



## WRAIR Clinical Trials Center and International Collaborator Network

WRAIR develops vaccines, drugs and diagnostics for endemic and emerging diseases that pose a threat to military operations and readiness. To achieve its mission, WRAIR operates a clinical trial center on its main campus and has cultivated an international network of collaborators with state-of-the-art labs and medical clinics.

Through this network of independent yet affiliated clinical trial sites, WRAIR provides a unique and effective platform to conduct research and assess diagnostics, candidate vaccines and therapeutics in endemic settings around the globe. WRAIR helps develop and sustain in-country scientific and technical expertise needed to conduct state-of-the-art research to the highest ethical standard.

WRAIR's Clinical Trials Center, international research directorates and network of nearly 20 collaborating sites play a critical role in the Institute's disease surveillance and product development efforts. Together, the sites have successfully conducted Phase I-IV clinical studies and played a role in the licensing of several vaccines and therapeutics.



## WRAIR Clinical Trials Center (CTC)

WRAIR's CTC has focused capabilities to test candidate drugs and vaccines aimed at preventing and treating infectious diseases. It's structured for maximum agility, allowing it to quickly pivot to target and test products that are a top priority to DOD and national security. The Center, an outpatient facility located on WRAIR's Main Campus in Silver Spring, Md., has conducted more than 140 trials with an average of 5-10 new trials per year, encompassing up to 7,000 or more study visits annually related to diseases ranging from anthrax to Zika.

- Supports Phase 0-II trials and acts as a site for larger Phase III trials. In the past 5 years, the CTC has successfully filled recruitment for 96% of its trials.
- Has conducted studies on malaria, dengue, influenza, anthrax, Zika, Ebola, MERS-CoV, Marburg, hantavirus, *Staphylococcus aureus* and *E. coli*, as well many first-in-human studies including those for a novel adjuvant developed at WRAIR
- Conducted malaria human challenge studies for more than 20 years involving over 1000 volunteers

## Philippines

### *Philippines-AFRIMS Virology Research Unit (PAVRU), Cebu*

Established in 2011 in partnership with Chong Hua Hospital, PAVRU has supported two Phase III clinical trials. Each trial recruited around 2,000 volunteers, and volunteer visits per day exceed 100 during peak trial times.

**PAVRU participated in two consecutive pivotal multi-site Phase III dengue vaccine trials with 1500-10,000 visits per year.**

- Phase III Dengue vaccine trial, conducted from 2011 to 2016 in collaboration with Sanofi Pasteur, concluded with the licensure of Dengvaxia, the first ever vaccine against dengue virus
- A second Phase III trial, beginning in 2015 and ongoing, tests the safety and efficacy of the Takeda Pharmaceutical TDEN tetravalent dengue vaccine recently shown to be efficacious

## Cambodia

### *Anlong Veng Referral Hospital*

AFRIMS, the national malaria program in Cambodia (CNM) and the Royal Cambodian Armed Forces (RCAF) established highly-integrated clinical trial capabilities in 2008. The clinical sites are strategically located at the epicenter of multi-drug resistance.

- Participated in Phase III study that evaluated tafenoquine in Cambodian volunteers and provided essential data for the drug filing application with the FDA
- Study that examined malaria chemoprophylaxis among Royal Cambodian Armed Forces enrolled 1,050 volunteers
- Helped develop and test a number of licensed and FDA-approved products, including diagnostics for malaria and G6PD deficiency; multiple clinical trials with antimalarials
- Ongoing Phase I-III clinical trials per year on influenza, malaria and enteric diseases with 100% recruitment success rate for all studies and less than 5% loss to follow up

**Only site approved to conduct FDA-regulated study of Tafenoquine in Cambodia**



### *Kratie Referral Hospital*

Established in 2015, this site has supported therapeutic efficacy study of Malarone for the treatment of multi-drug resistant strains of *Plasmodium falciparum* malaria, as well as the current clinical trial of new drug combinations.

