM
Natick, MA

U.S. Army Research Institute of Environmental Medicine

USAMRICD
Aberdeen PG, MD

U.S. Army Medical Research Institute of Chemical Defense

TATRC
Ft. Detrick, MD

Telemedicine and Advanced Technology Research Center

USACEHR
Ft. Detrick, MD

U.S. Army Center for Environmental Health Research

Intramural Overseas Research Laboratories

Critical Resource in Global
Infectious Disease Research

USAMRIID, Fort Detrick

NAMRU-3, Cairo

WRAIR/NMRC, Silver Spring

AFRIMS, Bangkok

USAMRU-K, Nairobi

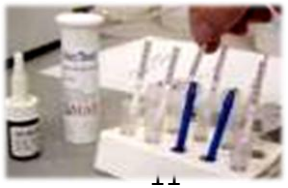
NAMRU-6, Lima

USAMRU-G, Tbilisi

NMRC-Asia, Singapore/
NAMRU-2, Cambodia

Program Portfolio

	Research Effort	Advanced Development	Fielded Products
Parasitic Diseases	• Malaria drug (CDD) • Malaria vaccine (CDD) • Leishmaniasis	• Intravenous Artesunate (CPD) • Tafenoquine • Topical Paromomycin drug (CPD)	• Atovaquone/Proguanil (Malarone®, 2000) • Doxycycline (Vibramycin®, 1992) • Halofantrine (Halfan®, 1992) • Mefloquine (Lariam ®, 1989) • Sulfadoxine-Pyrimethamine (1983) • Chloroquine-Primaquine Tablets (1969) • Primaquine (1952) • Chloroquine (1949)
Viral Diseases	• Dengue (CDD) • Hemorrhagic fevers • Scrub Typhus • HIV Global (CDD) • Acute respiratory disease research • Chikungunya vaccine development	• Dengue Tetravalent (CDD) • HIV Regional (CDD)	• Adenovirus 4 & 7 (1980) – (2011) • Japanese Encephalitis - cell based (2009) • Hepatitis A (1995) • Japanese Encephalitis (1992) • Hepatitis B (1981)
Diagnostics Developm	• Point-of-need devices (CDD) • Biofire Filmarray NGDS assay development • ESKAPE pathogens,	• Biofire Filmarray NGDS - Malaria, Dengue, Chikungunya	• Malaria Rapid Diagnostic Test (2007) • Leishmania Rapid Diagnostic Device (2014) • 5 hour antimicrobial susceptibility testing transitioned to industry (Accelerate Diagnostics) Expect FDA aproval in 2017



FIED

Program Portfolio

	Research Effort	Advanced Development	Fielded Products

Bacterial Diseases	• Clinical studies using current antibiotics for the prevention of infection post surgery
	  • Intrasite vancomycin
	  • Bismuth-thiol
	• Preclinical studies with novel therapeutic agents for the treatment of wound infections
	  • Broad-spectrum conjugate vaccine
	  • Gallium citrate
	  • Antifungal (VT-1598)
	  • Recombinant interleukin-12
	  • Activated adult mesenchymal stem cells
	• Preclinical studies with novel anti-infective delivery systems for the treatment & prevention of wound infections
	  • Anti-infective human skin substitute
	  • Antimicrobial nanoemulsion (NB-201)
	• Diarrheal (CDD)
		• Rapid Microbiological Diagnostics for MDRO Quantitative Identification	• Antimicrobial Prescribing Practices - Prevention of Infections Associated With Combat-Related Injuries (series of publications. *J. Trauma* 2011)
			• Arbekacin (FDA-approved for Single site study at Walter Reed National Military Medical Center)
			• Recognition and Comprehensive Management of Invasive Fungal Infections in War Wounds - JTTS Clinical Practice Guideline approved 1 Nov 2012
			• Meningococcus (A, C, Y, W-135) (1981)
			• Oral Live Typhoid Ty21A (1989)
			• Sentrex BioSponge™ - added to FSS 1 Apr 2015

