An Evaluation of Prescreen Recruitment Data: Enrolling Racial/Ethnic Minorities in Phase I HIV Vaccine Clinical Trials

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American Public Health Association
138th Annual Meeting and Expo
November 6-10, 2010
Denver, CO

Clinical Trials Core
Vaccine Research Center
National Institute of Allergy and Infectious Disease
National Institutes of Health
US Department of Health and Human Services

Learning Objectives

1. Understand barriers to participation of racial/ethnic minorities Phase I HIV vaccine clinical trials

2. Identify at least two structures, institutions, or barriers that may preclude participation of racial/ethnic minorities in clinical trials

3. Provide at least one recruitment method and/or community engagement activity for overcoming barriers to participation in clinical trials

4. Discuss the appropriateness of reviewing protocol eligibility criteria to ensure a diverse population of healthy volunteers for participation in clinical trials

Diverse Populations in Clinical Trials

- The NIH Revitalization Act of 1993 (amended in 2001) mandates that women and minorities be included in all NIH-funded research
- Diverse populations in clinical trials are necessary to ensure generalizable results
- Health disparities can impede diverse enrollment in healthy volunteer studies
- Strict eligibility criteria for Phase I trials make enrolling diverse populations particularly challenging

Phases of Clinical Research

Phase I
Researchers test an experimental drug or treatment in a small group of people (20–80) for the first time. The purpose is to evaluate its safety and identify side effects.

Phase II
The experimental drug or treatment is administered to a larger group of people (100–300) to determine its effectiveness and to further evaluate its safety.

Phase III
The experimental drug or treatment is administered to large groups of people (1,000–3,000) to confirm its effectiveness, monitor side effects, compare it with standard or equivalent treatments, and collect information that will allow the experimental drug or treatment to be used safely.

HIV/AIDS Statistics

Rates of newly diagnosed HIV infections (CDC, 2008):

- 52% non-Hispanic Blacks
- 17% Hispanic/Latinos

Rates of participation in National Institute of Allergy and Infectious Diseases (NIAID)-funded HIV Phase I HIV vaccine clinical trials (Djomand, 2005):

- 7% African-Americans
- 3% Hispanic/Latinos
- 3% other racial/ethnic minority

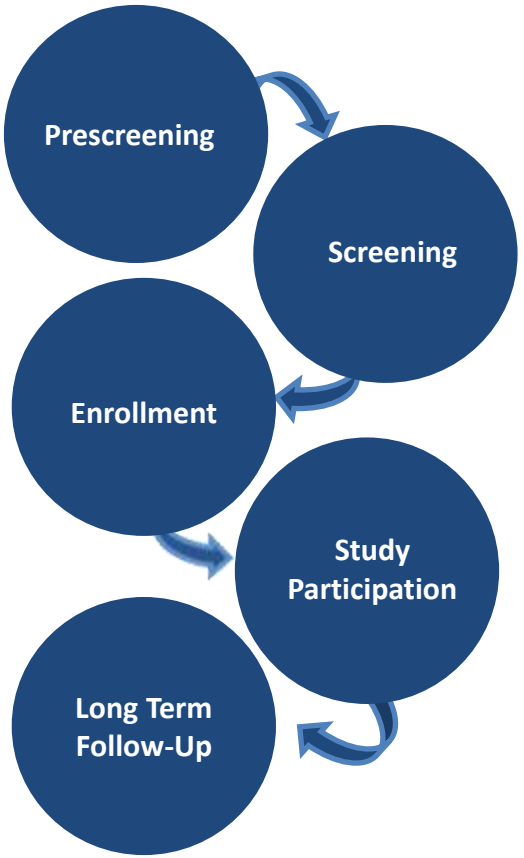
Mission of the VRC

To conduct research that facilitates the development of effective vaccines for human disease.

The primary focus of research is the development of vaccines for HIV/AIDS.

