



Infectious Diseases

UNCLASSIFIED

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US Army Medical Research and Materiel Command

8 March 2017



Disclaimer



The views expressed in this presentation are those of the author(s) and may not reflect the official policy or position of the Department of the Army, Department of Defense, or the U.S. Government.





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

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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



Diagnostics



Treatment



Insect Vector Control

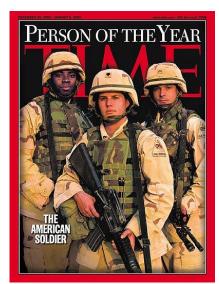




What Makes the MIDRP Unique?



- ➤ 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





• Pre Exposure/Pre-Deployment

Provide Immunity Before

Understand Epidemiology,

Develop and Test Candidate

Pathophysiology, and

Exposure

Immunity

Products



Long Term Treatment/ Management

Pointsor

Capability Neso

Sourions

ETEC Vaccine

HIV Vaccine

HFRS Vaccine

· Deployed in the Field

- Reduce Risk of Exposure to **Pathogens**
- Reduce Risk of Illness (LDD)
- **Identify Agents**
 - **New Drugs**
- **Vector Control Products**
- **Blood Screening Tools**
- Human Diagnostics -**Vector Detection**

MTF/Definitive Care

- Reduce Exposure to **Nosocomial Pathogens**
- Identify Agents of Wound Infections
- Optimize Wound Infection Management
- **New Drugs and Biologics**
- Diagnostics
- **Environmental Decontamination Products**
- **Bio-Marker Discovery**

- Malaria Vaccine
- · Dengue Vaccine

- · Improved Bed Net
- Tafenoquine
- IV Artesunate
- Topical Paromomycin Leishmania Rapid
 - Diagnostic Device
- Non-DEET Repellants

- · 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 **Active Dengue fever** Chikungunya/Onyong-nyong, Ross **MIDRP River Fever Effort** Norovirus Mers-CoV and other Emerging Inf. Vaccine, Diseases prophylactic or **MDR Bacteria** treatment Ebola hemorrhagic fever/Marburg available Influenza **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

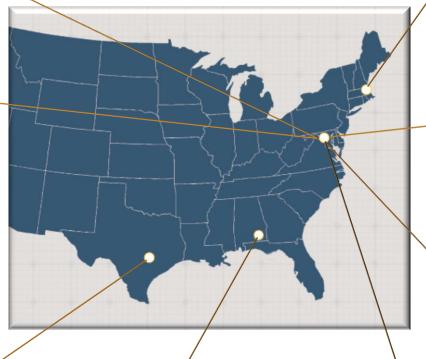


WRAIR

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





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

Telemedicine and Advanced Technology Research Center





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



U.S. Army Aeromedical Research Laboratory



USACEHR

Ft. Detrick, MD

U.S. Army Center for Environmental Health Research





Intramural Overseas Research Laboratories





USAMRIID, Fort Detrick



WRAIR/NMRC, Silver Spring



NAMRU-6, Lima



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USAMRU-K, Nairobi

AFRIMS, Bangkok

NAMRU-3, Cairo



USAMRU-G, Tbilisi

NMRC-Asia, Singapore/
NAMRU-2, Cambodia



Program Portfolio



S STATES OF	3.5		Si Rong to Sue
	Research Effort	Advanced Development	Fielded Products
Parasit ic Diseas	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 Table s (1969) Primaguine (1952)
Viral Diseas	 Dengue (CDD) Hemorrhagic fevers Scrub Typhus HIV Global (CDD) Acute respiratory disease research Chikungunya vaccine development 	 Dengue Tetravalent (CDD) HIV Regional (CDD) 	• Adenovirus 4 (4 7 4 6 1 980) – (2011) • Japanese Encephalitis - cell based (2009) • Hepatitis A (1995) • Japanese Encephalitis (1992) • Hepatitis B (1981)
Diagno cs Develor	devices (CDD)	• 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



Program Portfolio



To STATES OF THE					
	Research Effort	Advanced	Fielded Products		
	Clinical studies using current antibiotics for the prevention of infection post surgery Intrasite vancomycin Preclinical studies with novel therapeutic agents for the treatment of wound infections Broad-spectrum conjugate vaccine Gallium citrate Antifungal (VT-1598) Recombinant interleukin-12 Preclinical studies With novel The cities and dult with novel Infective delivery systems for the treatment & prevention of wound infections Anti-infective human skin substitute Diarrhadin (CDD) al nanoemulsion (NB-201)	Rapid Microbiological Diagnostics for MDRO Quantitative Identification	 Antimicrobial Prescribing Practices - Prevention of Infections Associated With Combat-Related Injuries (series of publications. <i>J. Trauma</i> 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 - <u>JTTS</u> 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-	 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