Vector Ctrl & Radio-protects	• Repellents/Insect control • Insect identification • Arthropod-Vector Detection Device (CDD)	• Bednet • CO2 Generator Mosquito Trap • AV-RDD Chikungunya Virus	• Combined Camo Face Paint (2013) • Alternate Repellent System (2013) • Arthropod Vector Rapid Detection Device for Dengue (2012) • Rift Valley Fever virus Vector Detection Assay (2011) • West Nile Virus detection Kit (2001) • Amifostine (Ethyol®, 1995) • DEET-based Insect Repellent (1946)

Task Areas

Army

- Parasitic Diseases Research
  - Anti-Parasitic Drug Development
  - Malaria Vaccine Research
- Viral Diseases
  - Flavivirus Vaccine Research
  - Lethal Virus (Hantann, Puumala) Countermeasures
- Bacterial Diseases
  - Prevention of Diarrheal Diseases
  - Rickettsial Diseases
- Vector Control
  - Identification and Control of Insect Vectors of Infectious Diseases

DHP

- Parasitic Disease Research
  - Defense Malaria Assistance Program
- Viral Diseases
  - Military HIV Research Program
  - Acute Respiratory Diseases/Emerging Infectious Diseases
- Bacterial Diseases
  - Combat wound Infection Prevention, Management & Treatment
  - Combatting Antibiotic Resistant Bacteria
- Vector Control
  - Deployed Warfighter Protection Program
- Diagnostic Systems for Infectious Diseases
- Bio-preparedness Research Platform
  - Joint West Africa Research Group

MIDRP Accomplishments

USAMRMC PLAYS A KEY ROLE IN CURRENT VACCINE DEVELOPMENT EFFORTS

- HIV
  (TIME 2009 -Top 10 Medical Breakthroughs)
- Malaria
  (Time 2011 - Top 10 Medical Breakthroughs)
- Dengue

Vaccination with ALVAC and AIDSVAX to Prevent HIV-1 Infection in Thailand

Immune-Correlates Analysis of an HIV-1 Vaccine Efficacy Trial

Safety and Immunogenicity of a Tetravalent Live-Attenuated Dengue Vaccine in Flavivirus-Naive Infants

Investigational Malaria Vaccine Protects Healthy U.S. Adults for More than One Year
PfSPZ Vaccine Is First to Show Durable, Sterile Protection in People with No Prior Infection

