SUMMARY OF CHANGES
INCLUDED IN THE
FULL PROTOCOL AMENDMENT TO:

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 1.0, dated October 10, 2003

THE AMENDED PROTOCOL IS IDENTIFIED AS
VERSION 2.0 AND DATED MAY 24, 2004

Each HPTU will submit this amendment, the corresponding protocol version 2.0, and the associated study informed consent forms to its Institutional Review Board (IRB)/Ethics Committee (EC). The Division of AIDS Regulatory Affairs Branch will submit this amendment to the U.S. Food and Drug Administration (FDA) for inclusion in the study Investigational New Drug application.

The study will open to enrollment under Version 2.0 upon receipt of IRB approval, protocol registration with the DAIDS Regulatory Compliance Center, and activation by the HPTN CORE.

SUMMARY OF REVISIONS

On January 2, 2004, the Division of AIDS, NIAID, NIH, received written comments on HPTN 052 from the U.S. Food and Drug Administration. The FDA comments include suggestions for changes to the protocol document, and submission of additional information related to the study such as adding the exclusion of participants younger than 18 years of age, providing the U.S. standard of care for the prevention of mother-to-child-transmission (which is HAART provided at the beginning of the 2nd trimester of pregnancy, and 4-6 weeks post-birth), and providing additional risk information related to HIV transmission in the informed consent forms. Other changes to the protocol document include information reflecting additional ART study drugs that have become available since Version 1.0, significant revisions to the study product and toxicity management sections that were already part of the protocol, addition of a Division of AIDS Expedited Adverse Event Reporting Manual reflecting a revised adverse event reporting system within the Division of AIDS, and general clarification and updating of information, and minor wordsmithing.

The changes included in this protocol amendment are summarized in the following table:

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Headers/Footers				
Footer	Change	HPTN 052 Final Version 1.0, October 10, 2003	Final Version 2.0, May 24, 2004	Updated Protocol Version Number and Date
Front Matter				
Cover Page	Change	IND: TBD	IND: 68,535	The FDA assigned this IND number to the submission containing this protocol.
Cover Page	Change	Final Version 1.0 October 10, 2003	Final Version 2.0 date will be placed here	Updated Protocol Version Number and Date
Cover Page	Addition	None	Bristol Myers Squibb, Inc.	Supplying atazanavir to of study
Protocol Co-Chairs	Deletion	Susan Buchbinder	None	Susan Buchbinder has decided not to participate in the study.
Protocol Team Roster	Deletion	Contact information for Susan Buchbinder	None	Susan Buchbinder has decided not to participate in the study.
Protocol Team Roster	Change	Room 106, First Floor, Bldg 3 Fax: +44 (0) 20 8966 4707	Building 38, 2 – 61 Fax: +44 (0) 20 8966 8044	Revision to Edde Loelinger's contact information
Protocol Team Roster	Change	Room 5115	Room 4115	Revision to Ana Martinez's contact information.
Protocol Team Roster	Addition	None	Gary D. Thal, M.D. Associate Director, Scientific Operations Bristol-Myers Squibb Company 777 Scudders Mill Road Mail Code: P11-14 Plainsboro, NJ 08536 phone: 609-897-4423 fax: 609-897-6068 email: gary.thal@bms.com	Added information for BMS representative.
Investigator of Record Signature Page	Addition	None	Bristol Myers Squibb, Inc.	Supplying atazanavir, ddI, and d4T
Investigator of Record Signature Page	Change	Final Version 1.0 / October 10, 2003	Final Version 2.0 / May 24, 2004	Updated Protocol Version Number and Date

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Front Matter (Continued)				
List of Abbreviations and Acronyms	Addition	None	ATV, atazanavir PPD, purified protein derivative (of tuberculin) FHI, Family Health International	Acronyms added to protocol.
Schema	Addition	Approximately 1750 total, with a maximum of 90 who will take part in the run-in period.	Approximately 1750 couples total, with a maximum of 90 couples who will take part in the run-in period.	Added for clarity.
Schema	Change	The ART drugs currently available through the study are Combivir® [3TC/ZDV] and its components (zidovudine [ZDV] and lamivudine [3TC]), nevirapine (NVP), and tenofovir (TDF). Due to this limited supply of ART study drugs, the study will begin with a run-in period where the starting regimen will be Combivir® [3TC/ZDV] and NVP. ZDV, 3TC, and TDF will be available for toxicity management or virologic failure. The sites may choose to use other ART drugs if they can provide them via non-National Institutes of Health [NIH] resources, or if participants can afford to buy them.) Enrollment beyond the run-in period will continue only if additional ART study drugs are obtained by the study. If the study is not able to provide additional ART study drugs, the study will be stopped.	The ART drugs available for the run-in period of the study are Combivir® [3TC/ZDV], ATV, EFV, NVP, TDF, 3TC, ddI-EC, and d4T; available for the full study are Combivir® [3TC/ZDV], 3TC, NVP, and TDF. Before the full study can be initiated, at a minimum, another nucleoside (such as ddI), and a protease inhibitor (such as ATV or Kaletra® [lopinavir/ritonavir]) must be available for the length of the full study. The study team has not yet secured commitments for these types of drugs for the full study. Therefore, HPTN 052 will begin with a run-in period using the ART drugs currently available. While the run-in period is being conducted, it is planned to pursue commitments for the full study. If commitments are not obtained, the full study will not proceed, and the study will end.	Updated to state that atazanavir, efavirenz, ddI, and d4T have been added to the available ART drugs. Revised for clarity.
Schema	Deletion	HIV virolgic failure will also be measured in this study, and will be defined as HIV RNA = 1000 copies/mL at week 16 of ART therapy or later.	None	Inappropriate information for schema.

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Front Matter (Continued)				
Schema	Change	Boston, Massachusetts, USA	Boston, Massachusetts, United States of America	U.S.A is spelled in full to match that of all participating countries listed
Schema	Deletion	San Francisco, California, USA	None	Site no longer participating in the study.
Section 1: Introduction				
1.1, Background, first paragraph	Change	The Joint United Nations Programme on HIV/AIDS (UNAIDS) estimates that 42 million adults and children were living with the human immunodeficiency virus (HIV) or living with acquired immunodeficiency syndrome (AIDS) at the end of 2002, of which 5 million were new infections occurring in 2002 alone.[1] Of the 42 million, 29.4 million are in sub-saharan Africa[1]	The Joint United Nations Programme on HIV/AIDS (UNAIDS) estimates that 40 million adults and children were living with the human immunodeficiency virus (HIV) or living with acquired immunodeficiency syndrome (AIDS) at the end of **2003**, of which 5 million were new infections occurring in 2003 alone.[1] Of the 40 million, 31.6 million are in sub-saharan Africa[1]	Text has been updated to include 2003 data

