

Walter Reed Army Institute of Research (WRAIR)

WRAIR's Contributions to the Vaccine Enterprise

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WRAIR

Walter Reed Army
Institute of Research
Soldier Health • World Health

NATIONAL VACCINE ADVISORY COMMITTEE

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Soldier Health. World Health.

Infectious diseases are a constant threat to the soldier and global citizen in both conflict and peacetime

- WRAIR researchers contributed to the development of multiple U.S. licensed vaccines (ex: flu, Hep A, oral adenovirus)
 - Unique expertise, capabilities and resources
 - Play key role in current leading vaccines for HIV, dengue, malaria
 - Currently assisting with development of several Ebola vaccines and a MERS vaccine



Requirements to Products

The U.S. Military acquires vaccines in a very similar fashion to the way in which it acquires any medical product or device

- A military requirement for a vaccine is determined by consultation with Combatant Command Surgeons, the Military Infectious Diseases and Preventive Medicine (Public Health) communities, and the Defense Health Agency (DoD)
- Prioritizations are made by the equity holders above and the U.S. Army Medical Research and Materiel Command in terms of intramural funding and in-kind resources
- Target Product Profile like guidance is provided by a process informed from pharma and military acquisition communities (Decision Gate)

Valley of Death

The U.S. Military integrates pre-clinical/early clinical and advanced development testing using an acquisitions model

- Research and Technology groups (laboratories like WRAIR and RIID) are funded with monies to push products up to and through phase 1 human testing
- Once a product is approaching phase 1 testing, a Technology Transfer Agreement is written between the R&T group and the US Army Medical Materiel Development Activity/MRMC
- USAMMDA and it's Advanced Development team have separate monies to pull products across the Valley of Death
- IPTs, IIPTs, Board of Governors

