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MHRP
U.S. MILITARY HIV RESEARCH PROGRAM

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Thai Government to Support HIV Vaccine Study

Building on the Success of the RV144 Thai HIV Vaccine Trial

On 29 August, the Kingdom of Thailand announced their commitment to build on the success of the landmark RV144 Thai HIV vaccine study. The announcement was made at the AIDS Vaccine Efficacy Consortium (AVEC) Summit for an AIDS-Free Generation in Thailand.

"The government of Thailand has given high priority to the HIV epidemic and we strongly believe that the development of an effective vaccine is possible. We are fully committed to playing a constructive role," said His Excellency Pradit Sintavanarong, Thailand's Minster of Public Health.

The Army-led HIV vaccine efficacy trial conducted in Thailand, RV144, provided the first evidence in humans that a safe and effective preventive HIV vaccine is possible. The Thai government will take a leadership role by supporting a future HIV vaccine efficacy study and assist in establishing a flexible biologics manufacturing capability that could support HIV vaccine production in Thailand.

"The Thai government is showing important leadership in taking HIV research to the next step," said Col. Jerome Kim, Principal Deputy of MHRP.

Read more about the AVEC Thailand initiative on page 2.

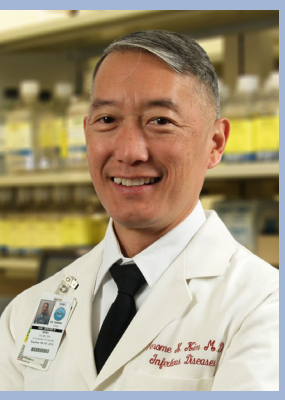
Pictured left to right: U.S. Ambassador to Thailand Kristie Kenney; Nirut Kunnawat, Advisor to the Minister of Science and Technology, Thailand; Dr. Pradit Sintavanarong, Minister of Public Health, Thailand. Together, the U.S. and Thailand have committed to create the needed capacity to further the development of an HIV vaccine working toward the shared vision of an AIDS-free generation.

The Summit attracted more than 160 international participants who discussed the UNAIDS "three zeros" goal for eradicating HIV/AIDS with a focus on the importance of developing a vaccine to prevent HIV infection. U.S. Ambassador to Thailand Kristie Kenney also addressed attendees. "Some of our most exciting partnership work with Thailand has been on HIV. Today we have the opportunity to step our efforts up a notch towards our united goal of an HIV-free generation," said Ambassador Kenney.

Other speakers included prominent Thai scientists, leaders from private industry and NIAID, CDC and UNAIDS. The Ministry of Public Health and the Ministry of Science and Technology of the Kingdom of Thailand organized the Summit, along with the U.S. Embassy in Thailand and the U.S. Army Medical Research and Materiel Command, which has worked with the government of Thailand on HIV vaccine research and development for more than 20 years. The Global HIV Vaccine Enterprise and the Bill and Melinda Gates Foundation also supported the event.

IN THIS ISSUE

More About the AVEC Thailand Initiative Col. Jerome Kim, MHRP Principal Deputy



What is AVEC Thailand?
In 2012, a working group comprised of public and private organizations called the AIDS Vaccine Efficacy Consortium (AVEC) formed with the mission to accelerate the development and testing of a pox-protein HIV vaccine prime-boost regimen in Thailand. This initiative will complement the Pox Protein Public-Private Partnership (P5) efforts to build on the RV144 results.

How will AVEC help fight HIV in Thailand?
AVEC seeks to build an effective public-private partnership (PPP) committed to providing the resources necessary for future HIV vaccine trials. Should the vaccine prove efficacious, AVEC Thailand is committed to ensuring public health access to the HIV vaccine in Thailand.

What was the importance of the recent AVEC Summit?
At the Summit, the Minister of Public Health, Pradit Sintavanarong, and a senior advisor to the Minister of Science and Technology announced their commitment to support a future efficacy study building on RV144 and establish a flexible biologics manufacturing capability in Thailand.

What role is the Thai Government playing in this initiative?
The Thai government is key to the long-term success of this initiative that will serve Thailand's public health and economic interests. This effort is connecting government, academia, industry and not-for-profits to tackle major public health challenges.

How will this initiative benefit Thailand?
Establishing a flexible biologics manufacturing capability in Thailand could support HIV vaccine production and also help address critical Thai public health needs, Thai national health security needs and regional disease burden. This biomanufacturing base could also enable more innovative translational research in Thailand and is a stated goal of the Thai government, utilizing its highly-skilled work force, providing innovative economic development, and complementing Thai strengths in clinical vaccine development.