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Section 1: Introduction (continued)				
1.1, Background, second paragraph	Change	As such, it is clear that prevention of HIV will depend on a multi-pronged strategy that employs all available biological and behavioral prevention interventions. The UNAIDS and AIDS Control and Prevention (AIDSCAP) approach – including safer sex counseling, provision of condoms, and sexually transmitted disease (STD) control – has had considerable success in some countries. Vaccines[2] and topical microbicides[3] have entered into clinical testing, and male circumcision may also be studied as a means of prevention.	Several different approaches to HIV prevention are being planned, or studies are on-going. For example, the UNAIDS and AIDS Control and Prevention (AIDSCAP) approach has focused on safer sex counseling, provision of condoms, and sexually transmitted disease (STD) control. This approach to HIV prevention includes an "ABC "(Abstinence, Be Faithful, Condoms) campaign, which has had considerable success in Uganda[73]. In particular, monogamy and partner number reduction may play a critical role in HIV prevention, a goal that must be emphasized in all HIV prevention strategies, including with concomitant use of ART. A variety of other prevention interventions include vaccines[2], and topical microbicides[3], treatment of bacterial vaginosis, the diaphragm, male circumcision, and other antiretroviral therapy studies (e.g. pre-exposure prophylaxis).	Text has been updated to include more recent references.
1.3.3, Other Applications of Antiretroviral Therapy for Prevention	Addition	None	ART might also be used as pre-exposure (PREP) or Post Exposure (iPEP and nPEP) prophylaxis to prevent HIV acquisition. This subject has recently been reviewed[74]. Three trials to determine the efficacy of PREP are planned. USPH Guidelines regarding PEP for needlestick or occupational exposure to HIV (iPEP) are available[75, 76], and updated guidelines for nPEP will be released in 2004 (see MMWR 1997, 1998 for current recommendations and concerns[77, 78]).	FDA request

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Section 1: Introduction (continued)				
1.3.3, Other Applications of Antiretroviral Therapy for Prevention	Addition	None	Briefly, experiments with primates suggest that ART provided within 48-72 hours of exposure to HIV and continued for a full 28 days will provide at least partial protection from HIV. However, such use of ART is expensive, and adherence to the regimen is difficult because of toxicity. The benefit of nPEP in humans has not been established. The cost-benefit ratio is very unfavorable because of the limited efficiency of transmission of HIV after any single sexual exposure [74]. Accordingly, while nPEP should be available for special circumstances (eg. after sexual assault), it is not recognized as a credible public health HIV prevention strategy, and would not be recommended for routine usage in HIV discordant couples in a steady relationship.	FDA request
1.3.4.1, Antiretroviral Drugs, first sentence, and EFV, NVP, TDF, ATV, ddI-EC, and d4T sections	Change/Addition	The ART drugs that are available now for use in the run-in period and full study are Combivir® [3TC/ZDV] and its components (ZDV and 3TC), NVP, and TDF. Refer to Version 1.0 for original text regarding efavirenz, nevirapine, and tenofovir.	The ART drugs that are available now for use in the run-in period and full study are Combivir® [3TC/ZDV], ATV, EFV, NVP, TDF, 3TC, ddI-EC, and d4T. Refer to Version 2.0 for revised text for efavirenz, nevirapine, tenofovir, and new text for atazanavir, ddI, and d4T.	Updated background information for efavirenz, nevirapine, and tenofovir, and added new information for atazanavir, ddI, and d4T.
1.3.4.3, HIV-1 Drug Resistance, first and third paragraph	Change	…except the two in the U.S…. and …(excluding the two U.S. sites)…	…except the one in the U.S…. and …(excluding the one U.S. sites)…	Necessary correction as only one U.S. site will be participating in the study.

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Section 1: Introduction (continued)				
1.3.4.3, HIV-1 Drug Resistance, fourth paragraph	Addition	While resistance testing in HPTN 052 is not designed to guide patient management (except at U.S. sites),	While resistance testing in HPTN 052 is not designed to guide patient management (except at U.S. sites where it is the standard of care),	Added to explain why U.S. sites will use resistance testing to guide patient management.
1.3.4.3, Drug resistance following NVP prophylaxis, first paragraph	Addition	None.	The long term clinical impact of these mutations are unclear.	DAIDS Medical Officer request.
1.3.5, HIV Primary Care and Counseling Considerations, second paragraph	Change	The HIV primary care being delivered in this study is derived from WHO/UNAIDS guidelines in combination with local standards of care at the study sites, and will include systematic attention to vitamin deficiency, STDs, tuberculosis, endemic infections (*e.g.* enteric parasites and malaria), expected opportunistic pathogens, and other AIDS-related conditions.	At non-US sites, the HIV primary care delivered in this study is derived from WHO/UNAIDS guidelines in combination with local standards of care at the study sites, and will include systematic attention to vitamin deficiency, STDs, tuberculosis, endemic infections (*e.g.* enteric parasites and malaria), expected opportunistic pathogens, and other AIDS-related conditions.	Changed to clarify how primary care at non-U.S. sites will be determined.
1.3.5, HIV Primary Care and Counseling Considerations, second paragraph	Change	Participants will receive prompt and effective symptomatic care as clinically indicated per local guidelines and locally-developed study operating procedures (SOPs).	For US sites, participants will receive care in line with local standards of care provided at the particular study site. All participants will receive prompt and effective symptomatic care as clinically indicated per local guidelines and locally-developed study operating procedures (SOPs).	Changed to explain how primary care at U.S. sites will be determined.
1.4, Study Implementation Plan	Change	Refer to Version 1.0 for original text.	Refer to Version 2.0 for revised text.	Changed to reflect the addition of efavirenz, atazanvir, ddI, and d4T, and that ZDV will not available as a single agent.

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Section 2: Study Objectives And Study Design				
2.2, Secondary Objectives, second paragraph	Addition	The secondary objectives will be evaluated through clinical procedures, laboratory evaluations, and behavioral assessments outlined in Section 5.0, and Appendix I A and B.	<u>The primary objective will be evaluated per the algorithm outlined in Appendix 2; AIDS-defining illnesses are defined in Appendix III.</u> The secondary objectives will be evaluated through clinical procedures, laboratory evaluations, and behavioral assessments outlined in Section 5.0, and Appendix I A and B, <u>Appendix III, Appendix IV, and AACTG's Appendix 60 – Diagnoses Appendix, which can be found in the Study Specific Procedures (SSP) Manual.</u>	Added to reference additional information added to the protocol.
2,3, Study Design, first paragraph	Change	Accrual of a maximum of 90 participants into the run-in period will require 3 months, and all couples will be followed until the last couple enrolled completes their 6-month follow-up visit. Accrual of a maximum of 1660 participants into the full study will require approximately 18 months total, and all couples will be followed until the last couple enrolled completes their 60 month follow-up visit.	Accrual of a maximum of 90 couples into the run-in period will require 3 months, and all couples at each site will be followed until the last couple enrolled completes their 6-month follow-up visit. Accrual of a maximum of 1660 couples into the full study will require approximately 18 months total, and all couples will be followed until the last couple enrolled completes their 60 month follow-up visit.	Changed for clarity.
2.3, Study Design, Definition of Arm 2	Addition	Arm 2: HIV primary care without initiation of ART until the participant has two consecutive measurements of a CD4+ cell count $\leq$ 200 cells/mm^3, or develops an AIDS-defining illness.	Arm 2: HIV primary care without initiation of ART until the participant has two consecutive measurements of a CD4+ cell count $\leq$ 200 cells/mm^3, or develops an AIDS-defining illness (defined in Appendix III).	Added to reference additional information added to the protocol.