WRAIR CONUS and OCONUS Platforms

Text Version

Additional Research Sites

- Tanzania
- Uganda
- Cameroon
- Nigeria
- Mozambique

- Cambodia
- Vietnam
- Philippines
- Bangladesh
- Bhutan
- Nepal
- Mongolia

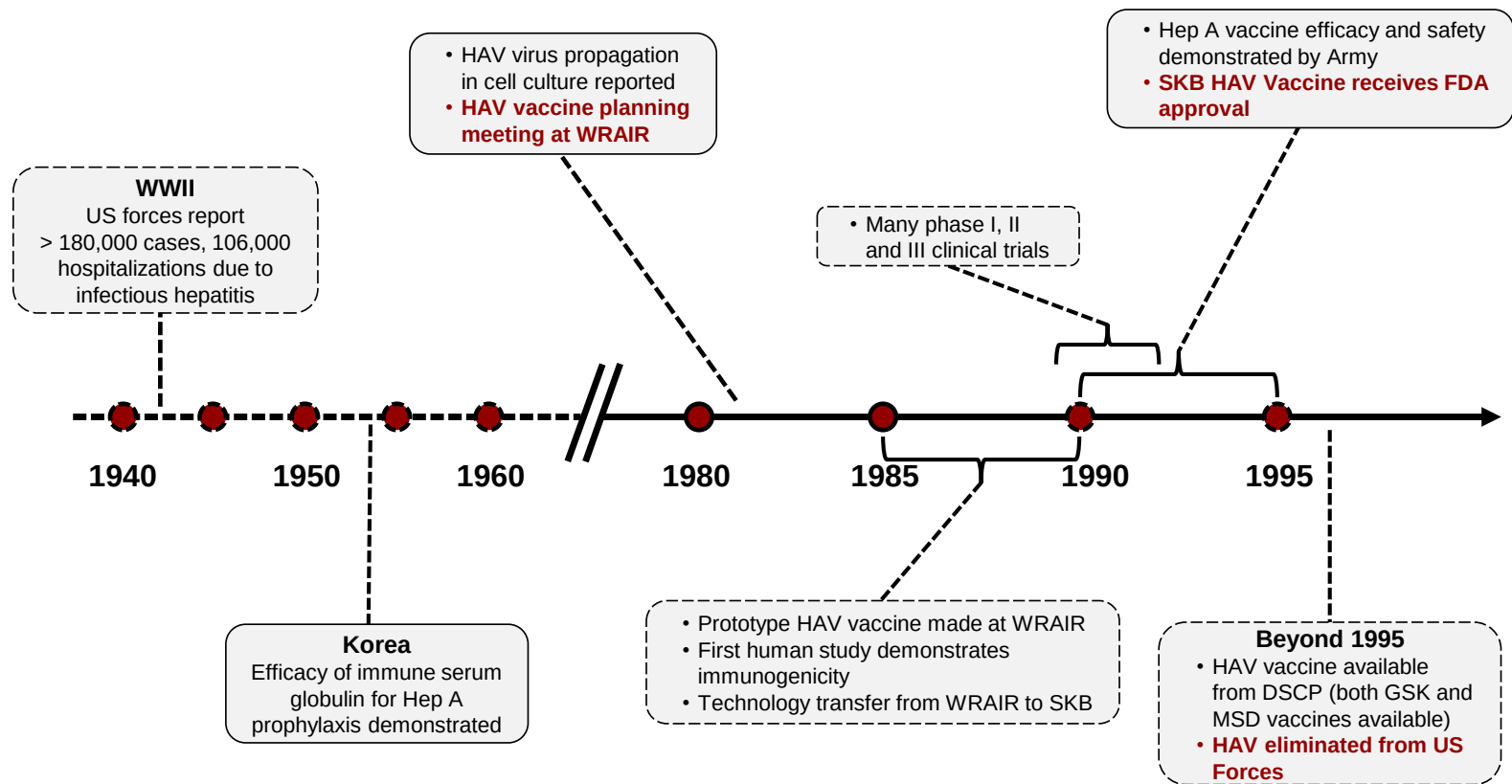


International research capabilities, expertise, and relationships

>2,000 military, civilian, support personnel

Effective Product Development: Hepatitis A Vaccine

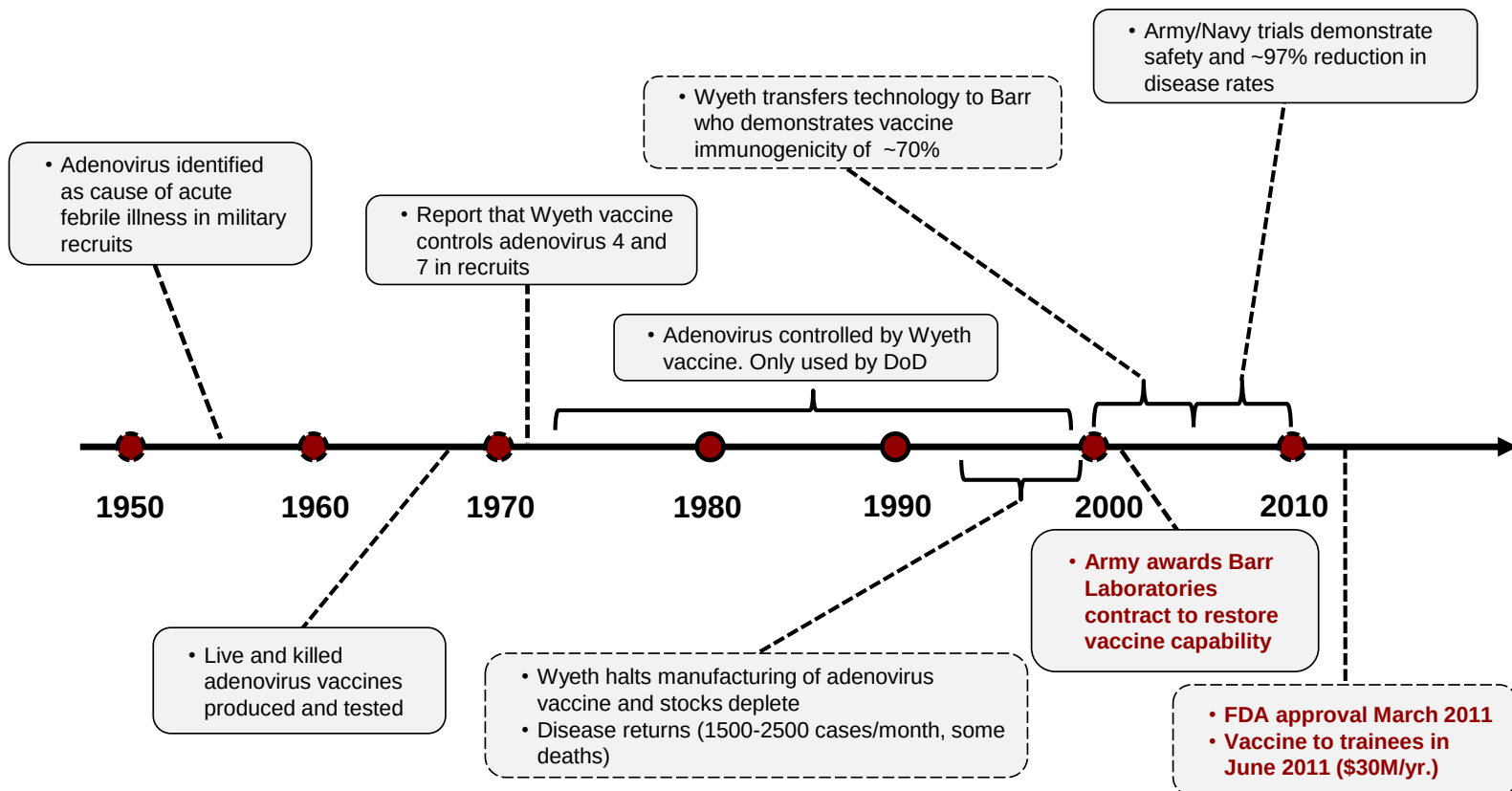
Text Version



- Time from HAV vaccine planning meeting at WRAIR to licensing approval leading to HAV elimination from US forces

Effective Product Development: Adenovirus Types 4 and 7 Vaccine

Text Version



- Time from Army awarding Barr Laboratories the contract to restore vaccine capability to FDA approval and vaccine reaching trainees
- These two types of *adenovirus* have caused severe outbreaks of respiratory illness among military recruits

WRAIR: Human Clinical Trials

- Highly experienced
 - Conducted 35 clinical studies to evaluate malaria vaccine candidates
- Full spectrum of services for clinical trial execution
 - Idea → Execution → FDA reporting
- Co-located with numerous research assets
 - Animal research facilities and Insectary
 - Product manufacturing facility (GMP)
 - Basic and applied science labs



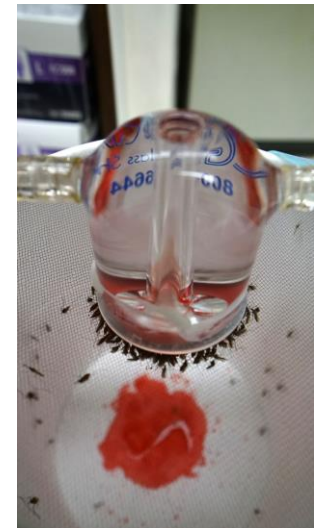
Extensive Collaborations