# Clinical Research Collaborator Network

## Africa

For more than 50 years, the U.S. military has maintained a substantial program for infectious disease research in Kenya. These collaborations have expanded to eight countries under the U.S. Army Medical Research Directorate–Africa (USAMRD-A), which is headquartered on the campus of the Kenya Medical Research Institute (KEMRI) in Nairobi. Many of the studies in Africa have been led by WRAIR’s Military HIV Research Program (MHRP) with support from HJF.

### Kenya

#### *KEMRI-Kombewa Clinical Research Centre*

The Centre was established in 1998 and is located adjacent to the Kombewa County Hospital, which can be used for inpatient portions of studies. A new Clinical Research Centre was built in 2003 where researchers conduct Phase I-IV clinical trials on malaria vaccines and therapeutics, enteric diseases and Ebola.

- Testing new anti-malarial drug and completed Ebola Phase II vaccine clinical trial
- Completed Phase III testing of Coartem Dispersible formulation, tafenoquine, intravenous artesunate, other antimalarial drugs and zinc for diarrhea prevention; key site in RTS,S field studies and a variety of vaccine studies
- ~3000 visits/year on site, with >10,000 field visits/year and household surveys of >45,000 households biannually

#### *KEMRI-Kericho Clinical Research Centre (CRC)*

Established in 1999 in collaboration with KEMRI, a new CRC opened in 2012 where more than 50 studies have been completed. The Kericho CRC has conducted randomized, double-blind, placebo-controlled and IND/FDA-regulated studies from Phase I to IV.

- Vaccines against HIV, Ebola and polio; therapeutics against HIV, diarrhea, tuberculosis and opportunistic diseases/malignancies
- Chosen by several *Shigella* vaccine manufacturers to conduct three large scale multivalent *Shigella* vaccine trials

- NIH Networks – Part of National Institutes of Health Division of AIDS/AIDS Clinical Trials Group (ACTG) and IMPAACT, the maternal/child HIV treatment and prevention research network funded by the National Institute of Child Health and Human Development

**The Kericho CRC established Kenya’s first College of American Pathologist (CAP)-accredited laboratory**

### Nigeria

#### *Abuja Clinical Research Centre (CRC)*

The Abuja CRC was established in 2014 through a United States–Nigeria military-to-military partnership. The Centre receives additional laboratory support from the Nigerian Defence Reference Laboratory (ISO 15189 accredited by AALA). The site supports several cohort studies, and it has the capacity to see 10-20 vaccine trial participants per day.

- Conducted Two Ebola Vaccine Studies:
  - > The first Zaire Ebola vaccine trial in Nigeria enrolled 330 participants, exceeding the original sample size expectation for Nigeria by over 100%; participant retention rate of 99.4% at 12 months
  - > Phase II Ebola vaccine study enrolled 38 participants (22 healthy and 16 HIV+ adults); Participant retention rate of 89.5% at 12 months



## Tanzania

### *Mbeya Medical Research Centre (NIMR-MMRC)*

WRAIR has conducted HIV research in partnership with NIMR-MMRC since 1999.

- NIH Network – NIMR-MMRC is part of MHRP's Clinical Trial Unit for the National Institute of Allergy and Infectious Diseases (NIAID) HIV Vaccine Trials Network (HVTN). Studies include:
  - > HVTN 703 (AMP Study), a Phase I study testing broad and potent monoclonal antibody (bNAb) VRC01 for HIV prevention
    - > Phase II HVTN vaccine research trials
- Implementing a Phase IIb HIV vaccine trial evaluating two HIV vaccine regimens and a new pre-exposure prophylaxis (PrEP) agent (PrEPVacc)
- Completed Ebola Phase II vaccine study and an acute HIV infection cohort study
- Conducted three additional HIV vaccine studies (Phase I-II)

## Mozambique

### *Polana Caniço Health Research and Training Center (CISPOC), National Institute of Health (INS) (CISPOC-INS)*

In Maputo, Mozambique, WRAIR works with local researchers on HIV vaccine development and collaborates as part of MHRP's Clinical Trials Unit with NIAID/HVTN. Studies include:

- HVTN 703 (AMP Study), HVTN 705 vaccine trial, and PrEPVacc
- The site also completed HIV vaccine Phase I/II studies
- Completed Ebola Phase II vaccine study

## Uganda

### *Makerere University Walter Reed Project (MUWRP)*

WRAIR has been conducting HIV research in Uganda since 2002 with MUWRP, which has expanded and diversified to study a range of disease threats.

