

Letter of Amendment # 2 to:

HPTN 052: A Randomized Trial to Evaluate the Effectiveness of Antiretroviral Therapy plus HIV Primary Care versus HIV Primary Care Alone to Prevent the Sexual Transmission of HIV-1 In Serodiscordant Couples Version 2.0, May 24, 2004

FINAL Version: 13 July 2005

The following information impacts the HPTN 052 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 may also impact the sample informed consent. Your IRB/EC will be responsible for determining the process of informing subjects of the contents of this letter of amendment.

Please file this letter and any IRB/EC correspondence in your regulatory file and other pertinent files. You are NOT required to submit these documents to the Protocol Registration Office unless the changes result in a change to the informed consent for your site.

If the HPTN 052 protocol is amended in the future, this Letter of Amendment will be incorporated into the next version.

Summary of Revisions and Rationale

1. The Inclusion Criteria has been revised to update information concerning efavirenz in response to a recent change in the pregnancy category of the drug. The category has been changed from Category C (Risk of Fetal Harm Cannot Be Ruled Out) to Category D (Positive Evidence of Fetal Risk). The new category classification requires a change to the inclusion criteria regarding reproductive documentation requirements.
2. The Study Procedures section and the corresponding schedule of evaluations have been corrected to collect demographic information at enrollment instead of at screening. This corrects a minor mistake in the protocol.

Implementation

Modifications outlined below are indicated by ~~strikethrough~~ or **bolded** text.

Revision 1 Section 3.1.1 Inclusion Criteria, Index Case

THE FOLLOWING INCLUSION CRITERIA MARKED WITH AN ARROW WILL APPLY ONLY DURING THE RUN-IN PERIOD:

- For female participants of reproductive potential, a negative serum or urine pregnancy test performed within 48 hours before initiating study treatment.

NOTE: “Reproductive potential” is defined as ~~girls~~ **females** who have reached menarche or women who have not been post-menopausal for at least 24 consecutive months (i.e., who have had menses within the preceding 24 months) or have not undergone surgical sterilization (e.g., hysterectomy, bilateral oophorectomy, or salpingotomy).

- Female participants who are participating in sexual activity that could lead to pregnancy (BUT not receiving EFV) must use at least one reliable method of contraception while receiving the protocol-specified drugs and for 6 weeks after stopping the medications.
- Female participants ~~who are~~ participating in sexual activity that could lead to pregnancy and are receiving EFV must agree to use two reliable methods of contraception: a barrier method of contraception (condoms or cervical cap) together with another reliable form of contraception (condoms, with a spermicidal agent; a diaphragm or cervical cap with spermicide; an IUD; or hormonal-based contraception) while receiving the protocol-specified drugs and for 6 weeks after stopping the drugs. Another ART drug may be substituted for EFV if participants are not able, or willing, to use two concurrent forms of contraception, or they will be excluded (if another ART drug is not available).
- Female participants who are without reproductive potential, as defined above, or whose male partner(s) have undergone successful vasectomy ~~with documented azoospermia or have documented azoospermia for any other reason~~, are eligible without requiring the use of contraception. ~~Participant reported history is acceptable documentation of menopause, hysterectomy, bilateral oophorectomy, or tubal ligation.~~ **Acceptable documentation for sterilization or menopause for female participants would include written communication of a procedure signed by a licensed clinician or clinical staff, an operative report, a discharge summary, or a FSH measurement elevated into the menopausal range as established by the site laboratory. For male participants, a laboratory report of azoospermia to document successful vasectomy is required. If only self-reported history is available for sterilization (male or female) or menopause, the female participant must use a barrier method of contraception with a possible second method required at the discretion of the site study physician.**

Revision 2 Section 5 STUDY PROCEDURES, CLINICAL PROCEDURES, AND LABORATORY EVALUATIONS

5.1.1.1 Administrative, Behavioral, and Regulatory Procedures Both Index Case and Partner

- Screening informed consent
- ~~Demographic information~~

5.2.1 Administrative, Behavioral, and Regulatory Procedures – Both Index and Partner

- Study informed consent
- **Demographic information**

Appendix I. A. Schedule of Procedures and Evaluations – Index Case

	Screening	Enrollment	Week 2	Monthly (other than quarterly/yearly)	Quarterly	Yearly	Partner Serocoverts	Confirmed Virologic Failure
Administrative, Behavioral and Regulatory Procedures								
Informed consent (screening or study informed consent form)	X	X						
Demographic information	X	X						

Appendix I. B. Schedule of Procedures and Evaluations – Partner

	Screening	Enrollment	Week 2	Monthly (other than quarterly/yearly)	Quarterly	Yearly	Partner Serocoverts	Confirmed Virologic Failure
Administrative, Behavioral and Regulatory Procedures								
Informed consent (screening or study informed consent form)	X	X						
Demographic information	X	X						