The 50 Best

Inventions

Of the Year



USAMRMC PLAYS A KEY ROLE IN CURRENT VACCINE DEVELOPMENT

EFFORTS

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

Investigational Malaria Vaccine Protects

PfSPZ Vaccine Is First to Show Durable,

Sterile Protection in People with No Prior

Healthy U.S. Adults for More than One Year

Dengue

medicine

The NEW ENGLAND JOURNAL of MEDICINE

DECEMBER 3, 2009

VOL. 361 NO. 23

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

Supachai Renks-Ngarm, M.D., Punnee Pitisattithum, M.D., D.T.M.H., Sorachai Nitayaphan, M.D., Ph.D., int Kaeskungwal, Ph.D., Joseph Chiu, M.D., Robert Paris, M.D., Nakorn Permiri, M.D., Chawetsan Namwak, M.D. de Souza, Ph.D. (Jazabert Adema, M.D., Michael Benerous, M.D. Sarisy Garunathan, M.D., Jim Tartagia, Ph.D., John G., McNeil, M.D., Donald F. Francis, M.D., D.Sc., Donald Stablen, Ph.D., Deboah L. Birx, M.D., Suparnit Chimarithust, M.D., Chirasak Khamboonnang, M.D., Parastr Thengcharton, M.D., M.D., Merlin L. Robb, M.D., Nelson L. Michael, M.D., Ph.D., Poyura Kunasol, M.D., and Jerome H. Kim, M.D., for the MOPH-TAVEG (investigators*)

The NEW ENGLAND JOURNAL of MEDICINE

DETABLISHED IN 1912

DD11 5 2012

VOL 266 NO 14

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

Barton F. Haynes, M.D., Peter B. Gilbert, Ph.D., M., Juliana McEirath, M.D., Ph.D., Susan Zolla-Parces, Ph.D., Georgia D. Tormass, Ph.D., S. Murir Allem, Ph.D., Durit Evans, Ph.D., Durit C. Monteficir, Ph.D., Chitzopor Karnassuk, Ph.D., Amergaper Gistherth, M.D., Ph.D., Haub's, Liao, M.D., Ph.D., Arleby Janes, Ph.D., George K. Levis, Ph.D., Constance Williams, B.S., Alvarbaro Pietre, Ph.D., Yoyi Forg, Ph.D., Holly Janes, Ph.D., Maghid Rey, Ph.D., Kill Birger, Ph.D., Kender Karassus, Ph.D., Although Rey, Ph.D., Kill Rey, Ph.D., Challer, Ph.D., Selly A. Sockerter, Ph.D., Charles Andrews, Sc.M., Phillip W. Berman, Ph.D., Nicole Frahm, Ph.D.

LETTER

Increased HIV-1 vaccine efficacy against genetic signatures in Env V2

Morgane Rollandi¹⁸, Paul T. Eddeteni¹⁸, Brendran B. Larseni¹⁸, Sodai Tiovanabuturi, İnris Sanders-Bu. Alan C. deCampi¹, Curis Carrico¹⁸, Sergey Menis¹⁸, Craig A. Magaret², Hasan Ahmed², Michal har Philip Konoga², Soehal Nariya¹, Julia N. Stoddard¹, Kim Wong², Hong Zhao², Wenjie Deng², Branc Shana Howelf², Adam Bates³, Michelle Lazzaro², Annemarie O Sullivari, Esther Lett, Andrea Bratightscharin Assensadrachark², Robert D. Coronell², Mark S. Gelsouas², Senachal Mitzyaphani³, Supa Merlin L. Robb³, Jason S. McLellan³, Ivelin Georgies³, Peter D. Kwong³, Jonathan M. Carlson⁵, Nel William R. Schler⁵, Peter B. Gibers⁵, James J. Mulliras⁵ & Jerome H. Klur⁵, Peter B. Gibers⁵, James J. Mulliras⁵ & Jerome H. Klur⁵

Beth Israel Deaconess





National Institute Allergy and

MACCINES

Medical Center

Protective efficacy of multiple vaccine platforms against Zika virus challenge in rhesus monkeys

Peter Abbinsh, "Raffat A. Laroena," Raffat A. De La Barrera, "Carleidae A. Britonsh," Belavard T. Moselva, "Michael Bjord, Marriach Killman," Streng Li, Dould Syndys, Orlin Nanayahlara, "Empo Nilyanandam, Noe B. Mercado, "Erica N. Berelachi," Orlin Nanayahlara, "Empo Nilyanandam, Noe B. Mercado, "Erica N. Berelachi, Particla B. Glight, "Debug Health Strength Strength," Series S. Berelachi, Farticla B. Glight, "Debug Health," Series Sandam, "Engolden Marian, Katherien Molloy," Mayari Sustry, "George B. Neubauer, "Kathryn E. Stephenson," Jean Ferre S. Pereng, "Debug M. de A. Gustern, "Januarian Missanore," Richard G. Jarman, "Remeth H. Edele," Nelson L. Michael, Sephen J. Thomas, "Rometh H. Edele," Nelson L. Michael, Sephen J. Thomas, "Dan H. Baroud-H.