What are the chances for success?
These types of PPPs have been successfully established in many countries including Brazil and India. Having a formal commitment from the Thai government at this Summit helps ensure that this initiative will move forward. At the Summit, the founder of the Korean company Celltrion spoke about their success as the first company to license a biosimilar in Europe—biosimilars are biological "drugs" like insulin or some of the newer monoclonal antibodies that are used therapeutically. Celltrion was co-founded by the maker of AIDSVAX (VaxGen) to be able to manufacture AIDSVAX if the Vax003 and 004 trials were successful. When efficacy was not found, the company retooled, won a large Contract Manufacturing Organization contract and is now the global leader in biosimilar programs.

Who is a part of AVEC?
The Ministry of Public Health and the Ministry of Science and Technology of the Kingdom of Thailand, the U.S. Embassy in Thailand and the U.S. Army Medical Research and Materiel Command form the core membership.

RV 368 TRUST Study

The RV368/TRUST study, a cohort study that recently began in Nigeria, will evaluate the impact of providing HIV medical and prevention services to Nigerian MSM at a Trusted Community Center that supports this high-risk population. This study aims to engage and retain individuals in the MSM community in HIV care and treatment, and better understand social and behavioral approaches for HIV prevention. In addition, researchers will assess the prevalence, incidence and risk factors for HIV and STIs in this high-risk population.

MHRP will focus on viral and host genetic factors among those infected, and characterize their influence on disease pathogenesis and response to ART. A total of 1,200 participants will be enrolled at two urban centers in Abuja and Lagos Nigeria. Recruitment will be aided by Respondent Driven Sampling, where researchers rely on their participants to recruit other participants.

RV368 is a collaborative study that will be carried out by key personnel from the U.S. Military HIV Research Program, Walter Reed Program Nigeria; Population Council Nigeria; The Johns Hopkins University Bloomberg School of Public Health; Institute of Human Virology, University of Maryland School of Medicine; and the Institute of Human Virology, Nigeria.

The African Cohort Study now enrolling participants

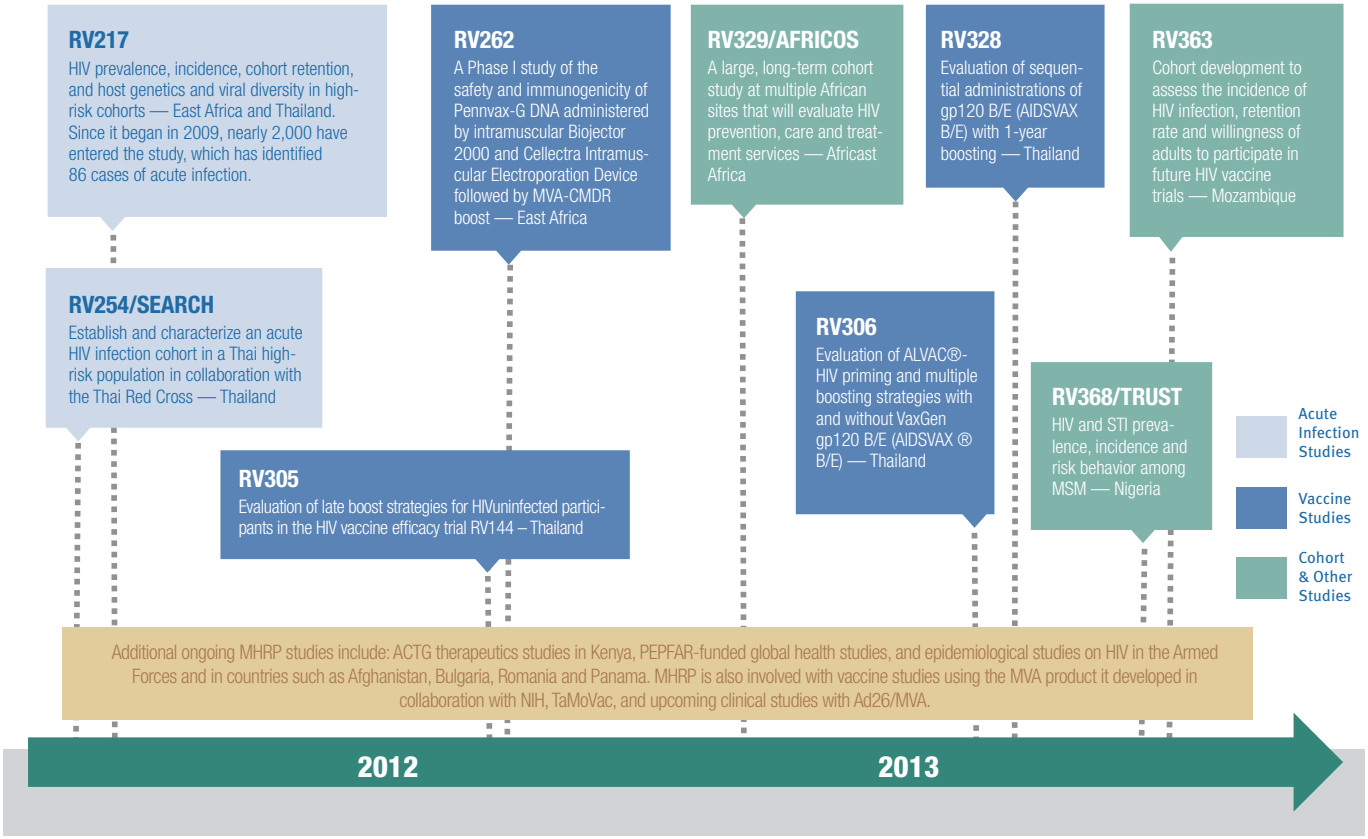
The African Cohort Study, also known as AFRICOS or RV392, is taking place at a dozen research sites in Uganda, Kenya, Tanzania and Nigeria. The study officially launched in January 2013 at the Kayunga District Hospital in Uganda after two years of preparatory work. The site has already enrolled more than 100 participants. One other site, South Rift Valley in Kenya, has also started enrolling participants.

