Letter of Amendment

Date: 06 October 2011
Re: Letter of Amendment #1 for HPTN 068, Version 1.0, 06 October 2010
Title: Effects of cash transfer for the prevention of HIV in young South African women
To: IRB/EC
From: HPTN 068 Protocol Team

The following information impacts the HPTN 068 study and must be forwarded to your Institutional Review Board (IRB)/Ethics Committee (EC) as soon as possible for their information and review. This must be approved by your IRB/EC before implementation.

The following information minimally impacts the sample informed consents. Your IRB/EC will be responsible for determining the process of informing subjects of the contents of this letter of amendment (LoA).

Upon receiving final IRB/EC and any other applicable Regulatory Entity (RE) approval(s) for this LoA, sites should implement the LoA immediately. Sites are still required to submit an LoA registration packet to the DAIDS Protocol Registration Office (PRO) at the Regulatory Support Center (RSC). Sites will receive a registration notification for the LoA once the DAIDS PRO verifies that all the required LoA registration documents have been received and are complete. An LoA registration notification from the DAIDS PRO is not required prior to implementing the LoA. A copy of the LoA registration notification along with this letter and any IRB/EC correspondence should be retained in the site’s regulatory files.

All deleted material is noted by strikethrough text (strikethrough) and additions to the protocol are noted by bold type (bold). The following sections of the protocol are affected by this LoA:

Addition of CD4 cell count testing at annual follow-up visits for young women who are HIV-positive at enrollment or any follow-up visit

Section 5.2.3 12, 24, and 36 month Follow-up Visits, page 14

- Store plasma and dried blood spots (all participants, regardless of HIV testing results)
- **Draw blood for CD4 cell count (HIV positive young women only)**

Section 8.4 Benefits, page 29

There may be no direct benefits for individuals who participate in the study, though they may benefit by learning their HIV or HSV-2 status and from learning more about HIV and HSV-2 prevention. **HIV positive young women may benefit from knowing their CD4 cell count.**
Section 9.1.2  CD4 Testing, page 32

A CD4 cell count is performed at the first any visit where one or both of the HIV rapid tests are reactive. In general, a participant will only have one CD4 cell count obtained during the study. In cases where a reactive HIV rapid test is obtained, but HIV infection is not confirmed, a second CD4 cell count should only be obtained in cases where HIV infection was not confirmed after a first reactive HIV rapid test result is obtained (e.g., if test results from a prior visit indicate that the participant was not HIV-infected). In these cases, the CD4 cell count testing should be repeated at a subsequent the next visit where a reactive HIV rapid test is obtained, provided it is at least if it is more than 6 months after the first previous CD4 cell count was obtained. Additionally, all young women found to be HIV positive at enrollment or at any follow-up visit will receive CD4 testing at each annual follow-up visit.

Section 9.3.2  QC for CD4 cell count determination, page 33

CD4 cell count testing will be performed at local laboratories for any subject with confirmed HIV infection. Additionally, all HIV-positive young women will receive CD4 cell count testing at each annual follow-up visit.

Appendix IB. Schedule of Visits and Procedures –Young Women, page 40

<table>
<thead>
<tr>
<th>Administrative, Behavioral, and Regulatory Procedures</th>
<th>Screening</th>
<th>Baseline/Enrollment</th>
<th>12-months</th>
<th>24-months</th>
<th>36-months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verify young woman meets all eligibility criteria</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obtain young woman's consent/assent</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Verify young woman's ongoing consent/assent</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Re-consent young woman if she has reached 18 years of age since last study visit</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obtain/update locator information</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Provide Appointment for Baseline Visit</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Young woman’s questionnaire</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Pre and Post Risk Reduction Counseling</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Schedule follow-up visit for repeat blood draw if necessary</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>
A CD4 cell count is performed at the first \textbf{any} visit where one or both of the HIV rapid tests are reactive. In general, a participant will only have one CD4 cell count obtained during the study. In cases where a reactive HIV rapid test is obtained, but HIV infection is not confirmed, a second CD4 cell count should only be obtained in cases where HIV infection was not confirmed after a first reactive HIV rapid test result is obtained (e.g., if test results from a prior visit indicate that the participant was not HIV-infected). In these cases, the CD4 cell count testing should be repeated at a subsequent the next visit where a reactive HIV rapid test is obtained, \textbf{provided it is at least} if it is more than 6 months after the first previous CD4 cell count was obtained. Additionally, all young women found to be HIV positive at enrollment or at any follow-up visit will receive CD4 testing at each annual follow-up visit.

A CD4 cell count is drawn at each follow-up visit on all young women determined to be HIV-positive at enrollment or after any follow-up visit.

