# Implications of HIV Testing Outside of the Study During Preventative HIV Vaccine Trials in the US

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HIV VACCINE TRIALS NETWORK

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## Objective

To assess the number of participants and reasons for having HIV testing performed by non-study providers in preventative HIV vaccine trials. To assess if events related to non-study HIV testing had a negative impact on trial participants' quality of life.

## Background

Participants on HIV vaccine trials who receive an HIV vaccine may test positive for HIV antibody, increasing their risk of social harms and potentially unblinding participants who receive a standard HIV test by providers outside of the study.
The HIV Vaccine Trials Network (HVTN) is an international clinical trials network dedicated to finding an effective and safe HIV vaccine. Participants enrolled in HVTN studies are provided HIV testing at protocol-specified visits and upon request.
On September 22, 2006, Revised Recommendations for HIV Testing of Adults, Adolescents, and Pregnant Women in Health-Care Settings were issued by the US Centers for Disease Control.
"Major revisions from previously published guidelines are as follows:
For patients in all health-care settings
HIV screening is recommended for patients in all health-care settings after the patient is notified that testing will be performed unless the patient declines (opt-out screening).
Persons at high risk for HIV infection should be screened for HIV at least annually.
Separate written consent for HIV testing should not be required; general consent for medical care should be considered sufficient to encompass consent for HIV testing.
Prevention counseling should not be required with HIV diagnostic testing or as part of HIV screening programs in health-care settings. "
These recommendations for increased HIV testing in health-care settings could potentially lead to more vaccine trial participant's receiving HIV testing by non-study providers.
Data presented below from HVTN Phase I and II vaccine trials reflect the impact of non-study HIV testing prior to wide-spread implementation of the CDC recommendations.

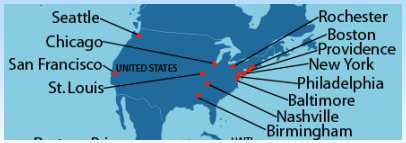


**Figure 1.** *US HIV Vaccine Trial Network (HVTN) Sites*

## Methods

The HVTN initiated 15 phase I and one phase II preventative HIV vaccine trials in the United States since January 2004. Participants were recruited and seen for study visits at 13 study sites located in 12 U.S. cities (see Figure 1). Participants had to be 18-50 years of age, HIV-1 negative and in general good health at study entry.
The timing of study procedures varied by protocol. Typically HIV testing and risk reduction counseling were done every 3 months. Testing was performed by the HVTN HIV diagnostic laboratory using an algorithm that distinguishes between vaccine induced seropositivity and true HIV infection. Also, as part of their visits, participants were asked, typically every 6 months, if they had received any HIV testing from non-study providers. Participants were counseled to receive all HIV testing through the study site to avoid false positive tests.
Participants may experience discrimination because of their participation in an HIV vaccine trial, because others may think they are HIV infected or at high risk of HIV infection. Participants were asked to report to site staff any events that the participant felt had a negative impact upon their quality of life and were related to trial participation. Details of the event were captured on a Social Impact Log (Figure 2). Impact of the event on the participant's quality of life was self-determined. Events related to off study HIV testing may or may not have actually involved having an HIV test performed by a non-study provider.
Rates and 95% confidence intervals (CIs) of off study HIV testing and social impacts related to off study HIV testing were calculated assuming a Poisson distribution. For off study testing, person-years of follow-up were calculated as time from enrollment to last assessment of off study testing. For social impacts, person-years were calculated as time from enrollment to last study visit.

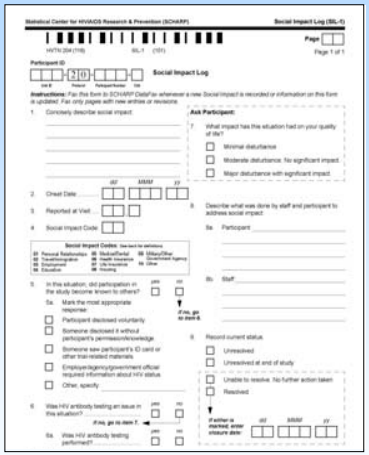


**Figure 2.** *Social Impact Log Case Report Form*
This form is used to capture negative social impact events as reported by the participant.