The study, supported by MHRP's Global Health Programs and funded by the President's Emergency Plan for AIDS Relief (PEPFAR), will enroll 3,600 adults, including a subset of HIV-uninfected participants to facilitate the evaluation of prevention strategies. Participants will be followed every 6 months and the study has been initially approved for 15 years.

By following study participants, researchers will be able to evaluate current HIV treatment and prevention strategies, as well as gain valuable information about the varied sub-types of HIV across Africa. Additionally, researchers will collect data about co-infections such as TB and malaria and non-infectious conditions like heart disease.

MHRP Clinical Studies at a Glance

This graphic represents a snapshot of MHRP's current major clinical research activities. Most of the studies are supported by the National Institute of Allergy and Infectious Diseases and the U.S. Army.



RV144 Follow-up Immunogenicity Study RV306 Begins

MHRP initiated several follow-on clinical studies to conduct intensive immunogenicity research on the RV144 vaccine regimen that are funded by NIAID and the U.S. Army. The data from these studies are informing future clinical research by providing insights into the immune mechanisms generated by the RV144 regimen and the effects of an additional boost.

One study, RV306, recently began screening in September. Researchers are using the RV144 vaccine regimen to compare additional vaccine boosts and gather more immunogenicity data in 360 new volunteers. Dr. Punnee Pitisuttithum with Mahidol University is the study Principal Investigator. It will be conducted at three sites: the Vaccine Trial Centre at Mahidol University and the Royal Thai Army Armed Forces Research Institute of Medical Sciences (AFRIMS), both in Bangkok, and the Royal Institute for Health Sciences in Chiang Mai.

Another immunogenicity study, RV305, began in April 2012 in Thailand to evaluate re-boosting in volunteers who participated in the RV144 study. Initial data should be available later this year on RV305.

The RV306 study began screening volunteers on Tuesday, 24 September in Thailand. This auspicious occasion occurred on Mahidol Day, which commemorates the passing of Prince Father Mahidol Adulyadej, the "Father of Thai Modern Medicine."

New Program in Tanzania Aims to Respond to and Reduce Gender-based Violence

The Southern Highlands region of Tanzania experiences one of the highest HIV prevalence rates in the country. The epidemic in this area is fueled in part by a societal acceptance of gender-based violence, which limits a woman's ability to negotiate safe sexual practices. In Mbeya more than 67% of women have experienced some form of partner violence, which is higher compared to the statistics reported for Tanzania overall and nearly double the rate reported in the U.S.