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Section 2: Study Objectives And Study Design (continued)				
2.3, Study Design, fourth, fifth, and sixth paragraphs	Change	The starting regimen available for the run-in period is Combivir® [3TC/ZDV] and NVP. The starting regimen for the full study is Combivir® [3TC/ZDV] and NVP or EFV (if it becomes available through the study), where the choice of the NNRTI will be at the discretion of the study clinicians. Also available for the run-in period and full study are the components of Combivir® [3TC/ZDV], and TDF, for toxicity management or virologic failure. The sites may choose to use other ART drugs if they can provide them via non-NIH resources, or if participants can afford to buy them (*e.g.* if during the run-in period a site can provide EFV for the starting regimen, they may do so).	The starting regimen available for the run-in period is Combivir® [3TC/ZDV] and EFV or ATV (choice of 3rd drug in the "triple combination" is at the discretion of the study clinician during the run-in period). Also available for the run-in period are ATV, EFV, NVP, TDF, 3TC, ddI-EC, and d4T for toxicity management or virologic failure. The starting regimen for the full study will be determined when additional ART drugs become available, but will include Combivir® [3TC/ZDV]. In addition to Combivir® [3TC/ZDV], the full study has commitments for NVP, TDF, and 3TC.	Original paragraph split up into 3 paragraphs for clarity; changed to reflect the addition of efavirenz, atazanavir, ddI-EC, d4T, and to reflect that ZDV will not be available as a single agent
2.3.1, Criteria For Switching Antiretroviral Therapy Regimen Due to Virologic Failure, second paragraph	Deletion	For study sites outside of the U.S., index cases will switch ART due to virologic failure based on the following definition that is deemed appropriate for the majority of settings in which this study will take place:	For study sites outside of the U.S., index cases will switch ART due to virologic failure based on the following definition that is deemed appropriate for settings in which this study will take place:	Deleted for clarity.
2.3.2, Index Case and Partner Follow-Up Visit Schedule, second paragraph	Deletion	For example, for a couple enrolled on September 15, follow-up visits will be targeted to take place on October 15, November 15, December 15, etc.	None	Deleted for clarity.
2.3.3.3, Partner, second paragraph	Change	In cases where the index case dies (based on self-report or verification if available, *e.g.* death certificate or notice) or the partnership has permanently ended (based on self-report), the partner's participation in the study will end.	In cases where the index case dies (based on partner report, or verification if available, *e.g.* death certificate or notice) or the partnership has permanently ended (based on self-report), the partner's participation in the study will end.	Revised for clarity.

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Section 3: Study Population and Screening Recruitment and Enrollment Procedures				
3.1.1, Index Case, second bullet, third bullet, and text following fourth bullet	Change/Addition	Refer to Version 1.0 for original inclusion/exclusion criteria	Refer to Version 2.0 for revised criteria.	Second and third bullets revised for clarity. Changed to reflect exclusion of pregnant women in the run-in period, and updated information related to contraception requirements.
3.1.2, Partner, third bullet	Change	Plans to maintain a sexual relationship with partner.	Plans to maintain a sexual relationship with the person who is enrolled in the study with them.	Revised for clarity.
3.1.3, Both Index Case and Partner, first bullet	Deletion	Men and women age ≥ 18 years. Note: participants < 18 years may enroll with the agreement of the site investigator plus legal guardian/representative written informed consent.	Men and women age ≥ 18 years.	FDA request.
3.2.1, Index Case, third bullet	Addition	In cases where the participants' starting regimen contains NVP, documented or suspected acute hepatitis within 30 days prior to enrollment, irrespective of AST (SGOT) and ALT (SGPT) values.	In cases where the participants' starting regimen contains ATV or NVP, documented or suspected acute hepatitis within 30 days prior to enrollment, irrespective of AST (SGOT) and ALT (SGPT) values.	Additional information related to atazanavir.
3.2.1, Index Case, fourth bullet	Change	Current or previous AIDS-defining illness (as defined by WHO-Derived AIDS Case definition in Appendix III), and/or opportunistic infection (note: active TB, as defined by the AACTG Appendix 60 International Diagnoses Appendix, is an exclusion, as well as currently being on intensive phase of TB treatment, but previously treated cases of pulmonary TB may be waived at the discretion of the study clinician. Specific guidelines for TB treatment at each site will be included in the SSP.)	Current or previous AIDS-defining illness (as defined in Appendix III.) (Note: active TB, as defined by the AACTG Appendix 60 - Diagnoses Appendix, is an exclusion, as well as currently being on intensive phase of TB treatment, but previously treated cases of pulmonary TB may be waived at the discretion of the study clinician. Specific guidelines for TB treatment at each site will be included in the SSP Manual.)	A more specific definition of AIDS-defining illnesses has been added to the protocol.

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Section 3: Study Population and Screening Recruitment and Enrollment Procedures (continued)				
3.2.1, Index Case, added as fifth bullet	Addition	None	Pregnancy (run-in period only). NOTE: Breastfeeding is allowed at enrollment, however, during the run-in period, women may <u>not</u> be on a regimen containing study-provided ATV the entire time they are breastfeeding.	Added to reflect exclusion of pregnant women in run-in period. Breastfeeding note added per BMS request.
3.2.2, Both Index Case and Partner, added as last bullet	Addition	None	Incarceration in a correctional facility, prison, or jail; and involuntary incarceration in a medical facility for psychiatric or physical (e.g. infectious disease) illness.	BMS request.
Section 4: Study Treatment Considerations				
4.0, Study Treatment Considerations, first paragraph	Change	The run-in period will employ a starting regimen of Combivir® [3TC/ZDV] and NVP. The full study will employ a starting regimen of Combivir® [3TC/ZDV] and NVP or EFV (if available), where the choice of the NNRTI will be at the discretion of the study clinicians. Also available for the run-in period and full study are the components of Combivir® [3TC/ZDV], and TDF, for toxicity management or virologic failure.	The run-in period will employ a starting regimen of Combivir® [3TC/ZDV] and EFV or ATV. Also available for the run-in period are ATV, EFV, NVP, TDF, 3TC, ddI-EC, and d4T for toxicity management or virologic failure. The full study starting regimen will be determined when additional ART drugs become available, but will include Combivir® [3TC/ZDV].	Changed into two paragraphs for clarity, and to reflect the addition of efavirenz, atazanavir, ddI-EC, d4T, and to reflect that ZDV will not be available as a single agent. Also revised for clarity.

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Section 4: Study Treatment Considerations (continued)				
4.1.1, Antiretroviral Drugs, first paragraph	Change	The run-in period will employ a starting regimen of Combivir® [3TC/ZDV] and NVP. The full study will employ a starting regimen of Combivir® [3TC/ZDV] and NVP or EFV (if available), where the choice of the NNRTI will be at the discretion of the study clinicians. Also available for the run-in period and full study are the components of Combivir® [3TC/ZDV], and TDF, for toxicity management or virologic failure.	The ART study drugs currently available for the run-in period of the study are 3TC/ZDV, EFV, ATV, NVP, TDF, 3TC, ddI-EC, and d4T. The ART study drugs currently available for the full study are 3TC/ZDV, 3TC, NVP, and TDF. Study drugs will be provided by the study to participants while they are on study, and are being provided by, or purchased from: • 3TC/ZDV, 3TC: GlaxoSmithKline • EFV: Merck & Co., Inc. • ATV, ddI-EC, d4T: Bristol-Myers Squibb, Inc. • NVP: Boehringer-Ingelheim Pharmaceuticals, Inc. • TDF: Gilead Sciences, Inc.	Changed to reflect the addition of efavirenz, atazanavir, ddI-EC, d4T, and to reflect that ZDV will not be available as a single agent. Manufacturer names added per RCC/DAIDS request.