- HIV Research Studies – recently completed HIV-V-A004 Phase II HIV vaccine trial (Ad26 prime with MVA and protein boost); several other Phase I/II HIV vaccine studies
- Ebola/Marburg Vaccine Studies
  - > Phase I/II trials with Ad26 prime, MVA-BN-Filo boost vaccines and Ebola Sudan ChimpAd3 vectored vaccine
- Other emerging infections research and influenza and antimicrobial resistance surveillance

**In 2009, MUWRP launched the first Ebola vaccine clinical trial conducted in Africa, using an early-generation DNA vaccine candidate developed by the NIH.**

### *Fort Portal Regional Referral Hospital-MUWRP/JMEDICC Site*

The Joint Mobile Emerging Disease Intervention Clinical Capability (JMEDICC) was established in 2016 to accelerate development and deployment of medical countermeasures in a filovirus outbreak (Ebola/Marburg) by MUWRP, U.S. Navy, U.S. Army Medical Research Institute of Infectious Diseases and HJF.

- Conducting an observational study of sepsis; 570 visits/year
- Monitored Use of Unregistered and Investigational Interventions (MEURI) for outbreak preparedness



## Southeast Asia

Armed Forces Research Institute of Medical Sciences (AFRIMS) was established in Bangkok in 1961 as part of a cooperative agreement between the Royal Thai Army (RTA) and the U.S. Army. AFRIMS works with research sites in Thailand, the Philippines and Cambodia.

### Thailand

#### *Royal Thai Army Clinical Research Center (RTA-CRC), Bangkok*

The RTA-AFRIMS CRC has a clinical research site in Bangkok located on the RTA-AFRIMS campus. This site is in collaboration with the Phramongkutklao Hospital TB clinical unit.

- RTA-AFRIMS has conducted nine Phase I/II HIV vaccine trials including multi-site RV306 Phase II HIV vaccine trial and Phase II HIV-V-A004
  - Helped conduct the largest HIV vaccine trial to date, RV144, which showed modest efficacy
  - Retention rate 95-100 percent

#### *Vaccine Trial Centre (VTC), Mahidol University*

The VTC is a clinical facility located at the Faculty of Tropical Medicine in Bangkok that was established in 1960. The VTC has conducted a number of HIV vaccine clinical trials, and has been involved in vaccine research in diarrheal diseases, malaria and viral infections.

- RV305: ALVAC-HIV and AIDSVAX; MVA Boost with Mosaic inserts and Ad Type 26 vector; cohort study for future HIV trial
- Helped conduct the largest HIV vaccine trial to date, RV144, which showed modest efficacy
- VTC executes on average 2-3 studies annually with Phase I, II and III in various vaccine studies including cholera, malaria, rubella, varicella, HIV, influenza, HPV, acellular pertussis and tetanus

#### *Thai Red Cross AIDS Research Centre (TRCARC), Bangkok*

TRCARC is a major collaborating site with AFRIMS, South East Asia Research Collaboration in HIV (SEARCH) and MHRP. Studies focus on neuro AIDS, HIV immunology/virology, vaccine development, sexual health, opportunistic and co-infections.

- Nine clinical trials ongoing, including RV254, a collaboration with MHRP to identify acutely infected individuals and place them onto antiretroviral therapy immediately
- MHRP is conducting treatment interruption studies within the RV254 cohort as part of an effort to identify effective remission strategies

#### *AFRIMS-KRCH Clinical Center (AKCC), Sangkhlaburi*

Established in 1996, AKCC has conducted eight clinical trials; drug/small molecule/treatment strategy and malaria drug efficacy studies. Located in Sangkhlaburi, Western Thailand, Kanchanaburi Province, close to the Myanmar border.

#### *Phramongkutklao Hospital/AFRIMS Virology, Bangkok*

Completed multiple dengue vaccine clinical trials in children and adult volunteers; currently conducting one phase II clinical trial with 500-4,700 visits per year.