> "In Mbeya more than 67% of women have experienced some form of partner violence"

To address gender issues, MHRP's site in Tanzania, the Walter Reed Program, initiated a comprehensive Gender Based Violence and Violence Against Children (GBV/VAC) program in collaboration with the Tanzanian Ministry of Health and Social Welfare.

The program, supported by PEPFAR, aims to increase the availability, quality and utilization of GBV services as well as to reduce the societal acceptance of GBV. The 18-month pilot project will provide interrelated intervention components delivered at the health facility and community levels with the help of eight implementing community partners. The components of the comprehensive program include:

- Facility-based services for GBV survivors;
- Facility-based screening and referral in clinical settings;
- Clinic and community outreach;
- Community-based GBV prevention activities; and
- Referrals to psychosocial support, legal services and safe houses.

In addition to local partners, the project is also working with other PEPFAR-supported international organizations to deliver the interventions with the goal of reaching nearly 64,000 people throughout the project's pilot phase.

PEPFAR is in its second year of a GBV response initiative in three African countries including Tanzania. Additionally, PEPFAR is currently conducting an in-depth evaluation examining the effectiveness and overall impact of these interventions in the Mbeya area.

PEPFAR's Impact After 10 Years

Launched in 2003, the President's Emergency Plan for AIDS Relief (PEPFAR) is the largest effort by any nation to combat a single disease. PEPFAR, which began as an emergency response to AIDS in low-resource settings, is now focused on advancing the sustainability of the response. The program directly supports more than 5 million people on antiretroviral treatment—up from 1.7 million in 2008—a three-fold increase in only four years.

PEPFAR is more than numbers. Meet Joyline. She is here today because of PEPFAR. Born with HIV, she was brought to the Walter Reed Project (WRP) in Kenya as a child very ill and extremely small for her age. Doctors started Joyline on antiretroviral therapy (ART). She was the first pediatric patient at WRP to receive ARTs. Over time, Joyline continued to receive ART at WRP and her health improved.

Today, as a young woman, Joyline is preparing for her Kenya Certificate of Secondary Examination and she plans to attend college next year. She is thankful the PEPFAR care and treatment program was started in Kenya in time to save her life and hopes the program may continue so that others in need can receive treatment. Joyline expects to live her full life and she says she will be forever grateful to the doctors for their efforts to save her life.

Joyline, pictured on the left with her grandmothers in 2004 is now a young woman preparing to attend college thanks to the lifesaving antiretroviral therapy she received because of PEPFAR. In the 2013 photo Joyline is pictured on the left with friends at school.

While MHRP's primary focus is on developing a safe, globally effective HIV vaccine, the program provides prevention, care and treatment services in each of the African communities where research is conducted as well as with military communities under the Department of Defence HIV/AIDS Prevention Program (DHAPP). These services, funded through PEPFAR, provide an ethical, non-coercive environment to conduct clinical research. As a result, MHRP has built strong and trusting relationships with the communities, developed sustainable local healthcare capacity for HIV and other medical programs, and touched many lives like that of Joyline.

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Please submit your questions and comments via email to communications@hivresearch.org. Editors: Lisa Reilly, Stephanie Stevens

For more information visit: www.hivresearch.org. Connect with us on Facebook and Twitter!

The U.S. Military HIV Research Program (MHRP) conducts research to develop an effective preventive HIV vaccine and integrates prevention, treatment, diagnostics and monitoring as part of an international effort to protect U.S. and allied troops and reduce the impact of HIV infection worldwide. The MHRP network includes sites in Maryland, Kenya, Mozambique, Nigeria, Uganda, Tanzania, and Thailand.

See MHRP and RV144 Collaborators at AIDS Vaccine in Barcelona!

After the conference, find links to available MHRP presentations and posters on the MHRP website, www.hivresearch.org.