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Section 4: Study Treatment Considerations (continued)				
4.1.1, Antiretroviral Drugs, second and third paragraph	Change	The ART study drugs provided through this study will be distributed to the study sites by the NIAID Clinical Research Products Management Center (CRPMC). The study site pharmacist can obtain the ART study drugs by following the instructions provided in the latest version of the *Pharmacy Guidelines and Instructions for DAIDS Clinical Trial Networks*. The site pharmacist is required to maintain records of all ART study drugs received from the CRPMC and subsequently dispensed to study participants. Each study site is required to have a DAIDS Pharmacy Plan in place, which will be reviewed and approved by the DAIDS Pharmacy Affairs Branch (PAB).	Any other ART drugs used during the run-in period will be provided by non-study prescription. The ART study drugs provided through this study, with the exception of EFV, will be distributed to the study sites by the NIAID Clinical Research Products Management Center (CRPMC), and possibly through regional distribution facilities outside of the U.S. (as approved by the Division of AIDS). The provision of EFV will be managed by Family Health International (FHI) who will facilitate the purchasing of EFV locally (refer to SSP Manual for additional details). The study site pharmacist can obtain the ART study drugs available through the CRPMC by following the instructions provided in the latest version of the *Pharmacy Guidelines and Instructions for DAIDS Clinical Trial Networks*, and instructions in the SSP Manual. The study site pharmacist is required to maintain records of all ART study drugs received and subsequently dispensed to study participants. All unused study drugs are to be held until the study is completed, terminated, or otherwise instructed by the sponsor. Specific instructions will be provided for the final disposition of the study products.	Changed for clarity, and to reflect the possibility that EFV may be distributed by regional distribution facilities.

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Section 4: Study Treatment Considerations (continued)				
4.1.2, HIV Primary Care Agents, first sentence	Change	Each site will be responsible for purchasing and maintaining their own supply of the HIV primary care medications for this study.	Each site will be responsible for purchasing and maintaining their own supply of non-study drugs (HIV primary care medications**).**	Changed for clarity.
4.2, Regimens and Administration	Change/Addition	Table 8 outlines specifications related to the ART study drugs used for this protocol.	Table 3 outlines specifications related to the ART study drugs used for this protocol. All medications will be administered orally.	Table renumbering and information about the route of administration.
4.2, Regimens and Administration, Table 3	Addition	Refer to Version 1.0.	Refer to Version 2.0.	Atazanavir, ddI, and d4T have been added to the protocol.
4.3.2, Prohibited Medications, Table 4	Addition	Refer to Version 1.0.	Refer to Version 2.0.	Added additional prohibited concomitant medications
4.3.3, Precautionary Medications, Table 5	Addition	Refer to Version 1.0.	Refer to Version 2.0.	Added additional Prohibited Concomitant Agents with ATV, and other Protease Inhibitors
4.3.3, Precautionary Medications, Oral Contraceptives; Sildenafil and other Phosephodiesterase Type 5 (PDE5) Inhibitors and NNRTI's and PI's, Methadone; Rifampin and Rifabutin; Tenofovir; Atazanavir	Change	Refer to Version 1.0	Refer to Version 2.0	Included updated information consistent with AACTG 5175, and BMS request.

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Section 4: Study Treatment Considerations (continued)				
4.4, Adherence Counseling and Assessment, second paragraph	Deletion/ Change	The self-report adherence assessment will adapt items from the AACTG adherence assessment instruments. These measures ask individuals to recall the number of pills they took for varying time periods, including "yesterday," "the day before," and the "past four days." Additionally, it asks participants how they typically take their pills, using a Likert-type scale with anchor points ranging from "all of the time," to "sometimes" to "never." A similar assessment will be used. It is also planned to ask about discrete time periods as well as a "typical" week.	Measures may include asking individuals to recall the number of pills they took for varying time periods, including "yesterday," "the day before," and the "past four days." Additionally, it asks participants how they typically take their pills, using a Likert-type scale with anchor points ranging from "all of the time," to "sometimes" to "never." A similar assessment may be used.	Updated for refinement and clarity, since different measures may be applied in the study
4.5, Toxicity Management	Addition/Change	Refer to Version 1.0	Refer to Version 2.0	Updated for clarity and consistentcy with AACTG 5175.
4.5.4, Antiretroviral Therapy Dosage Reductions, Table 6	Addition	None	Information about atazanavir	Atazanavir added to protocol.
4.5.5.1, Rash	Change	Refer to Version 1.0	Refer to Version 2.0	Section completely revised per updated information, and consistency with AACTG 5175.
4.5.5.2, Lipase Elevations and Pancreatitis, first paragraph	Change	The enzyme abnormality that will be used for making diagnoses is the lipase level.	The primary enzyme abnormality that will be used for making diagnoses is the lipase level.	Clarification.
4.5.5.2, Lipase Elevations and Pancreatitis, at the end of second paragraph	Addition	None	(Pancreatic amylase also is acceptable.)	Additional information.

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Section 4: Study Treatment Considerations (continued)				
4.5.5.2, Lipase Elevations and Pancreatitis third paragraph, second bullet	Change	Grade 1 or 2: Follow participants and repeat lipase as soon as possible; within 2 weeks is optimal. If lipase remains elevated, but is Grade <3 and symptoms persist, then participants should either be considered to have clinical pancreatitis or continue to be followed at frequent intervals, depending on the best available clinical judgment. CT scan of the abdomen, if available, may be helpful in determining whether clinical pancreatitis is present.	Grade 1 or 2: Participants should be contacted as soon as the results are available, and instructed to return for clinical assessment and a repeat lipase level as soon as possible; within one to two days is optimal. If lipase remains elevated, but is Grade <3 and symptoms persist, then participants should either be considered to have clinical pancreatitis or continue to be followed at frequent intervals, depending on the best available clinical judgment. CT scan of the abdomen, if available, may be helpful in determining whether clinical pancreatitis is present.	Changed for clarity per FDA request.
4.5.5.3, CK Elevation	Change	CK will be measured only if participants develop clinical symptoms consistent with a diagnosis of myositis.	CK will be measured only if participants develop clinical symptoms consistent with a diagnosis of myopathy.	Corrected information.
4.5.5.4, Calculated Creatinine Clearance (for Participants Receiving TDF)	Deletion	Section Title: Grade ≥ 2 Creatinine for Participants Receiving TDF For confirmed Grade ≥ 2 increase in creatinine, TDF should be discontinued. Participants should be followed as medically indicated until the creatinine returns to Grade < 2. ddI-EC may be substituted for TDF.	None	Information contained in 4.5.5.14.
4.5.5.4, AST and ALT Elevation, Section number re-numbered; third paragraph	Change	For asymptomatic or symptomatic elevation of AST or ALT >10 × ULN (Grade 4), all medications should be discontinued and held until levels are Grade ≤ 2, at which time therapy may be reintroduced with the substitution of NFV for EFV or NVP, if applicable.	For asymptomatic or symptomatic elevation of AST or ALT >10 × ULN (Grade 4), all medications should be discontinued and held until levels are Grade ≤ 2, at which time therapy may be reintroduced with the substitution of a PI for EFV or NVP.	Changed for clarity, and BMS request.