Stages of Study Participation

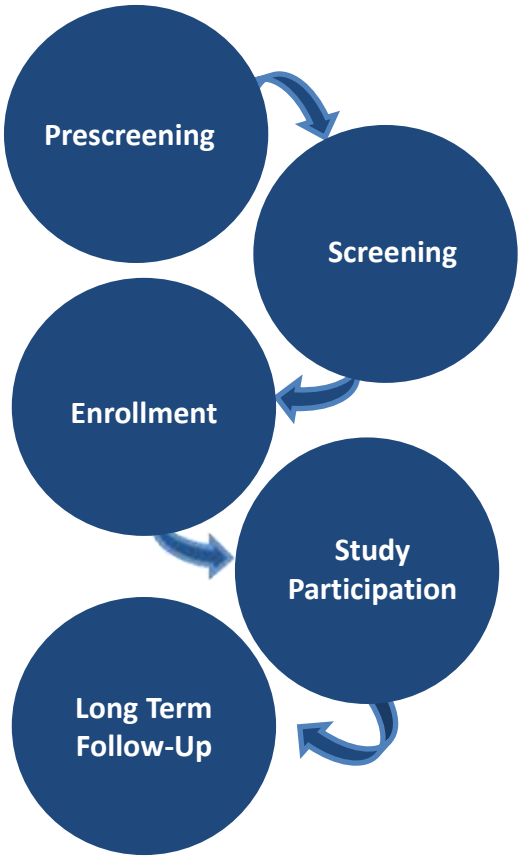
- Stage 1: Prescreening
- Stage 2: Screening
- Stage 3: Enrollment
- Stage 4: Study Participation
- Stage 5: Long Term Follow-Up



Stages of Study Participation

Stage 1: Prescreening

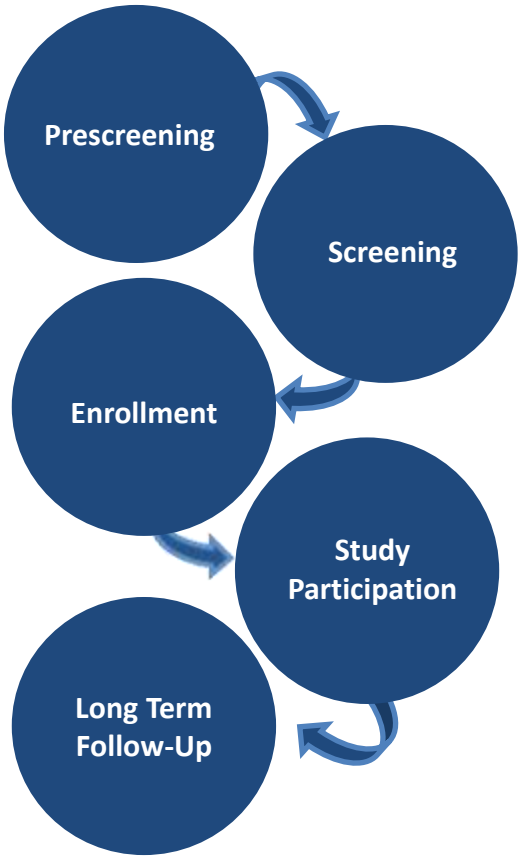
- Individuals interested in participating in a VRC study contact recruitment staff
- Recruitment staff provide a brief description of the study and obtain demographic and recruitment information
- If the volunteer is interested in being screened to determine eligibility for participation, recruitment staff conduct a prescreen questionnaire to determine appropriateness for clinical screening



Stages of Study Participation

Stage 2: Screening

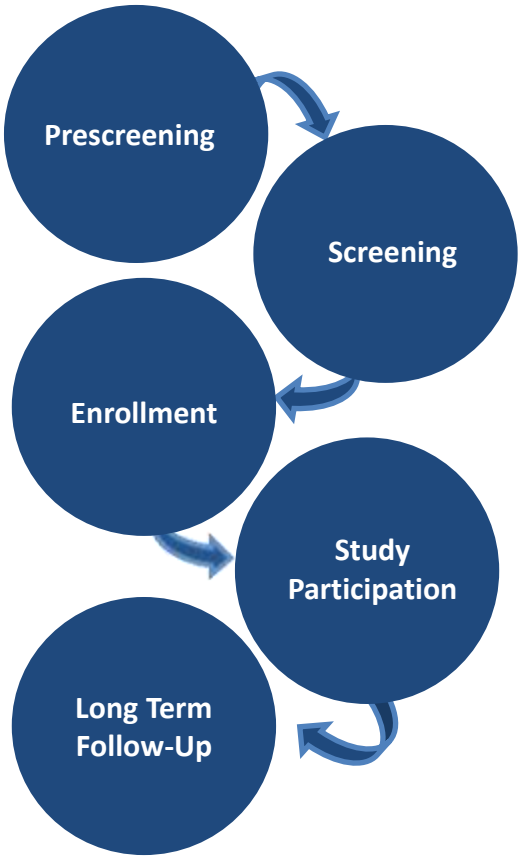
- Clinical staff discuss the study in detail (including review of informed consent documents)
- A detailed medical history is obtained
- A physical exam is conducted
- Blood tests are performed to complete the picture of current health status
- If clinical staff determine the volunteer is eligible for vaccine study participation, the volunteer is scheduled for an enrollment visit



