Walter Reed Army Institute of Research (WRAIR)

WRAIR’s Contributions to the Vaccine Enterprise

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NATIONAL VACCINE ADVISORY COMMITTEE
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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

International research capabilities, expertise, and relationships

>2,000 military, civilian, support personnel
Effective Product Development: Hepatitis A Vaccine

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

- WWII US forces report > 180,000 cases, 106,000 hospitalizations due to infectious hepatitis

- 1940
  - HAV virus propagation in cell culture reported
  - HAV vaccine planning meeting at WRAIR

- 1950
  - Efficacy of immune serum globulin for Hep A prophylaxis demonstrated

- 1960
  - Prototype HAV vaccine made at WRAIR

- 1980
  - First human study demonstrates immunogenicity

- 1985
  - Many phase I, II and III clinical trials

- 1990
  - Technology transfer from WRAIR to SKB

- 1995
  - HAV vaccine available from DSCP (both GSK and MSD vaccines available)

- Beyond 1995
  - HAV eliminated from US Forces

- 13 Years
Effective Product Development: Adenovirus Types 4 and 7 Vaccine

- Adenovirus identified as cause of acute febrile illness in military recruits
- Live and killed adenovirus vaccines produced and tested
- Wyeth halts manufacturing of adenovirus vaccine and stocks deplete
- Disease returns (1500–2500 cases/month, some deaths)
- Adenovirus controlled by Wyeth vaccine. Only used by DoD
- Wyeth transfers technology to Barr who demonstrates vaccine immunogenicity of ~70%
- Army/Navy trials demonstrate safety and ~97% reduction in disease rates
- Army awards Barr Laboratories contract to restore vaccine capability
- FDA approval March 2011
- Vaccine to trainees in June 2011 ($30M/yr.)

- 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
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

• 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
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 duel 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

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**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)

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


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
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 Help A prophylaxis demonstrated.

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- 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
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1994
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1995
- Hep A vaccine efficacy and safety demonstrates 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
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.)