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Section 4: Study Treatment Considerations (continued)				
4.5.5.4, AST and ALT Elevation; Section number re-numbered; Clinical (Symptomatic) Hepatitis with NVP or EFV	Change	They must discontinue NVP immediately if AST or ALT is even 2 × higher than baseline. If the study clinician determines that the participant has clinical hepatitis, and NVP cannot be excluded as the cause, NVP should be permanently discontinued.	If the study clinician determines that the participant has clinical hepatitis with or without LFT abnormality or regardless of the degree of LFT abnormality, and NVP cannot be excluded as the cause, NVP should be permanently discontinued and not restarted after recovery.	DAIDS Medical Officer request.
4.5.5.5, Anemia / Neutropenia / Thrombocytopenia, Section number re-numbered; first paragraph	Change	If a subject experiences treatment-limiting (in the opinion of the study clinician) anemia (hemoglobin $\geq$ 7.0 but < 7.9 g/dL), neutropenia, or thrombocytopenia, d4T or another appropriate nucleoside analogue (TDF, ddI) may be substituted for ZDV. If Grade 2 anemia is present at enrollment, d4T or another appropriate nucleoside analogue (TDF, ddI) may be substituted for ZDV at the start of Step 1 treatment. Participants with Grade 2 anemia considered treatment limiting in the opinion of the study clinician may have the ZDV dose reduced to 200 mg BID.	Participants who develop Grade 1 or Grade 2 (hemoglobin =7.0 but =7.9 g/dL), anemia, which is considered treatment limiting in the opinion of the study clinician, may have d4T substituted for ZDV.	Changed for clarity per FDA request, and for consistency with AACTG 5175.
4.5.5.5, Anemia / Neutropenia / Thrombocytopenia, Section number re-numbered; third paragraph	Addition	Participants with Grade 4 anemia or neutropenia attributed to ZDV will have treatment interrupted until the adverse event has returned to Grade ≤ 2.	Participants with Grade 4 anemia, neutropenia, or thrombocytopenia attributed to ZDV will have treatment interrupted until the adverse event has returned to Grade ≤ 2.	Added for consistency with AACTG 5175.
4.5.5.6, CNS Symptoms (for Participants on EFV);section number re-numbered	Change	Refer to Version 1.0	Refer to Version 2.0	Changed for consistency with AACTG 5175.

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Section 4: Study Treatment Considerations (continued)				
4.5.5.7, Peripheral Neuropathy (for Participants on ddI and d4T); Section number re-numbered	Addition	Title: Peripheral Neuropathy	Title: Peripheral Neuropathy (for Participants on ddI and d4T)	Added for clarity.
4.5.5.7, Peripheral Neuropathy (for Participants on ddI and d4T);Section number re-numbered	Change	Participants who experience symptoms consistent with peripheral neuropathy that is unrelieved with non-narcotic analgesics (Grade ≥ 3) should have d4T and/or ddI discontinued, and another medication such as TDF should be substituted.	For Grade = 3, participants who experience symptoms consistent with peripheral neuropathy that is unrelieved with non-narcotic analgesics (Grade = 3) must have d4T and/or ddI permanently discontinued, and another NRTI should be substituted.	Changed for consistency with AACTG 5175.
4.5.5.8, Nausea (with or without vomiting); Section number re-numbered; second paragraph	Change	In the event of intractable nausea despite medication, substituting d4T for ZDV is permitted.	In the event of intractable nausea for participants receiving ZDV, after pancreatitis, lactic acidosis, etc. have been ruled-out, substituting another NRTI for ddI orZDV is permitted.	Changed for consistency with AACTG 5175.
4.5.5.11; 4.5.5.12; 4.5.5.13; and 4.5.5.14	Addition	None	Refer to Version 2.0	Added sections per DAIDS, and consistency with AACTG 5175.
4.5.6, Drug Substitutions, Table 7	Changes	Refer to Version 1.0	Refer to Version 2.0	Information added for efavirenz, tenofovir, and ddI-EC.
4.5.7, Management of ART and Pregnancy, Contraception, and Breast-Feeding, first paragraph	Change	HPTN 052 will not provide prenatal care for women who become pregnant, postpartum testing, or care to infants born to women	While ART during pregnancy will be provided to participants on both arms of the study, prenatal care for women who become pregnant, postpartum testing, or care to infants born to women will not be provided through this study.	Changed for clarity of meaning.
4.5.7, Management of ART and Pregnancy, Contraception, and Breast-Feeding, second paragraph	Deletion / Addition	Women who become pregnant will be allowed to remain on study treatment and in follow-up after pregnancy informed consent has been obtained.	Refer to section 5.0 for additional procedures related to ART and pregnancy.	Wordsmithing for protocol consistency.

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Section 4: Study Treatment Considerations (continued)				
4.5.7.1, Pregnant Women on a Regimen Containing EFV	Change	If a woman is on EFV and becomes pregnant, EFV will be discontinued immediately and replaced with NVP for the full course of pregnancy. It will be at the discretion of the study clinician to determine whether a woman should remain on NVP following pregnancy or return to EFV.	Women who are taking EFV and become pregnant will immediately stop EFV and substitute a different ART drug for the full course of pregnancy. The study clinicians will determine which ART drug should be substituted for EFV, and whether the woman should return to EFV following pregnancy. In particular for pregnant women with CD4+ counts >250 cells/mm^3, an ART drug other than NVP should be considered.	Wordsmithing for clarity, and consistency with AACTG A5175.
4.5.7.3, Pregnant Women on a TDF or ATV-Containing Regimen	Addition	None	Data on the safety of TDF and ATV in pregnancy are limited; data on the appropriate dose of ATV for use in pregnancy has not yet been determined. During the run-in period, if a woman becomes pregnant while on a regimen containing ATV, ATV will be stopped and she will be placed on an appropriate substitute.	Added per consistency with AACTG A5175, and BMS request.
4.5.7.4, Pregnant Women on a Regimen Containing Two ART Drugs with Hepatic Toxicity Potential	Addition	None	Women who become pregnant on study should be monitored closely for liver toxicities when they are taking two hepatotoxic ARV drugs (e.g., d4T, NVP) concurrently.	Added per consistency with AACTG A5175.
4.5.7.6, Women Who Breast-feed, first paragraph	Change/ Deletion	Changes in ART for women who are breast-feeding while enrolled in HPTN 052 will be at the study clinician's discretion. EFV is an evaluable drug for use in HIV-exposed infants and HIV-infected children. For this reason, breast-feeding participants receiving EFV will be allowed to continue study drugs while breast-feeding.	During the run-in period, women who are breastfeeding must not take ATV. Other changes in ART for women who are breastfeeding while enrolled in HPTN 052 will be at the study clinician's discretion, and per package insert guidelines.	Wordsmithing for clarity. ATV information added per BMS request.

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Section 4: Study Treatment Considerations (continued)				
4.5.10, Management of ATV When Treating Tuberculosis	Addition	None	Participants who are taking ATV and require rifampicin for the treatment of active TB should either replace rifampicin with rifabutin or replace ATV with EFV, during the period of rifampicin treatment. Participants should wait approximately 2 weeks after stopping rifampicin before resuming ATV. Participants who receive rifabutin for the treatment of TB may remain on ATV. Refer to the ATV package insert.	Added per addition of atazanavir.
Section 5: Study Procedures, Clinical Procedures, And Laboratory Evaluations				
5.2.2, Clinical Procedures – Index Case, sixth bullet	Change	Chest x-ray	Chest x-ray (U.S. sites only: obtain PPD first. If > 5mm induration then chest x-ray is obtained. Refer to local SOP for instructions regarding treatment.)	Information added to accommodate U.S. standard of care.
5.3.4.2, Clinical Procedures – Index Case, eighth bullet	Addition	None	U.S. sites only: obtain PPD. If > 5mm induration then chest x-ray is obtained. (Refer to local SOP for instructions regarding treatment.)	Information added to accommodate U.S. standard of care.
5.3.6.1, Clinical Procedures –Index Case, fourth bullet	Change	Provide treatment (as clinically indicated)	Provide treatment (as clinically indicated. This refers to study-provided non-ART treatment. See Section 8.3 for more information.)	Revised for clarity.
5.4, Title	Addition	Procedures to be Followed in the Event of Pregnancy	Procedures to be Followed in the Event of Pregnancy or Breastfeeding	Added to include information about breastfeeding.