Stages of Study Participation

Stage 3: Enrollment

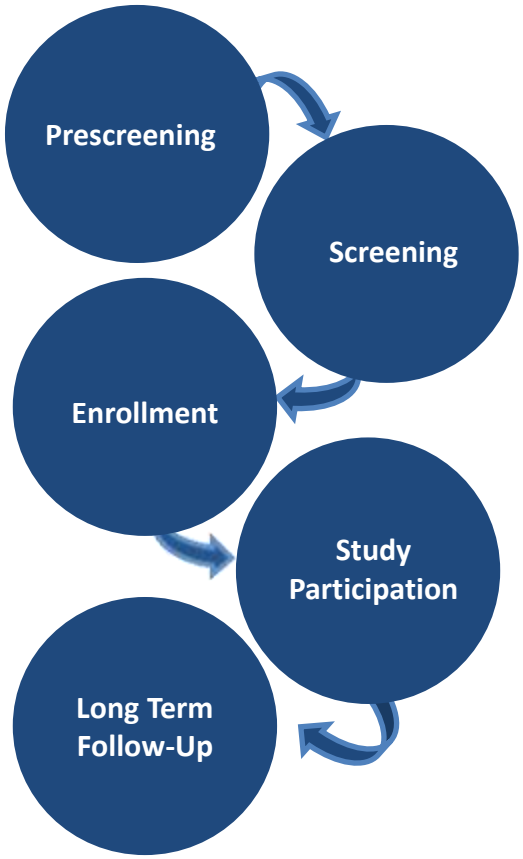
- Clinical staff review study and assess volunteer's understanding prior to enrollment
- Eligibility is confirmed prior to study enrollment
- Once a volunteer is enrolled, they receive their first vaccination
- Volunteers are monitored for a period of time after each vaccination
- Volunteers and staff set schedule for remaining study visits



Stages of Study Participation

Stage 4: Study Participation

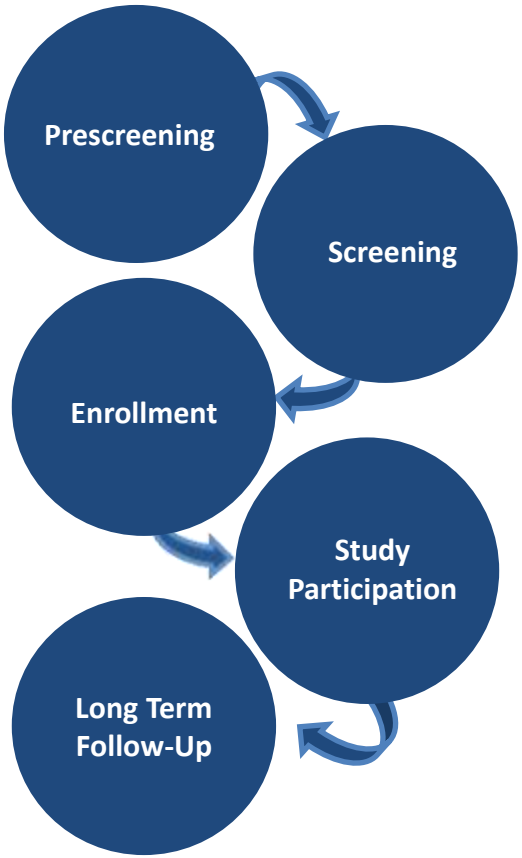
- Volunteers may receive additional vaccinations as indicated per protocol
- Reactogenicity information is collected throughout the vaccination phase of study participation
- Even after vaccination is completed, follow-up visits continue to be conducted to collect information about the effects of vaccination
- Safety data is collected throughout the course of the study