\textit{Assent to Participate in a Research Study – Young women under 18 years of age, page 43}

\textbf{What will you be asked to do for this research?}

\begin{itemize}
  \item Every year give a sample of blood from your arm so we can test it for HIV (the virus that causes AIDS) and another infection called herpes simplex virus, also called HSV-2 or herpes. \textbf{If you are known to be HIV positive at enrollment or any follow-up visit, a CD4 cell count will be performed at each annual visit instead of an HIV test. CD4 cells help your body fight viruses. A CD4 cell count measures the number of cells in a small amount of blood to see how well your body is fighting a virus like HIV. CD4 cell counts are important to monitor your health and to help your doctor decide whether or not to start HIV medications, or see if HIV medications you are taking are working.}
  \textbf{HIV and HSV-2 testing}

Sometimes an HIV test is not clearly positive or negative. If this happens, we will test your blood again until we know the result. The counselor will talk with you about the test results. \textit{This study does not}
provide care or treatment for HIV. If you are found to be HIV positive at enrollment or any follow-up visit, a CD4 cell count test will be performed at each annual visit instead of an HIV test.

Consent to Participate in a Research Study – Young Women Participants (age 18 years and over), page 51

**What will you be asked to do for this research?**

- Every year give a sample of blood from your arm so we can test it for HIV (the virus that causes AIDS) and another infection called herpes simplex virus, also called HSV-2 or herpes. If you are found to be HIV positive at enrollment or any follow-up visit, a CD4 cell count will be performed at each annual visit instead of an HIV test. CD4 cells help your body fight viruses. A CD4 cell count measures the number of cells in a small amount of blood to see how well your body is fighting a virus like HIV. CD4 cell counts are important to monitor your health and to help your doctor decide whether or not to start HIV medications, or see if HIV medications you are taking are working.

**HIV and HSV-2 testing**

Sometimes an HIV test is not clearly positive or negative. If this happens, we will test your blood again until we know the result. The counselor will talk with you about the test results. *This study does not provide care or treatment for HIV. If you are found to be HIV positive at enrollment or any follow-up visit, a CD4 cell count test will be performed at each annual visit instead of an HIV test.*

Consent to Participate in a Research Study – Adult Parent/Legal Guardian Participants, pages 59-60

All young women in the study will be asked to:

- Every year give a sample of blood so we can test it for HIV (the virus that causes AIDS) and another infection called herpes simplex virus, also called HSV-2 or herpes. **If the young woman is found to be HIV positive at enrollment or any follow-up visit, a CD4 cell count will be performed at each annual visit instead of an HIV test. CD4 cells help your body fight viruses. A CD4 cell count measures the number of cells in a small amount of blood to see how well your body is fighting a virus like HIV. CD4 cell counts are important to monitor your health and to help your doctor decide whether or not to start HIV medications, or see if HIV medications you are taking are working.**

**HIV and HSV-2 testing for the young woman**

Sometimes an HIV test is not clearly positive or negative. If this happens, we will test her blood again until we know the result. The counselor will talk with the young woman about the test results. *This study does not provide care or treatment for HIV. If the young woman is found to*
be HIV positive at enrollment or any follow-up visit, a CD4 cell count test will be performed at each annual visit instead of an HIV test.

Change in method of sample selection

Section 3.2 Sample Selection, page 10

...The young woman will be required to re-consent at age 18 if she is a minor at baseline. If after the consent procedure, the young woman or parent/legal guardian chooses not to participate, the refusal and reason for refusal will be recorded. Only one young woman per household may enroll in the study. If more than one eligible girl is in the household, girls in grades 9 or 10 will be selected first. If no young woman is in grade 9, then grade 8 is next selected, followed by grades 10 and 11 respectively. If there are more than 2 girls in the grade grades being used as the selection criterion, 9 or 10 in the same household then young women will be randomly selected using the "next birthday" method. The same method will be used to select girls in grades 8 or 11 if there are multiple girls in the household not in grade 9 or 10.

Minor changes to the protocol

List of Abbreviations and Acronyms, page iv

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDSS</td>
<td>Households Health and Demographic Surveillance Site System</td>
</tr>
<tr>
<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
</tr>
<tr>
<td>HPTN</td>
<td>HIV Prevention Trials Network</td>
</tr>
<tr>
<td>HSV-2</td>
<td>Herpes Simplex Virus Type 2</td>
</tr>
<tr>
<td>HPTN</td>
<td>HIV-Prevention Trials Network</td>
</tr>
</tbody>
</table>

Protocol Team Roster, Page vi

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Letter of Amendment #1
HPTN 068, version 1.0
06 October 2010
Title on Investigator Agreement, Page ix

Effects of cash transfer and community mobilization for the prevention of HIV in young South African women

Section 1.1 Background, page 1

Using Health and Demographic Surveillance Site System (HDSS) data from South Africa, Barnighausen et al also found that each additional year of education reduced the hazard of HIV infection by 7% adjusting for sex, age, wealth, household expenditure, rural vs. urban/periurban residence, migration status and partnership status.  

The above information will be incorporated into the next version of the protocol at a later time if it is amended.