SANARIA
MALARIA ERADICATION THROUGH VACCINATION

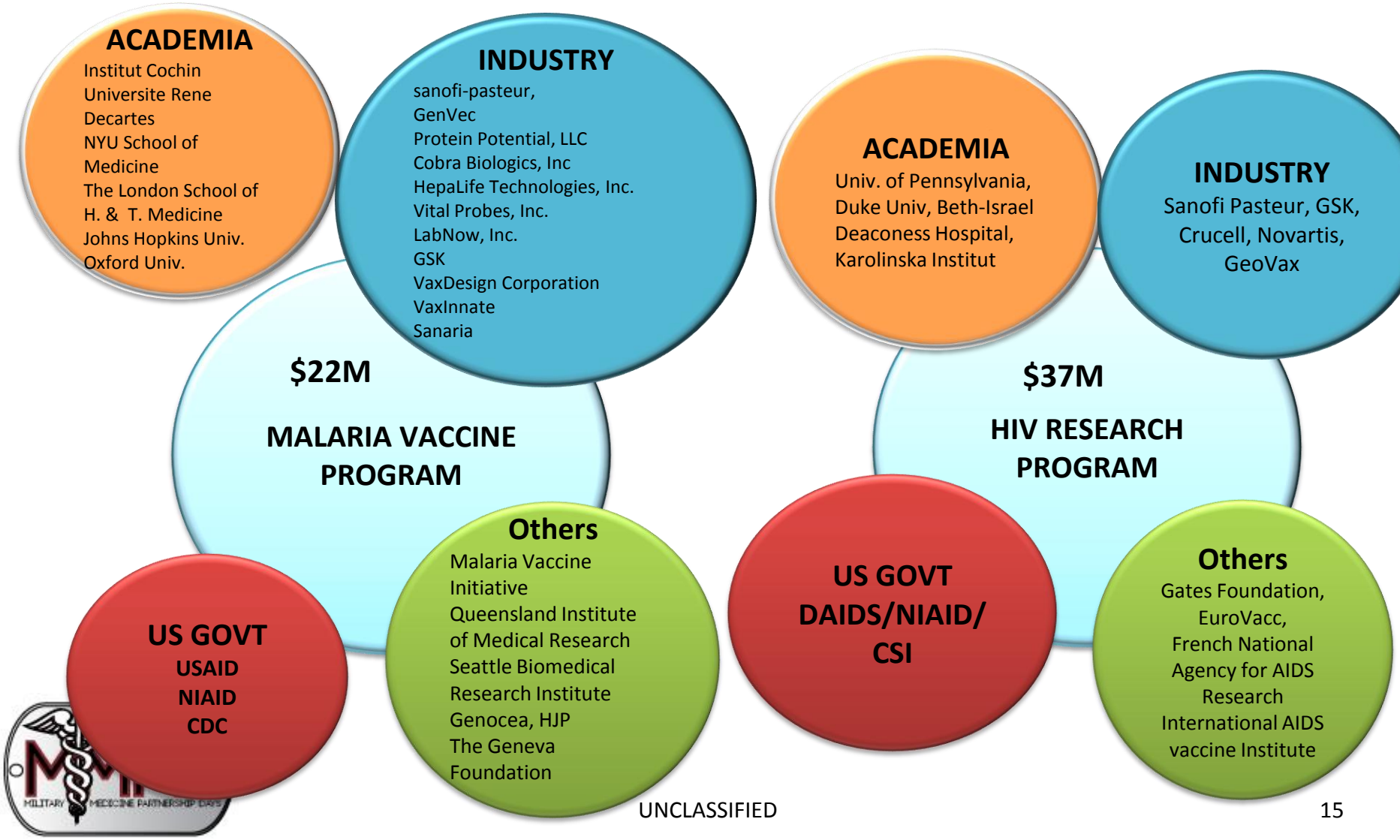
GSK's malaria candidate vaccine, Mosquirix™ (RTS,S), receives positive opinion from European regulators for the prevention of malaria in young children in sub-Saharan Africa.

Early clinical development was done in collaboration with WRAIR

Efficacy and Long-Term Safety of a Dengue Vaccine in Regions of Endemic Disease

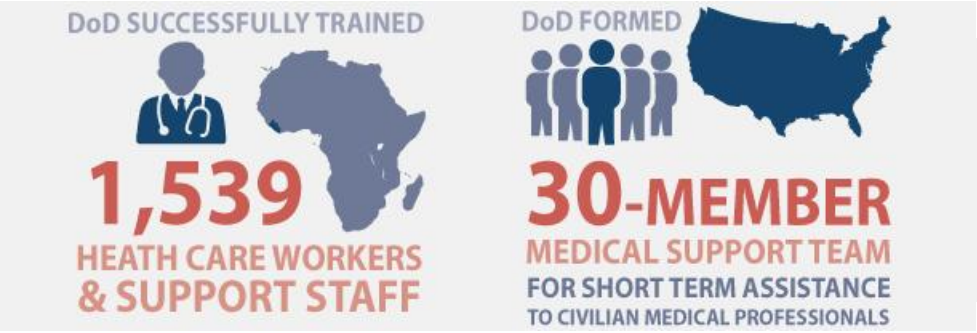
S.R.S. Hadinegoro, J.L. Arredondo-García, M.R. Capeding, C. Deseda, T. Chotpitayasunondh, R. Dietze, I.I. Hj Muhammad Hussain, H. Reynales, K. Limkittikul, D.M. Rivera-Medina, H.N. Tran, A. Bouckenooghe, D. Chansinghakul, M. Cortés, K. Fanouillere, R. Forrat, C. Frago, S. Gailhardou, N. Jackson, F. Noriega, E. Plennevaux, T.A. Wartel, B. Zambrano, and M. Saville, for the CYD-TDV Dengue Vaccine Working Group*