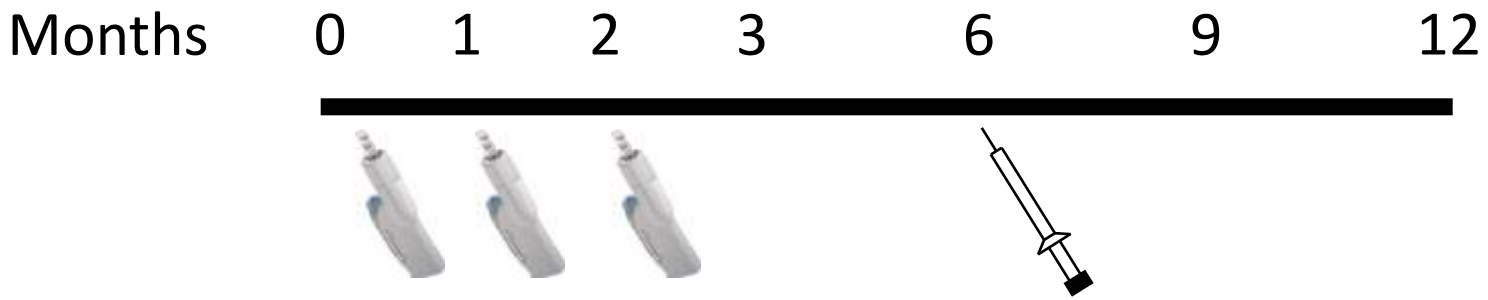
Stages of Study Participation

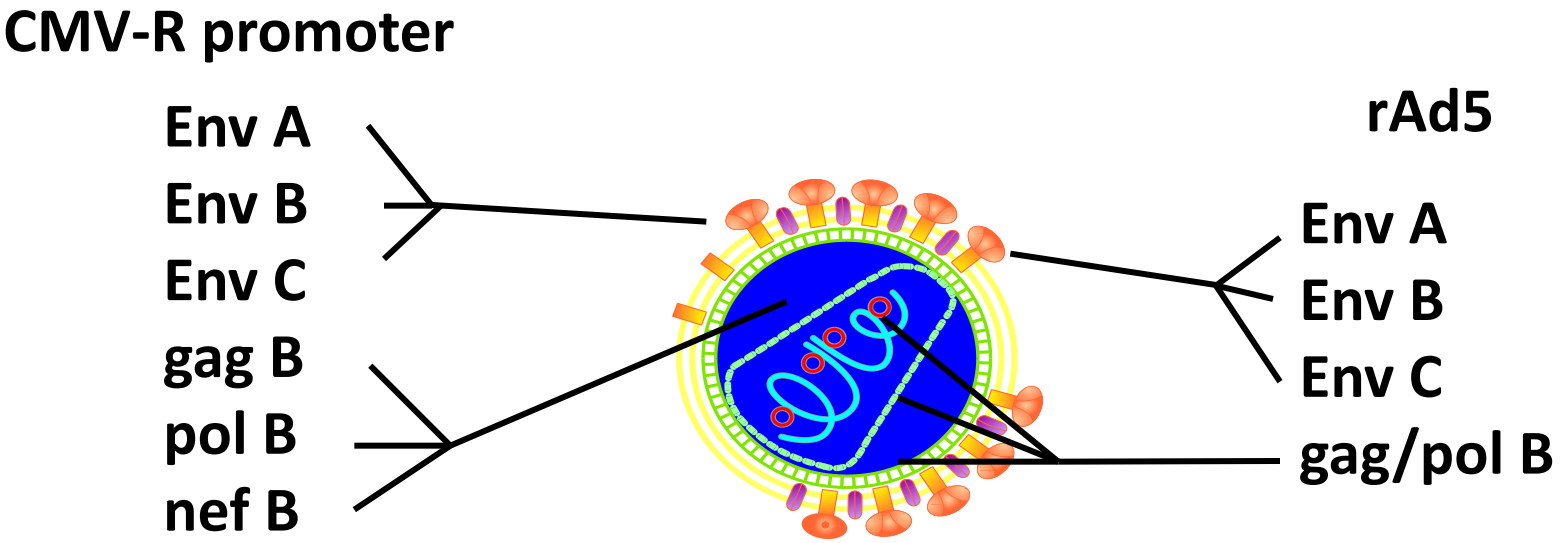
Stage 5: Long Term Follow-Up

- After active study completion is complete, volunteers may be followed on an annual basis to assess long-term outcomes
- For HIV vaccine study participants, VRC may offer free HIV testing even after study completion
- As information about studies is published, publications are shared with study participants