- Strong ties with international government, ministries of health, militaries
- Strategic partnership with NIAID/NIH
- Broad pharmaceutical company partnerships (Sanofi, J&J, Crucell, Novartis, GSK)
- Collaborative relationship with the Bill & Melinda Gates Foundation
- Extensive engagements with international normative bodies (WHO, UNAIDS) and Non Government Organizations

Infectious Diseases Research Successes

- Developed vaccines to prevent meningitis, Japanese Encephalitis and Adenovirus
- WRAIR led the first/only HIV vaccine study to show efficacy
 - Showed a preventive vaccine IS possible
- Play key roles in leading Dengue and Malaria vaccine candidates
- Advancing three Ebola vaccine candidates
 - Two US trials of Ebola candidate at WRAIR
 - Sites in Africa leveraged for Ebola vaccine research
- MERS Vaccine – first in man study



Vaccine Studies: RV144

The Thai HIV Vaccine Study

- First HIV vaccine to show modest effectiveness in preventing HIV in humans.
- Efficacy of ~60% at year 1; demonstrated 31.2% efficacy at end of study (3.5 years)
- Major international collaboration with 16,000 Thai volunteers



Building on Success of RV144

- Intensive Laboratory Studies

- Several papers published in *NEJM*, *Nature*, *Immunity*, *Cell*
- Provided clues why the vaccine protected some volunteers
- International collaboration with more than 120 scientists