Successful Program Partnerships

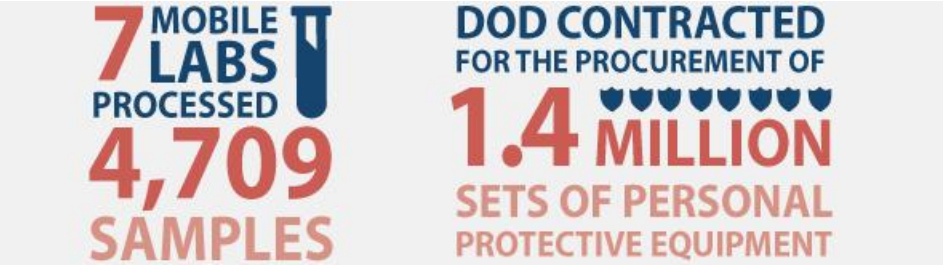


DoD Response to Ebola – Operation United Assistance

Health Care Training

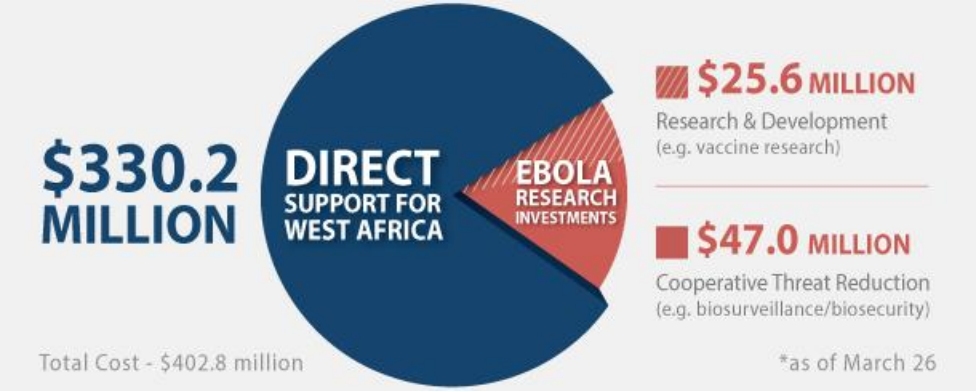


Mobile Labs & Personal Protective Equipment



Ebola Treatment Units/ Monrovian Medical Unit

DoD Ebola-Related Costs



MMPD
MILITARY MEDICINE PARTNERSHIP DAYS

Ebola Treatment Units (ETUs) & DoD Labs as of 15 Dec 2014

ETU Build End State:

Up to 17 ETUs and MMUs, transition to a self sufficient NGO.