HIV Vaccines – VRC Approach





HIV Vaccine Studies at VRC

Phase I eligibility criteria are generally strict to minimize variables during initial product discovery

In 2009, the criteria for participation in a VRC Phase I HIV vaccine study included:

- 18 – 50 years old*
- Low risk for HIV infection
- Ability to provide informed consent
- Ability to provide government-issued ID
- Generally healthy (no major chronic conditions)
- Ability to comply with appointment schedule

* Rollover participants had an age limit of 55

VRC 012

A Phase I Clinical Trial of the Safety and Immunogenicity of an HIV-1 Adenoviral Vector Serotype 35 Vaccine, VRC-HIVADV027-00-VP (rAd35-EnvA): Dose Escalation as a Single Agent and Prime-Boost Schedules with an HIV-1 Adenoviral Vector Serotype 5 Vaccine, VRC-HIVADV038-00-VP (rAd35-EnvA), in Uninfected Adults

Part I:	**Day 0**:	
Group 1 (n=5)	rAd35-EnvA 10^9	
Group 2 (n=5)	rAd35-EnvA 10^{10}	
Group 3 (n=5)	rAd35-EnvA 10^{11}	
Part II (Prime/Boost):	**Day 0**:	**Week 12**:
Group 4A (n=10)	rAd35-EnvA 10^{10}	rAd5-EnvA 10^{10}
Group 4B (n=10)	rAd5-EnvA 10^{10}	rAd35-EnvA 10^{10}

VRC 015

A Phase I, Open-Label Clinical Trial to Evaluate the Safety, Tolerability and Immunogenicity of a Multiclade Recombinant HIV-1 Adenoviral Vector Vaccine, VRC-HIVADV014-00-VP, in Uninfected Adults Randomized to Needle or Biojector Methods of Intramuscular Injection

Group 1 *(vaccine naïve)*:	**Day 0**:
Group 1a (n=10)	rAd5 via needle/syringe
Group 1b (n=10)	rAd5 via Biojector
Group 2 *(previously vaccinated)*:	**Day 0**:
Group 2a (n=10)	rAd5 via needle/syringe
Group 2b (n=10)	rAd5 via Biojector

Adenoviral Exposure Considerations

Rates of adenoviral exposure vary by region, but in North America:

- Estimated Ad5 exposure is 50-60% of population
- Estimated Ad35 exposure is 20% of population

VRC 012 required:

- No previous Ad5 exposure (<12)
- No previous Ad35 exposure (<12)

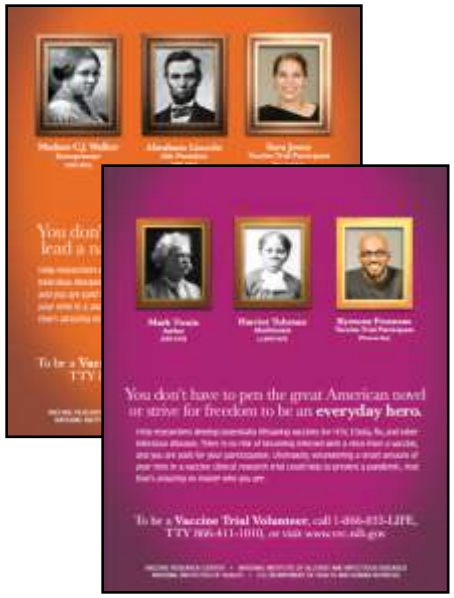
VRC 015 required:

- Group 1: at least 40% of enrollees had to have **low** Ad5 exposure ($\leq$500)
- Group 2: at least 40% of enrollees had to have **high** Ad5 exposure (>500)

Volunteer Recruitment

Volunteers are recruited for participation in VRC HIV vaccine clinical trials through a myriad of mechanisms:

- Community outreach
- Mass transit
- Newsprint
- Internet
- Radio



Volunteer Recruitment

VRC recognizes that a single approach will not reach everyone, so to address the need for diversity, the VRC ensures:

- Diverse recruitment team
- Educational materials available in multiple languages
- Frequent partnering with minority-serving organizations
- Variety of promotional materials that appeal to different populations

Possible Outcomes of Prescreening

- **Did Not Qualify**

  Based on questions asked by recruitment staff at prescreening, the volunteer does not meet eligibility criteria for participation.