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

- Follow up Clinical Studies

- Early effect nearly 60%
- Add a boost to extend and increase the immune response
- Test in different risk groups and geographic areas
- MHRP is part of the P5 Collaboration



BILL & MELINDA
GATES foundation



Ongoing HIV Vaccine Studies

- **Ad26/MVA/Protein (A004)**
Janssen/J&J HIV vaccine study in Thailand and Uganda
- **Heroin/HIV vaccine**
NIDA sponsored vaccine to combat dual epidemics
- **gp145 (NIAID)**
MHRP-developed protein for use in clinical studies
- **DNA adjuvant study (RV460)**
Clinical study in Kenya using novel adjuvants developed at WRAIR

RV144 Follow-up Studies

RV305 and RV306

Immunogenicity studies in Thailand testing late boosts

P5 studies (HVTN)

Clinical studies using subtype C vaccines

WRAIR Vaccine R&D

Malaria Vaccines

- RTS,S – early clinical development thru WRAIR- GlaxoSmithKline collaboration
 - Additional studies extending time between boosts
- Radiation-attenuated Sporozoites (PfSPZ) with Sanaria and NMRC
- New candidate vaccines targeting PfCelTOS, PfTRAP, to include novel vaccine platforms



Dengue Vaccines

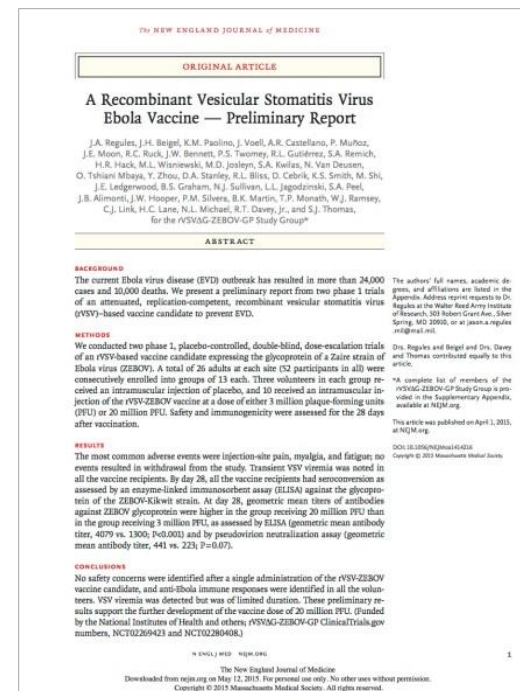
- Collaborating with industry partners on several candidate vaccines for dengue virus
- Identified new strains of dengue fever in Peru

WRAIR developed the Human Malaria Challenge Model

Ebola Vaccine Testing - US

- Completed Phase I clinical testing of VSV-EBOV vaccine candidate
 - Agile: Initiated study within 11 weeks
 - Leveraged established expertise and capabilities
 - Showed vaccine was safe, generates immune response
 - Informed dosing for larger clinical trials

Conducted in collaboration with NIH, other DoD, WHO and corporate partners



MHRP Ebola Vaccine Research in Africa

- HIV vaccine research infrastructure in Uganda leveraged for several Ebola vaccine studies:
 - Conducted first Ebola vaccine clinical trial in Africa in 2009
 - Currently testing NIH's ChAd3 vaccine (RV 422)
- Conducted the largest long-term follow up study on Ebola survivors
 - Showed long-term adverse health effects last 2+ years in survivors of 2007-2008 *Bundibugyo* ebolavirus (BDBV) outbreak in Uganda
- ChAd3 Phase II Ebola vaccine trial began in 2015 in Abuja, Nigeria GSK/(RV 429)



Kibuuka H, et al. *Lancet*. 2015 Apr 18;385(9977):1545-54.

Clark DV, et al. *Lancet Infect Dis*. 2015 Apr 21. pii: S1473-3099(15)70152-0.