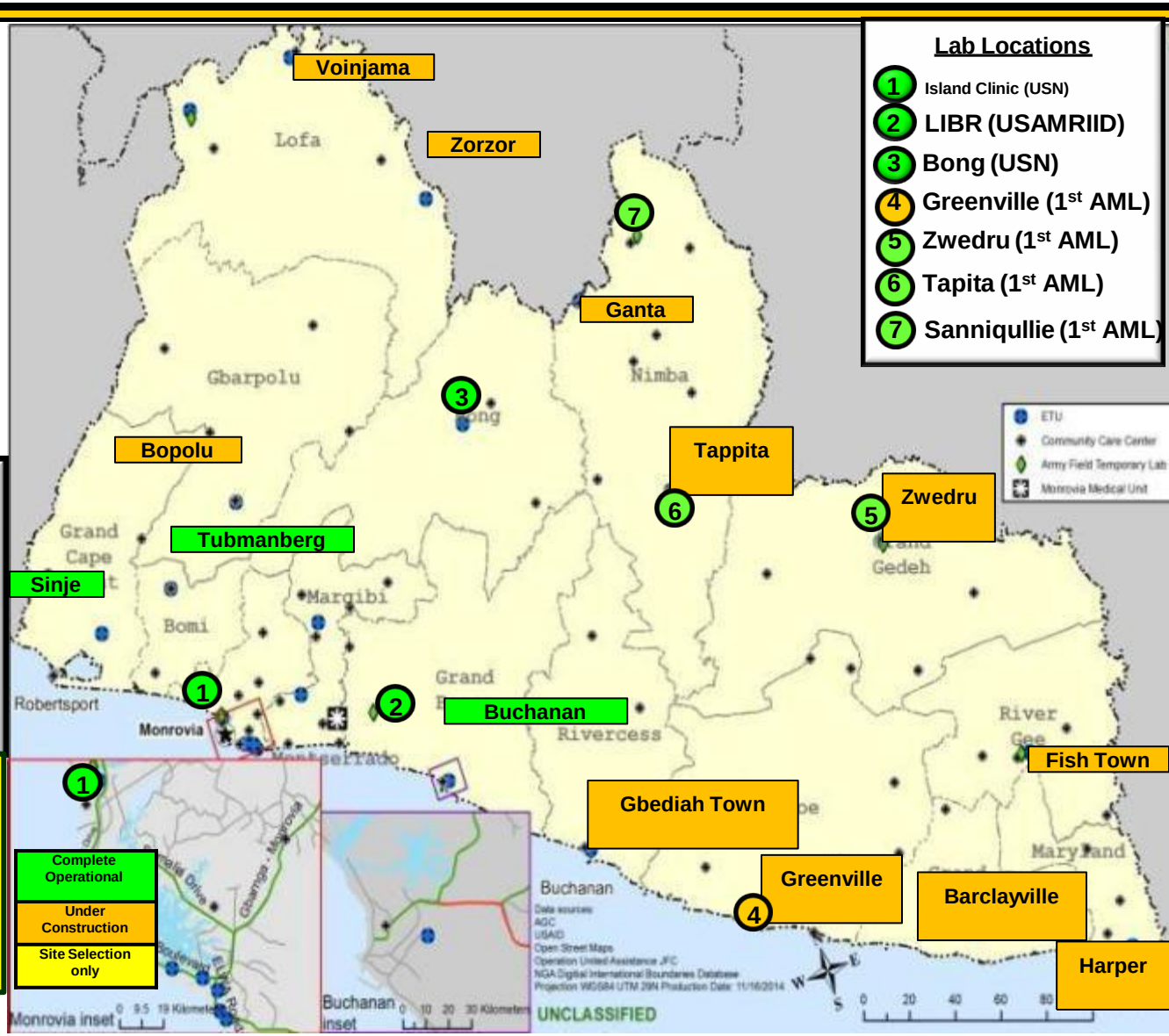
1 x US (Buchanan) (100 Bed)
1x AFL/US (Gbediah Town) (50 Bed)
2x AFL (Tubmanberg, Sinje) (100 Bed) 6 x LOGCAP (Ganta, Tappita, Zorzor, Voinjama, Barclayville, Bopolu) (50 Bed)
4 x WHH (Zwedru, Harper, Fishtown, Greenville) (50 Bed)
2 x WFP (Old Mod & SKD) JFC refuel only
1 x IMC (Kakata) JFC (PPE only)

DoD Lab

Labs conduct Ebola Virus Disease (EVD) laboratory testing to identify and communicate the infection of local nationals with EVD IOT prevent the spread of the disease.