- **Voluntarily Discontinued**

  After expressing initial interest in participating in an HIV vaccine study, the volunteer opts not to continue participation.

  (*includes those who do not respond to repeated contact attempts and those who do not keep scheduled screening appointments*)

- **Screened**

  After prescreening with recruitment staff, the volunteer is scheduled for and keeps at least one screening appointment.

Possible Outcomes of Screening

- **Did Not Qualify**

  Based on screening procedures, including lab tests and physical exam findings, the volunteer does not meet eligibility criteria for participation.

- **Voluntarily Discontinued**

  After initiating the screening process, the volunteer opts not to continue participation prior to study enrollment.

  (*includes those who do not respond to repeated contact attempts and those who do not keep scheduled screening appointments*)

- **Enrolled**

  After completing screening procedures with clinical staff, the volunteer is enrolled into a vaccine study and receives at least one study injection.

Voluntarily Discontinuing During Screening

Due to the voluntary nature of clinical research, volunteers may choose at any time to discontinue participation for any reason. In 2009, reasons VRC volunteers gave for choosing to discontinue participation both during prescreening and screening included:

- Concerns about vaccine-induced seropositivity (VISP)
- Geographic constraints/inconvenience
- Inability to meet time commitment
- Loss to follow-up (passive declination)

Voluntarily Discontinuing During Screening

- Time commitment was a concern for all races/ethnicities
- In the absence of protocol ineligibility, the most common reason for voluntarily discontinuing for all races/ethnicities was concerns regarding VISP
- Geographic constraints as a reason for discontinuing participation can be largely attributed to both the unique requirements of accessing the NIH campus and the cyclical nature of employment in the DC area

Protocol Ineligibility During Screening

Despite a desire to participate in research, some volunteers do not meet eligibility criteria for a Phase I trial. Reasons include:

- Substance use that might preclude compliance
- Sexual history (Phase I studies require low risk of HIV infection)
- High body mass index (obesity)
- Chronic medical conditions (i.e. hypertension, diabetes)
- Medical eligibility criteria unrelated to volunteer safety (i.e. previous adenoviral exposure, history of certain allergic reactions)

Protocol Ineligibility During Screening

- More than three-fourths of those ineligible for high BMI/obesity were racial/ethnic minorities
- The majority of those ineligible due to chronic medical conditions were racial/ethnic minorities
- Two-thirds of those ineligible due to health behaviors (e.g. sexual history and substance use) were racial/ethnic minorities

General Observations

- Racial/ethnic minorities express interest in HIV vaccine trials at the same rate as whites
- Racial/ethnic minorities progress from prescreen to screen at lower rates than whites
- Racial/ethnic minorities enroll in HIV vaccine studies at lower rates than whites
- Differences in accrual rates by race/ethnicity can be attributed to:
  - Higher rates of medical conditions
  - Sexual history
  - Substance use

VRC Recruitment and Enrollment Goals

- Evaluate vaccines in a diverse population
- Obtain results that are relevant to all those at risk for HIV
- Continually collect and analyze information regarding interested populations

Diversity Considerations

- Eligibility disparity, not lack of interest
- Different definitions of what it means to be healthy
- Better diversity in recent years, but not yet representative sample
- Small sample size of Phase I trials makes diversity particularly challenging
- Unique challenges of conducting trials within federal government

Eliminating Barriers to Participation

- The importance of ensuring diversity while maintaining safety should be stressed in all facets of clinical research
- Active collaboration by the scientific community and the general population will facilitate communication
- Educational initiatives are necessary for both study participants and scientific researchers to ensure common understanding
- Researchers must be aware of unique conditions present within a specific community when designing clinical trials

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