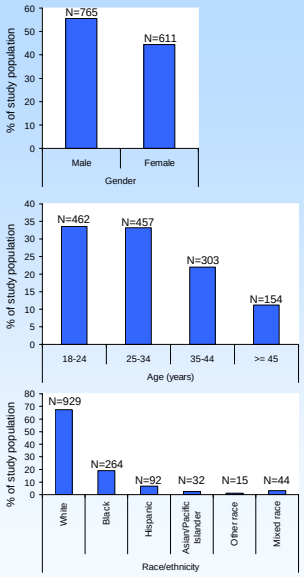


**Figure 3.** *Demographics of Study Participants (N=1376)*
2 of 1378 participants are missing demographic information.

| Reason | N | % |
|---|---|---|
| Part of non-study medical exam or medical provider recommended | 32 | 41.0 |
| Jail or drug treatment program requirement | 7 | 9.0 |
| Requirement of another research study | 7 | 9.0 |
| Military or job requirement | 5 | 6.4 |
| Participate in free HIV testing program | 5 | 6.4 |
| To sell or donate blood | 5 | 6.4 |
| Health or life insurance requirement | 4 | 5.1 |
| Recent or possible high-risk exposure to HIV | 4 | 5.1 |
| Wanted to know HIV status | 4 | 5.1 |
| Wanted to be testing with partner | 3 | 3.8 |
| Travel/immigration requirement | 1 | 1.3 |
| To know if developed antibodies to the vaccine | 1 | 1.3 |

**Table 1.** *Reasons for Off-study HIV Testing*

| Impact on Quality of Life | Description |
|---|---|
| **Major** | Obstetrician's office refused to provide care unless participant had HIV testing done by them. Site offered to provide HIV testing results to provider, but participant decided to have no further contact with provider. |
| **Moderate** | Participant attempted to enroll in a medical research study at another institution and was refused due to a positive HIV antibody test. That institution referred the participant's name to the State Dept of Health. Site staff provided HIV testing documentation to the other institution and DOH to clarify that the participant was not HIV positive. |
| | Participant was denied life insurance and suspected that this was related to study participation. Site staff planned to provide HIV testing results to company. |
| | Participant wanted to participate in another HIV research study that required HIV testing but decided not to because of vaccine trial requirement of no off study testing . |
| **Minimal** | Outside study provider wanted to perform HIV testing. Site planned to follow-up with outside provider. |
| | Participant wanted to be a liver donor and liver clinic wanted to perform HIV test. For other reasons, participant was not considered a suitable donor. |
| | Participant disclosed participation in the vaccine study to his Army reserve officer so he would not be tested for HIV by the military. |
| | HIV testing required for taking a job in Canada. Site provided study HIV test results to Canadian officials. |

**Table 2.** *Negative Social Impact Events Related to Off-study HIV Testing*

## Results

1378 participants were enrolled between 12 January 2004 and 06 September 2007. Participants were primarily male (55.6%), less than 35 years of age (66.8%), and white (67.5%). (Figure 3)
The rate of off study HIV testing was low for the time period under study. Among the 1378 participants, 61 participants reported a total of 78 tests performed by non-study providers. The rate of off study testing was 6.9 per 100 person-years of follow-up [95% CI: 5.4, 8.6]. The most common reason for testing was "part of a routine medical exam or medical provider recommended" (32 tests). Other reasons are listed in Table 1. There were no statistically significant differences by gender or age in reporting non-study HIV testing. The differences between race/ethnicity groups was significant (p=0.01), with 2.5% of whites reporting off study testing, 6.4% of blacks, 5.4% of Hispanics, and 1.1% of others.
Eight participants reported a negative social impact related to either a non-study request for HIV testing (5 events) or having a non-study test performed (3 events). The rate of social impacts related to non-study HIV testing was low, 0.6 per 100 person-years of follow-up [95% CI 0.2, 1.1].
One event was considered by the participant to have had a major impact on her quality of life; three events were considered as moderate impact, and 4 as minimal (Table 2). No statistically significant differences were observed by gender, age or race/ethnicity.

## Conclusions

Although outside testing rates and social impacts related to HIV testing are relatively low, the updated CDC HIV testing guidelines potentially increase the likelihood of participants receiving HIV testing outside of the study, with increasing risk for social harm for participants..