All ETU Build Complete – 30 DEC 14

All Labs Operational – NLT 23 DEC 14

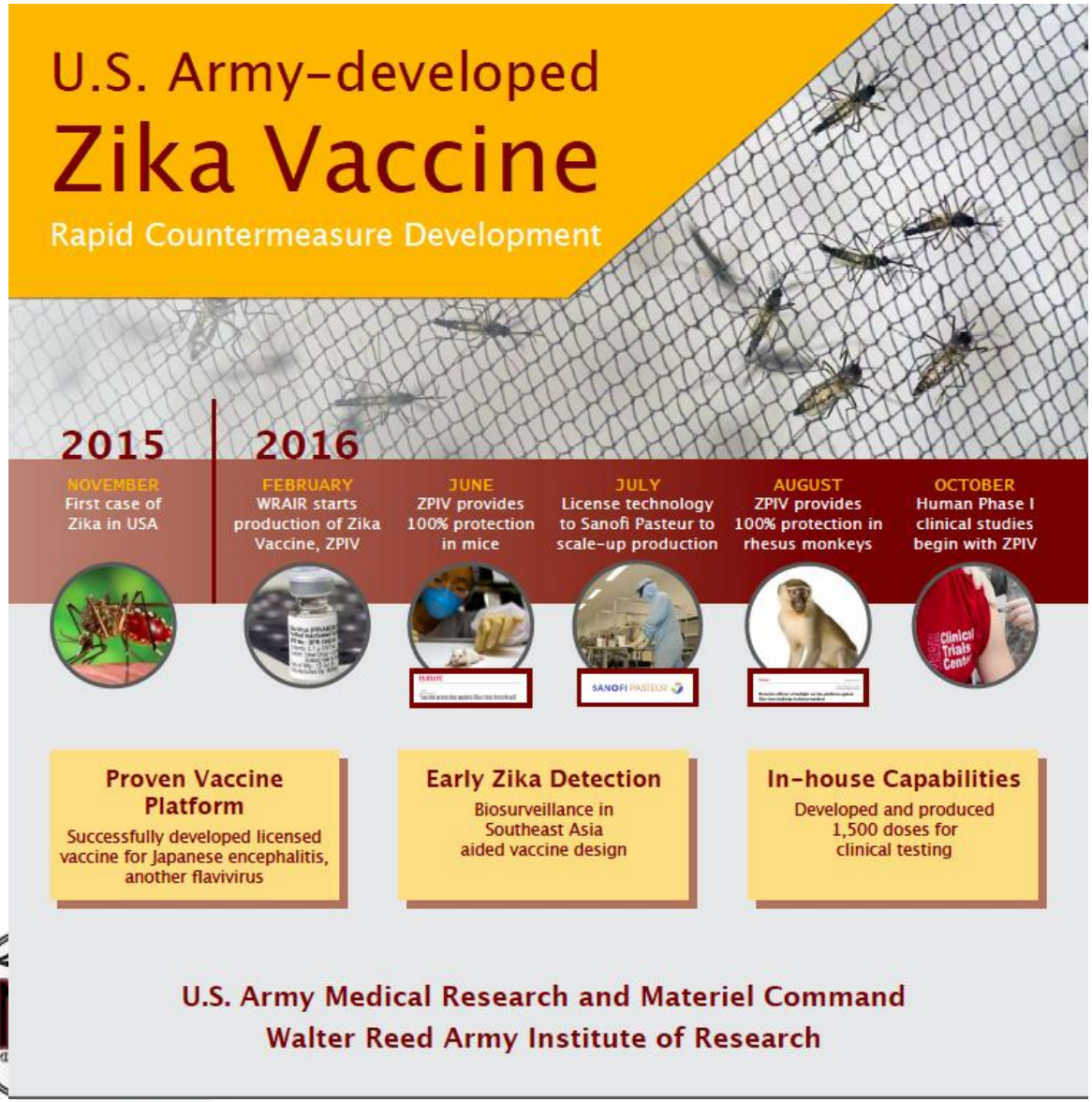


Response to Zika - Timeline

Walter Reed Army Institute of Research and Beth Israel Deaconess Medical Center Zika Virus Vaccine collaboration