Date	Title	Presenter	Session Type
Tuesday, 8 October	Comparative Analysis of Binding Antibody Responses elicited by a Cross-Section of Human HIV-1 Vaccine Clinical Trials	Dr. Shelly Krebs (MHRP)	Oral Abstract 11:00 am
	V2 Peptide Binding to HIV-1 Variants and Interaction of HIV-1 with a4b7 Integrin Receptor	Dr. Tina Peachman (MHRP)	Poster
	Comparable Antigenicity and Immunogenicity of Multimeric Forms of a Novel, Acute HIV-1 Subtype C gp145 Envelope for Clinical Development	Dr. Lindsay Wieczorek (MHRP)	Poster
	HLA Class II Genes Interact with the Immune Correlates from the RV144 Vaccine Efficacy Trial and Impact HIV-1 Acquisition	Dr. Rasmi Thomas (MHRP)	Poster
	Genetic and Immunological Evidence for a Role of Env-V3 Antibodies in the RV144 Trial	Dr. Morgane Rolland (MHRP)	Poster
	Engaging and Recruiting MSM in HIV Research: Experiences from the Early HIV Capture Cohort Study in Kampala, Uganda	Lillian Mutengu (Makerere University Walter Reed Project, Uganda)	Poster
	Human HIV-1 Vaccine Induced Antibody Durability and Env IgG3 Responses*	Dr. Kelly E. Seaton (Duke University)	Poster
	A V2 Conformational Immunodominant Epitope Recognized by Human Monoclonal Antibodies*	Dr. Susan Zolla-Pazner (NYU School of Medicine)	Poster
	Antibody Responses to Recombinant gp120, gp70 V1V2 Proteins and Cyclic V2 Peptide in Thai Phase I/II Vaccine Trials using Different Vaccine Regimens	Dr. Chitraporn Karnasuta	Poster
	Qualification of the Particle Diffusion Assay for Single Particle Tracking	Dr. Wiriya Rutvisuttinunt (AFRIMS, Thailand)	Poster
	Heterogeneity of anti-V2 ADCC Ab Responses and Implications for Vaccine Development*	Dr. Justin Pollara (Duke University)	Poster Discussion 4:53 pm
	Distinct HIV-Specific Antibody Fc-Profiles in RV144 and VAX003 Vaccinees*	Dr. Amy Chung (Ragon Institute)	Poster Discussion 5:01 pm
Wednesday, 9 October	Adenovirus 5 hexon-Specific CD4 T Cells are More Susceptible to HIV and Preferentially Depleted During Infection Compared to CMV-Specific CD4 T Cells	Dr. Haitao Hu (MHRP)	Poster
	Siglec-1 on Macrophages is a Major Infectivity Receptor for HIV-1: Differential Effects of GM-CSF and M-CSF on HIV-1 Entry and Replication	Dr. Mangala Rao (MHRP)	Poster
	Performance of the Determine HIV 1/2 Ag/Ab Combo Rapid Test on Serial Samples from an Acute Infection Study (RV217) in East Africa and Thailand	Leigh Anne Eller (MHRP)	Poster
	Stability of an an Acute HIV-1 Tanzanian Subtype C gp145 Envelope Protein for Clinical Development	Dr. Gary Matyas (MHRP)	Poster
	New Insight in HIV-1 Evolution during Acute Infection gained through Dense Sampling and Targeted Deep Sequencing (TDS)	Dr. Gustavo Kijak (MHRP)	Poster
	Recruitment and Retention of Urban Population in Vaccine Trials in Uganda	Dr. Hannah Kibuuka (Makerere University Walter Reed Project)	Poster
	Host-genetic Polymorphism in Fc RIIC Associated with HIV-1 Vaccine Efficacy in RV144 Trial*	Shuying S. Li (SCHARP)	Poster
	Preliminary Evaluation of Mucosal Immune Responses with Mucosal Tissue Explants in Humans Vaccinated with ALVAC/AIDSVAX B/E during the ongoing RV305 trial*	Dr. Carolina Herrera (Imperial College London)	Poster
	Investigation of Antibody Responses Induced in RV305 a Late Boost Vaccination of HIV-1 Uninfected Volunteers that Participated in RV144, a Thai Trial	Maj. Nicos Karasavvas (AFRIMS)	Poster
	Evaluation of Peripheral and Mucosal Cellular Immune Responses induced by Late Boost Strategies in HIV-negative Participants prior enrolled in RV144*	Dr. Alexandra Schuetz (AFRIMS, Thailand)	Poster
	Early and Continuous Engagement of the CAB is Essential to the Successful Implementation of Invasive Procedures in Clinical Trials	Patchara Charuthamrong (AFRIMS, Thailand)	Poster
Thursday, 10 October	Looking Back to Move Forward: Understanding ALVAC/AIDSVAX Immune Responses	Lt. Col. Robert O'Connell (USAMC-AFRIMS, Thailand)	Plenary 11:20 am

*Denotes RV144-related study by MHRP Collaborator