#### *Kamphaeng Phet-AFRIMS Virology Research Unit (KAVRU)*

Established in 1980, conducts emerging virus research and advanced clinical trials in collaboration with local hospitals. Previous clinical trials resulted in licensure of Japanese encephalitis and Hepatitis A vaccines.

**AFRIMS, WRAIR's Thailand Directorate, played a key role in the pivotal efficacy trial (60,000 volunteers) that led to the licensure of the Japanese encephalitis vaccine in 1992 and the next-generation vaccine in 2009. AFRIMS also supported trials leading to licensure of a hepatitis A vaccine and led the RV144 Thai HIV vaccine study, which showed partial efficacy.**

## Community Engagement

WRAIR prioritizes meaningful community engagement with the broadest array of community and research team stakeholders. WRAIR is committed to the concepts of Good Participatory Practice Guidelines and engages Community Advisory Boards (CABs) to ensure community engagement throughout the entire lifecycle of clinical research.





## Multi-site Clinical Trials Conducted within the WRAIR Network

- Ebola Vaccine — 7 sites in U.S. and Africa; n=575  
RV456: Two-Part, Phase II Study to Evaluate Two Prime-Boost Regimens of Vaccines for Ebola Ad26. ZEBOV and MVA-BNFILO
- HIV Vaccine — 3 sites in Thailand, n=367  
RV306: Randomized, Doubleblind Evaluation of Aventis Pasteur Live Recombinant Alvac-HIV (vCP1521) Priming and Multiple Boosting Strategies with and without VAXGEN gp120 B/E (AIDSVAX B/E)
- HIV Vaccine — 2 sites Uganda and Thailand, n=60 per site  
A004: Phase I/IIa Study HomologousAd26 Mosaic Vector Vaccine Regimens or Ad26 Mosaic and MVA Mosaic Heterologous Vector Vaccine Regimens
- DNA HIV Vaccine — 4 sites in U.S. and Africa, n=98  
RV262: Phase I HIV vaccine study (DNA prime/MVA boost)
- Broadly Neutralizing Antibodies for Treatment (Cure) of HIV — 4 sites in E. Africa and Thailand, n=24  
RV398: Safety and Virologic Effect of a Human Monoclonal Antibody, VRC-HIVMAB060-00-AB (VRC01) with Broad HIV-1 Neutralizing Activity, Administered Intravenously to Adults During Early Acute HIV Infection
- Acute HIV Infection — 4 sites in Africa, n=3,435  
RV217 (ECHO): HIV-1 Prevalence, Incidence, Cohort Retention, and Host Genetics and Viral Diversity in High Risk Cohorts in East Africa
- African Cohort Study (AFRICOS) — 12 sites in four African countries, n=3,500

## About WRAIR

WRAIR dates back to 1893 and is the most diverse biomedical research laboratory in the DOD. Housed in a state-of-the-art laboratory facility located in Silver Spring, Maryland, WRAIR provides unique research capabilities and innovative medical solutions to a range of Force Health Protection & Readiness challenges currently facing U.S. service members, along with threats anticipated during future operations.

WRAIR maintains sleep suites; an insectary for vectors of militarily important diseases such as malaria, dengue fever, and leishmaniasis; biosafety level 3 laboratories; accredited animal research facilities; a clinical trial center for conducting human studies for vaccines and therapeutics; and a Good Manufacturing Practice-compliant bioproduction facility.



## Study Collaborators

HJF | U.S. National Institutes of Health (DAIDS/NIAID/VRC) | USAMRIID Naval Medical Research Center | Centers for Disease Control and Prevention HIV Vaccine Trials Network | AIDS Clinical Trials Group Boston University School of Public Health | Beth Israel Deaconess Medical Center Profectus Biosciences | Inovio Pharmaceuticals, Inc. | GeneOne Life Science, Inc | GSK Novartis | Janssen Vaccines & Prevention B.V./J&J | Sanofi | ViiV Healthcare President's Emergency Plan for AIDS Relief (PEPFAR) | DOD-GEIS | ...and many more

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