Date	Event
2012-2015	WRAIR SEA sites detect ZIKV via passive surveillance
28 Jan 2016	Dan Barouch begins development of mouse and rhesus ZIKV challenge models and DNA/Ad vaccines
08 Feb 2016	WRAIR starts production of engineering lots of ZPIV vaccine
09 Mar 2016	BIDMC vaccinates mice with DNA vaccines to test in a murine challenge model
21 Mar 2016	Dan Barouch calls Nelson Michael seeking ZIKV collaboration
18 Apr 2016	WRAIR sends ZPIV vaccine to BIDMC to test in a murine model and rhesus monkey model
25 Apr 2016	BIDMC vaccinates mice with ZPIV vaccine to test in a murine challenge model
25 Apr 2016	BIDMC vaccinates 32 rhesus monkeys with ZPIV or placebo to test in the primate challenge model
28 Jun 2016	WRAIR and BIDMC publish murine protection data for ZPIV and BIDMC DNA vaccine in *Nature*
15 Jul 2016	WRAIR finishes cGMP (clinical trial material) lot of ZPIV vaccine (1,500 doses). Release testing begins.
04 Aug 2016	WRAIR and BIDMC publish rhesus protection data for ZPIV & BIDMC DNA/RhAd52 vaccines in *Science*
30 Sep 2016	Projected date of ZPIV clinical trial release for human testing
Oct 2016	Projected date of initiation of ZPIV phase 1 studies at WRAIR, BIDMC, and two DMID/NIAID VTEU sites

Rapid Response to Zika



WRAIR Walter Reed Army Institute of Research
Beth Israel Deaconess Medical Center
NIH National Institute of Allergy and Infectious Diseases
BARDA

- WRAIR, Beth Israel Deaconess Medical Center, and the National Institute of Allergy and Infectious Diseases manufactured a Zika vaccine, tested it in rodents & primates and initiated a clinical trial in < 10 months.
- WRAIR manufactured 1,500 vaccine doses for a clinical trial which began in October, 2016. Seventy-five healthy adults were recruited to participate at WRAIR's Clinical Trial Center in Silver Spring, MD.
- WRAIR and Sanofi Pasteur have agreed to co-develop the Zika virus vaccine.
- USAMRIID, as part of the National Laboratory Response Network, received the Emergency Use Authorization Zika diagnostic assay from the CDC.

Strategic Science & Technology Research Gaps

- Hantann/Puumala Virus DNA Vaccine – Co-Development Partner
  - A Phase 2a Randomized, Double-Blind, Dose-Optimizing Study to Evaluate the Immunogenicity of Hantaan/Puumala Virus DNA Vaccine Administered to Healthy Adult Volunteers Using the TDS-IM Electroporation Delivery Device for Prevention of Hemorrhagic Fever With Renal Syndrome
- Next Generation Malaria Drug
  - "Substituted Triazines for Malaria Treatment and Chemoprophylaxis", U.S. Patent 9,334,246, issued 10 May 2016.
  - Phase 0 with 3 candidates scheduled for early FY18
- Novel drug delivery technologies for treatment/prevention of infectious disease
  - Sustained release or reduce toxicity
  - Passive prophylaxis – eliminate individual compliance issues with an emphasis on anti-malarials
- Broad spectrum antiviral drugs
  - Agents that are clinically effective for treating multiple viral families, including the potential for "designer" applications that would allow for selection of combinations of agents based on geographic deployment.

Working with MIDRP

- New Product Ideas Website - http://mrmc-npi.amedd.army.mil/
- Broad Agency Announcement - http://www.grants.gov
  - On the Grants.gov homepage, click the tab "SEARCH GRANTS";
  - In the "Funding Opp #" block, enter W81XWH-17-R-BAA1
- Peer Reviewed Medical Research Program http://cdmrp.army.mil/prmrp/
  - $278.7 million in FY16
  - 39 topic areas including: Emerging Infectious Diseases, Malaria, and Vaccine Development for Infectious Diseases

Questions?

For additional questions after the conclusion of the conference, send an email message to usarmy.detrick.medcom-usamrmc.mbx.mmpd@mail.mil