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Section 5: Study Procedures, Clinical Procedures, And Laboratory Evaluations (continued)				
5.4.1, Procedures for Pregnancy or Breastfeeding at Enrollment	Change	Pregnant or breastfeeding women are eligible for enrollment, and must agree to be randomized. Breastfeeding or pregnant women randomized to Arm 1 (immediate ART arm) should be prescribed ART drugs that are known to be safe during pregnancy or breastfeeding. (*e.g.* EFV, and the combination of ddI and d4T together should not be prescribed to these women.)	In the run-in period, pregnant women are <u>not</u> eligible for enrollment. In the full study, pregnancy or breastfeeding women are eligible for enrollment, and must agree to be randomized. Breastfeeding or pregnant women **on** Arm 1 (immediate ART arm) should be prescribed ART drugs that are known to be safe during pregnancy or breastfeeding. (*e.g.* EFV, and the combination of ddI and d4T together should not be prescribed to these women.) During the run-in period, women who are breast-feeding should not receive study-provided ATV as part of their regimen.	Added sentence to reflect the exclusion of pregnant women at enrollment in the run-in period.

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Section 5: Study Procedures, Clinical Procedures, And Laboratory Evaluations (continued)				
5.4.2, Procedures for Female Index Case on ART Who Becomes Pregnant During Study	Change	If the pregnant index case is already on a regimen containing EFV, EFV will be discontinued immediately and replaced with another NNRTI or PI during the remainder of the pregnancy. It will be at the discretion of the study clinician to determine whether a woman should remain on NVP following pregnancy or return to EFV.	A pregnancy informed consent must be obtained. If the pregnant index case is already on a regimen containing EFV, EFV will be discontinued immediately and replaced with another NNRTI or PI during the remainder of the pregnancy, chosen at the discretion of the study clinician. However, during the run-in period pregnant women must not receive a regimen containing study-provided ATV. At the time the site becomes aware a participant is pregnant, study-provided ATV must be stopped and an appropriate drug given as substitution. In addition, during the run-in period women not already on ART who become pregnant should not be given study-provided ATV at any time during their pregnancy. If during the run-in period the site has access to ATV outside of the study, it may be provided per study clinician discretion and/or package insert guidelines. It should be noted that ddI-EC and d4T must not be coadministered during pregnancy.	BMS request.
5.4.3, Procedures for Breastfeeding Women on ART, added sentence to end of original paragraph	Addition	None	If a woman is breastfeeding during the run-in period, she must not be provided a regimen containing study-provided ATV.	BMS request.
5.4.4, Title	Addition	Procedures for Women Not on ART	Procedures for Women Not on ART Who Become Pregnant	Added for clarity.

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Section 5: Study Procedures, Clinical Procedures, And Laboratory Evaluations (continued)				
5.4.4, Procedures for Women Not on ART Who Become Pregnant, first paragraph	Deletion/ Change	Pregnant index cases not on ART (Arm 2) should be followed per study procedures. Site clinicians can choose one of two options: 1) provide all such women the local standard of care for pMTCT (prevention of maternal to child transmission) available at the study site location; or 2) site clinicians can put such women on triple ART therapy. The ART in either option will be provided through the study. In the latter case, sites should contact the CMC for guidance as to when such women should be placed on triple therapy. In either case, the choice of pMTCT should be documented in the study participant's chart and on any applicable CRF's.	Pregnant index cases not on ART (Arm 2) will be followed per study procedures, and placed on a triple regimen of ART regardless of CD4 + cell count at approximately the beginning of the 2nd trimester of pregnancy (e.g. 12-14 weeks of pregnancy), and for 4-6 weeks following birth. The ART will be provided through the study. The choice of regimen for such women should be documented in the study participant's chart and on any applicable CRF's. The choice of the regimen must NOT include study-provided ATV, unless the site has access to it outside of the study. It should be noted that ddI-EC and d4T should not be coadminstered.	FDA request; BMS request.
5.4.4, Procedures for Women Not on ART Who Become Pregnant, third paragraph	Deletion	This study will not provide prenatal care for women who become pregnant, postpartum testing, or care to infants born to women. All women who become pregnant will be referred to local clinics or other research studies for prenatal and postpartum care.	None	Already stated in another section of the protocol.
5.6, Participant Withdrawal, second paragraph	Addition	None	Participants will be withdrawn from the study if they become incarcerated in a correctional facility, prison, or jail, or if they are involuntary incarcerated into a medical facility for psychiatric or physical illness (e.g. infectious diseases).	

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Section 6: Safety Monitoring And Adverse Event Reporting				
6, **Expedited Adverse Event Reporting**	Change	See Version 1.0 for original text.	See Version 2.0 for revised text.	Changed to reflect new DAIDS Expedited Adverse Event Reporting system.
Section 7: Statistical Considerations				
7.2.2, Table 8, Immunologic response of index case	Change/ Addition/ Deletion	• Time from enrollment to first measurement of CD4< 200 cells/mm^3. In Arm 2, this corresponds to time of enrollment to initiation of antiretroviral therapy (ART) • Time from initiation of ART to first measurement of CD4<200 cells/mm^3. • Time from initiation of secondary regimen to first measurement of CD4 < 200 cells/mm^3.	• Time from enrollment to immunologic failure. (Immunologic failure is defined as two consecutive measurements of CD4+ cell count < 200 cells/mm3, or develops as AIDS-defining illness). • Time from initiation of ART to immunologic failure . • Time from initiation of secondary regimen to immunologic failure.	Changed to more accurately define the term "immunologic failure."
7.7.2, Monitoring of Efficacy and Safety Endpoints	Change	For example, it is possible that, in the short-term, the "immediate" arm may have a lower rate of HIV acquisition and of AIDS related SAEs while possibly having a higher rate of cardiovascular and metabolic SAEs than the "delayed" arm.	For example, it is possible that, in the short-term, the "immediate" arm may have a lower rate of HIV acquisition and of AIDS related AEs while possibly having a higher rate of cardiovascular and metabolic AEs than the "delayed" arm.	The term "SAE" has been replaced with "AE" so that the regulatory meaning is not implied.
Section 8: Human Subjects Considerations				
No Changes				
Section 9: Laboratory Specimens And Biohazard Containment				
No Changes				

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Section 10: Administrative Procedures				
10.2, Study Coordination	Change	The SSP Manual – which will contain reference copies of the DAIDS SOPs for Source Documentation and Essential Documents, as well as the DAIDS SAE Reporting Manual for the AACTG, PACTG, CPCRA, and IRP and the DAIDS Table for Grading Severity of Adverse Experiences – will outline procedures for conducting study visits; data and forms processing; AE assessment, management and reporting; dispensing study medications and documenting drug accountability; and other study operations.	The SSP Manual – which will contain reference copies of the DAIDS SOPs for Source Documentation and Essential Documents, as well as the Manual for Expedited Reporting of Adverse Events to DAIDS and the DAIDS Table for Grading Adult and Pediatric Adverse Experiences – will outline procedures for conducting study visits; data and forms processing; AE assessment, management and reporting; dispensing study medications and documenting drug accountability; and other study operations.	This section has been revised to reflect changes to names of the DAIDS manual for reporting SAEs/EAEs and the DAIDS toxicity grading table.
Section 11: References				
Reference 1.	Change	UNAIDS. Joint United Nations Program on HIV/AIDS and World Health Organization: AIDS Epidemic Update. 2002.	UNAIDS. Joint United Nations Program on HIV/AIDS and World Health Organization: AIDS Epidemic Update. 2003.	Reference revision.
Whole Section	Addition	None	Added references 73-82	Additional references added to the text of the protocol.
Appendix I: A. Schedule Of Procedures And Evaluations – Index Case				
Directed history, con meds, physical exam	Deletion	Footnote included	Footnote removed	Discrepancy between table and text
Footnotes	Addition	3 = Perform at the first two months following initiation of antiretroviral therapy.	3 = Perform at the first two months following initiation of antiretroviral therapy. When starting NVP, perform LFTs at week 2, 4, 6, then monthly for first 20 weeks.	Addition of NVP monitoring.
Footnotes	Addition	None	6 = U.S. sites only: obtain PPD first. If > 5mm induration then chest x-ray is obtained.	Added to accommodate U.S. standard of care.