Ziao Vins. (ZIVV) in suppossible for a major engoling options: in the Americas and has been causally associated with their immorcation. The development of a stail and infective XIV vaccini is therefore an ungest global health priority. Here we demonstrate that three different vaccine platforms protect against ZIVV challenges in melass moreiges, a purplic inactivated vinus vaccine induced ZIVV-isseelin endurated inactivated vinus vaccine induced ZIVV-isseelin endurated inactivated vinus vaccined endurated vinus vaccined vac



Tropical Medicine and Hygiene

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

Veerachai Watanaveeradej, Sriluck Simasathien, Ananda Nisalak, Timothy P. Endy, Richard G. Jarman, Bruce L. Innis, Stephen J. Robert V. Gibbons, Sumetha Hengprasert, Rudiwilai Samakos Angkool Kerdpanich, David W. Vaughn, J. Robert Putnak, Ken Rafael De La Barrera and Mammen P. Mammen Jr.*



The NEW ENGLAND JOURNAL of MEDICINE



Top 10 Medical

Breakthroughs

BILL & MELINDA GATES foundation

GSK's malaria candidate vaccine, MosquirixTM (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

ORIGINAL ARTICLE

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



ACADEMIA

Institut Cochin
Universite Rene
Decartes
NYU School of
Medicine
The London School of
H. & T. Medicine
Johns Hopkins Univ.
Oxford Univ.

INDUSTRY

sanofi-pasteur,
GenVec
Protein Potential, LLC
Cobra Biologics, Inc
HepaLife Technologies, Inc.
Vital Probes, Inc.
LabNow, Inc.
GSK
VaxDesign Corporation
VaxInnate

\$22M

MALARIA VACCINE PROGRAM

Sanaria

US GOVT

USAID NIAID CDC

Others

Malaria Vaccine
Initiative
Queensland Institute
of Medical Research
Seattle Biomedical
Research Institute
Genocea, HJP
The Geneva
Foundation

ACADEMIA

Univ. of Pennsylvania, Duke Univ, Beth-Israel Deaconess Hospital, Karolinska Institut

INDUSTRY

Sanofi Pasteur, GSK, Crucell, Novartis, GeoVax

\$37M

HIV RESEARCH PROGRAM

US GOVT
DAIDS/NIAID/
CSI

Others

Gates Foundation,
EuroVacc,
French National
Agency for AIDS
Research
International AIDS
vaccine Institute



DoD Response to Ebola – Operation United Assistance



Health Care Training





Mobile Labs & Personal Protective Equipment

7 LABS PROCESSED 4,709
SAMPLES

FOR THE PROCUREMENT OF

1.4 MILLION

SETS OF PERSONAL

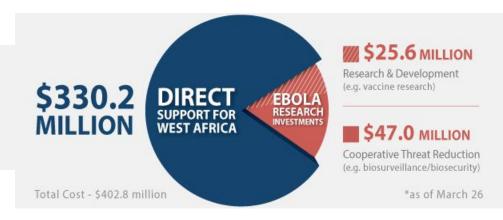
PROTECTIVE EQUIPMENT

Ebola Treatment Units/ Monrovian Medical Unit





DoD Ebola-Related Costs







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)

DoD Lab

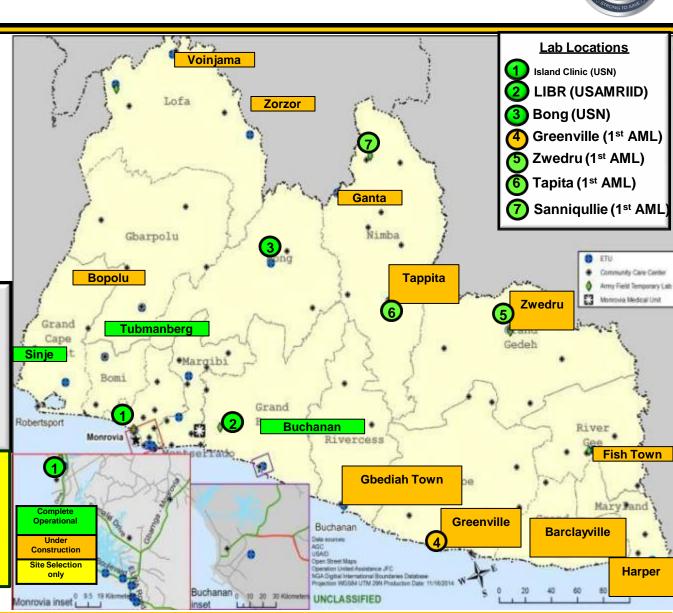
2 x WFP (Old Mod & SKD) JFC refuel only

1 x IMC (Kakata) JFC (PPE only)

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

<u>Date</u>	<u>Event</u>
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 $\it Nature$
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 \textit{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



U.S. Army-developed Zika Vaccine

Rapid Countermeasure Development

2015 First case of Zika in USA

WRAIR starts production of Zika Vaccine, ZPIV

2016





License technology to Sanofi Pasteur to scale-up production





Human Phase I clinical studies begin with ZPIV



Proven Vaccine Platform

Successfully developed licensed vaccine for Japanese encephalitis, another flavivirus

Early Zika Detection

Biosurveillance in Southeast Asia aided vaccine design

In-house Capabilities

Developed and produced 1.500 doses for clinical testing

U.S. Army Medical Research and Materiel Command Walter Reed Army Institute of Research



- 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 19 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