New Ebola Vaccine Research

- Phase 2 clinical trial to investigate the safety and immunogenicity of two Ebola vaccine regimens in healthy and HIV-infected subjects (RV456)
 - Ad26.ZEBOV and MVA-BN-Filo vaccine candidates
 - 575 volunteers, including HIV infected volunteers
- Collaboration between Janssen Pharmaceuticals and Walter Reed Army Institute of Research (MHRP)
 - With funding from Joint Vaccines Program – Joint Program Executive Office for Chemical and Biological Defense
- Participating Sites:

WRAIR CTC, USA	WRP-Kericho, Kenya
DODHP, Nigeria	MMRC, Tanzania
MUWRP, Uganda	CISPOC, Mozambique
Kombewa CRC, Kenya	

MERS First in Human Vaccine Study

- Phase 1 clinical trial to evaluate the safety and immunogenicity of a candidate vaccine for MERS-CoV (Middle East respiratory syndrome coronavirus).
- The vaccine (GLS-5300) was co-developed by Inovio Pharmaceuticals and GeneOne Life Science, Inc.
 - First MERS-CoV vaccine to be tested in humans
 - 75 participants at WRAIR's Clinical Trials Center in Silver Spring, MD
- MERS-CoV has infected more than 1,600 people and killed nearly 40% of those infected



WRAIR

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Committed to innovation and excellence, with military-specific focus to protect the health and readiness of the Warfighter

Vaccines Recently Developed at WRAIR

Malaria vaccine, RTS,S, co-developed at WRAIR and—after more than 25 years in development—clinical trial results showed up to 53% efficacy (Phase III 2011)

Oral adenovirus (type 4 and 7) vaccine (2011, 1980) to prevent respiratory infection

Japanese encephalitis vaccine (2009, 1992)

HIV Vaccine RV144—the first HIV vaccine regimen to show partial efficacy (Phase III 2009)

Hepatitis A vaccine (1995)

Meningococcal vaccines (Phase I)

HIV Vaccine, MVA-CMDR, testing in combination with Ad26 and DNA vaccines (Phase I and II)

Diarrheal disease (Shigella) candidate vaccine

WRAIR data helps formulate the annual influenza vaccine. WRAIR developed the first flu vaccine in 1948.



Text Version from slide 5
WRAIR CONUS and OCONUS Platforms
Additional Research Sites

USAMRU-K Nairobi, Kenya

- Tanzania
- Uganda
- Cameroon
- Nigeria
- Mozambique

USAMC-AFRIMS Bangkok, Thailand

- Cambodia
- Vietnam
- Philippines
- Bangladesh
- Bhutan
- Nepal Mongolia

USAMRU-G Tbilisi, Georgia

USAMRU-W Washington State

WRAIR/NMRC Silver Spring, Maryland Headquarters

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Effective Product Development: Hepatitis A Vaccine

1943 -VWVII

Us forces report 1900,000 cases, 106,000 Hospitalizations due to infectious hepatitis.

1954 - Korea

Efficacy of immune serum globulin for Hep A prophylaxis demonstrated.

1982

- HAV virus propagation in cell culture reported
- HAV vaccine planning meeting at WRAIR

1988

- Prototype HAV vaccine made at WRAIR
- First human study demonstrates Immunogenicity
- Technology transfer for WRAIR to SKB

1994

Many phase I, II and III clinical Trials

1995

- Hep A vaccine efficacy and safety demonstrated by Army
- SKB HAV Vaccine receives FDA approval

Beyond 1995

- HAV vaccine available from DSCP (both GSK and MSD vaccines available)
- HAV eliminates from US Forces

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Effective Product Development: Hepatitis A Vaccine

1961

Adenovirus identified as cause of acute febrile illness in military recruits

1968

Live and killed adenovirus vaccines produced and tested

1971

Report that Wyeth vaccine controls adenovirus 4 and 7 in recruits

1972-2000

Adenovirus controlled by Wyeth vaccine. Only used by DoD

2000-2005

Wyeth transfers technology to Barr who demonstrates vaccine immunogenicity of ~70%

2002

Army awards Barr Laboratories contract to restore vaccine capability

2005-2010

Army/Navy trials demonstrate safety and ~97% reduction in disease rates

1993-2000

- Wyeth halts manufacturing of adenovirus vaccine and stocks deplete
- Disease returns (1500-2500 cases/month, some deaths)

2012

- FDA approval March 2011
- Vaccine to trainees in June 2011 (\$30M/yr.)