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Appendix I: A. Schedule Of Procedures And Evaluations – Index Case (continued)				
Footnotes	Addition	None	7 = A swab should be taken for mulitplex PCR at any time an ulcer is observed upon examination for shipment to the HPTN CL.	Added for clarification.
Appendix I: B. Schedule Of Procedures And Evaluations – Partner				
No Changes				
Appendix II: HIV Antibody Testing Algorithm For Endpoint Ascertainment At Follow-Up				
No Changes				
Appendix III: WHO, CDC, And In-Country Derived AIDS Case Definition For Exclusion Criteria And Initiation Of ART While On Arm 2				
Appendix Title	Change	WHO-Derived AIDS Case Definition	WHO, CDC, and In-Country Derived AIDS Case Definition For Exclusion Criteria and Initiation of ART while on Arm 2	Title now accurately reflects the information in the appendix.
First Paragraph	Deletion/ Addition	The WHO-Derived AIDS Case Definition is defined as at least 2 major clinical signs and 1 minor clinical sign:	The following list will be used for purposes of excluding a person from the study, and for participants on Arm 2 of the study as criteria for initiation of ART despite CD4 + cell count.	The information contained in the appendix has been expanded to include CDC case definition, and country-specific AIDS-defining illness definitions where applicable.
Second Paragraph	Addition	None	For purposes of the study, a person will be considered to have AIDS if they meet these case definitions for AIDS. The list below also includes some specific conditions per the definition of AIDS in Brazil and Thailand, and is noted accordingly.	Additional information has been added to the protocol with regard to AIDS-defining illnesses.
Current WHO Case Definition for AIDS[1]	Changed	Table: Refer to Version 1.0 of the protocol.	The same information included in the table is now listed in this appendix.	Formatting change.
Current CDC Case Definition of AIDS[2] plus Country-specific Diseases for Brazil and Thailand	Addition	None	Refer to list in Version 2.0 of the protocol.	This list includes both the CDC Case Definition and country-specific AIDS-defining illness definitions where applicable.

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Appendix IV: HIV/AIDS Related or Defining Conditions for Inclusion into the Study Database (NOT for capture as an Adverse Event or Serious Adverse Event)				
This appendix has been added to Version 2.0 – it did not exist in Version 1.0. Refer to the Protocol Version 2.0 for the content. The subsequent appendix has been renumbered in Version 2.0 appropriately.				
Appendix V: Index Case and Partner Screening: Run-in Period and Full Study				
INTRODUCTION	Deletion	The screening tests for the study include interview questions and at least one blood test. You may also have another blood test, a physical exam, and a pregnancy test (if you are female. After the screening tests, you will find out if you are eligible for the research study. If you are eligible, the study staff will fully explain the research study to you and answer any questions you have. After the research study has been fully explained to you and if you decide to participate, you will be asked to sign another consent form.	None	Deleted because unnecessary information or repeated elsewhere.
DESCRIPTION OF THE STUDY, sentence added to first paragraph	Addition	None	The drugs being used in the study are approved by the United States Food and Drug Administration (U.S.FDA) for the treatment of HIV, but not approved for the prevention of HIV.	RCC/DAIDS request.

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Appendix V: Index Case and Partner Screening: Run-in Period and Full Study (continued)				
PURPOSE OF THE SCREENING TESTS	Addition	None	If you agree to be screened for the study you will have at least two visits over the course of several weeks, and each visit will last approximately one or two hours. You will be told the results of all of your screening tests as soon as they are available.	RCC/DAIDS request.
PROCEDURES: If you have HIV: last paragraph, add as second sentence	Addition	None	In order to participate in the study, you must have a long-term sexual partner who does not have HIV.	Verbiage was inadvertently left out.
CONFIDENTIALITY, first paragraph	Addition	None	Ethics Committee (EC)	RCC/DAIDS request.
CONFIDENTIALITY, fourth paragraph	Addition	None	Having a Certificate of Confidentiality does not prevent you from releasing information about yourself and your participation in the study.	RCC/DAIDS request.
RESEARCH-RELATED INJURY	Change	There is no program for monetary compensation or other forms of compensation for such injuries.	There is no program for monetary compensation or other forms of compensation for such injuries either through this institution or the U.S. National Institutes of Health (NIH).	Add for clarity.
PURPOSE OF THE STUDY, sentence added to first paragraph	Addition	None	The drugs being used in the study are approved by the United States Food and Drug Administration (U.S.FDA) for the treatment of HIV, but not approved for the prevention of HIV.	RCC/DAIDS request.
Study Groups, second paragraph	Deletion	The T-cell count is a bloodtest that we use to measure the amount of damage that HIV has done to the body. Regardless of which group you are in, you will be started on treatment *before* your T-cell count falls to a low level.	None	Appears in another section

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Appendix V: Index Case Enrollment: Run-in Period and Full Study (continued)				
PROCEDURES: First Study Visit (Enrollment): added sentence to third paragraph	Addition	None.	**[*NOTE: US site only – state that participant will receive PPD first, and if > 5mm induration then chest x-ray is obtained.*]**	Inadvertently omitted.
PROCEDURES: First Study Visit (Enrollment): changed and added a sentence to 4th paragraph	Addition/ Change	We will draw a blood sample (no more than 45 mL, which is about 7 teaspoons *[can be changed to local equivalent]*).	We will draw a blood sample (no more than 45 mL, which is about 9 teaspoons *[can be changed to local equivalent]*). Pregnant women are not allowed to enroll in the first part of the study (the run-in period), but will be allowed to enroll in the second part.	45 mL is equivalent to 9 teaspoons, not 7 teaspoons. Sentence added per RCC/DAIDS request.
PROCEDURES: First Study Visit (Enrollment): last paragraph	Change	You must understand that we do not know if anti-HIV drugs will prevent your partner from getting HIV from you, so you should avoid all activities where you could pass your HIV infection to someone else, even if you are taking the anti-HIV drugs.	You cannot count on anti-HIV drugs to prevent you from passing HIV to your partner, so you should avoid all activities where you could pass your HIV infection, even if you are taking the anti-HIV drugs.	FDA request.
IF YOUR PARTNER BECOMES INFECTED WITH HIV WHILE PARTICIPATING IN THIS STUDY: second paragraph	Change	We will draw blood (no more than 30 mL, which is about 4 teaspoons *[change to local equivalent]*).	We will draw blood (no more than 30 mL, which is about 6 teaspoons *[change to local equivalent]*).	30 mL is equivalent to 6 teaspoons, not 4 teaspoons.
RISKS and/or DISCOMFORTS: Anti-HIV Drugs: third paragraph	Change	We may have to draw your blood (no more than 30 mL, which is about 4 teaspoons [*can be changed to local equivalent*]) to figure out how well your drugs are working against the virus.	We may have to draw your blood (no more than 30 mL, which is about 6 teaspoons [*can be changed to local equivalent*]) to figure out how well your drugs are working against the virus.	30 mL is equivalent to 6 teaspoons, not 4 teaspoons.

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Appendix V: Index Case Enrollment: Run-in Period and Full Study (continued)				
RISKS and/or DISCOMFORTS: Anti-HIV Drugs: fifth paragraph, add as second sentence.	Addition	None	Suddenly stopping your treatment can cause an increase in the amount of HIV in your blood, and the virus can become resistant, which means that the drugs will no longer work.	Verbiage was inadvertently left out.
RISKS and/or DISCOMFORTS: Anti-HIV Drugs: last paragraph	Addition	None	*[Place information here regarding what the current recommendation is at your local site for initiation of antiretroviral therapy. If nevirapine is not recommended as first line therapy for treatment-naïve individuals, please state it here].*	FDA request.
RISKS and/or DISCOMFORTS: Pregnancy and Breastfeeding, number 1	Addition	Birth control drugs that prevent pregnancy given by pills, shots or placed under the skin (some birth control drugs will not work if you are taking certain anti-HIV drugs, your doctor will tell you if this is a problem for you);	Birth control drugs that prevent pregnancy given by pills, shots, the "patch", or placed on or under the skin (some birth control drugs will not work if you are taking certain anti-HIV drugs, your doctor will tell you if this is a problem for you);	RCC/DAIDS request.
RISKS and/or DISCOMFORTS: Pregnancy and Breastfeeding, third paragraph.	Deletion	If you become pregnant <u>while taking study medication</u>, you must notify the study doctor immediately.	If you become pregnant, you must notify the study doctor immediately.	The study doctor should be informed of all pregnancies as soon as possible.

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Appendix V: Index Case Enrollment: Run-in Period and Full Study (continued)				
Other Risks Associated with HIV transmission	Addition	None	• There are other risks involved with HIV transmission that you should know about. These risks are additional reasons why you and your partner must always wear a condom when having any kind of sex: • If the HIV in your partner's body is at a high level (called "viral load") it may make it easier to pass HIV to you. • If you or your partner has an ulcer on your penis or vagina, it may make it easier to pass HIV to you. • If you and your partner practice unprotected oral sex, it may make it easier to pass HIV infection to you. • Not being circumcised may make it easier to get HIV.	FDA request.
CONFIDENTIALITY, first paragraph	Addition	None	Ethics Committee (EC)	RCC/DAIDS request.
CONFIDENTIALITY, forth paragraph	Addition	None	Having a Certificate of Confidentiality does not prevent you from releasing information about yourself and your participation in the study.	RCC/DAIDS request.
RESEARCH-RELATED INJURY:	Addition	None	The study staff will monitor your health closely while you are in this study. You will have a study visit every month. If you have any health problems between visits, please contact the study staff. If you have a medical emergency that requires immediate care, [*insert site-specific instructions*].	Changed for clarity per FDA, and RCC/DAIDS comment.

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Appendix V: Index Case Enrollment: Run-in Period and Full Study (continued)				
RESEARCH-RELATED INJURY:	Change	[*Site-specific: insert institutional policy*] If you are injured as a result of being in this study, the study clinic will give you immediate necessary treatment for your injuries. You will then be told where you may receive additional treatment for your injuries. The cost of this treatment may be charged to you. There is no program to pay for the treatment of such injuries. You do not give up any legal rights by signing this consent form.	[*Sites to specify institutional policy*:] If you are injured as a result of being in this study, the [institution] will give you immediate necessary treatment for your injuries. You [will/will not] have to pay for this treatment. You will be told where you can get additional treatment for your injuries. There is no program for monetary compensation or other forms of compensation for such injuries either through this institution or the U.S. National Institutes of Health (NIH). You do not give up any legal rights by signing this consent form	Changed for clarity per FDA, and RCC/DAIDS comment.
Risk Table	Changes/ Additions	Refer to Version 1.0	Refer to Version 2.0	The risks for ZDV, EFV, NVP, TDF, d4T, ddI, and ATZ were updated or added according to the newest DAIDS' risk lists.
Appendix V: Partner Enrollment: Run-In Period And Full Study				
PURPOSE OF THE STUDY, sentence added to first paragraph	Addition	None.	The drugs being used in the study are approved by the United States Food and Drug Administration (U.S.FDA) for the treatment of HIV, but not approved for the prevention of HIV.	RCC/DAIDS request.
PURPOSE OF THE STUDY: Study Groups, added to paragraph.	Addition	None	During the study, one group will start anti-HIV drugs as soon as they join the study. Others will start the anti-HIV drugs later in the study, after their T-cell count *[or whatever term is commonly used locally]* is lower or if they become sick.	Verbiage was inadvertently left out.

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Appendix V: Partner Enrollment: Run-In Period And Full Study (continued)				
PROCEDURES: First Study Visit (Enrollment), add as second to last paragraph	Addition	None	If you and your partner are in Group 1, your partner will be given anti-HIV drugs. You will be told how to help your partner take these pills correctly.	Verbiage was inadvertently left out.
PROCEDURES: First Study Visit (Enrollment) last paragraph	Change	You must understand that we do not know if anti-HIV drugs will keep you from getting HIV from your partner, so you should avoid all activities where the HIV infection can pass to you, even if your partner is taking the anti-HIV drugs.	You cannot count on the anti-HIV drugs to prevent your partner from passing HIV to you. You should avoid all activities where HIV could pass to you, even if your partner is taking the anti-HIV drugs.	FDA request.
Other Risks Associated with HIV Transmission	Addition	None	• There are other risks involved with HIV transmission that you should know about. These risks are additional reasons why you and your partner must always wear a condom when having any kind of sex: • If the HIV in your partner's body is at a high level (called "viral load") it may make it easier to pass HIV to you. • If you or your partner has an ulcer on your penis or vagina, it may make it easier to pass HIV to you. • If you and your partner practice unprotected oral sex, it may make it easier to pass HIV infection to you. • Not being circumcised may make it easier to get HIV.	FDA request.
POTENTIAL BENEFITS, fourth paragraph	Change	Because your partner will be treated for HIV, your chance of getting HIV from your partner may be reduced.	Because your partner will be treated for HIV, your chance of getting HIV from your partner may be reduced, but no guarantee can be made.	RCC/DAIDS request.

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Appendix V: Partner Enrollment: Run-In Period And Full Study (continued)				
CONFIDENTIALITY, first paragraph	Addition	None	Ethics Committee (EC)	RCC/DAIDS request.
CONFIDENTIALITY, fourth paragraph	Addition	None	Having a Certificate of Confidentiality does not prevent you from releasing information about yourself and your participation in the study.	RCC/DAIDS request.
RESEARCH-RELATED INJURY:	Change	[*Site-specific: insert institutional policy*] If you are injured as a result of being in this study, the study clinic will give you immediate necessary treatment for your injuries. You will then be told where you may receive additional treatment for your injuries. The cost of this treatment may be charged to you. There is no program to pay for the treatment of such injuries. You do not give up any legal rights by signing this consent form.	The study staff will monitor your health closely while you are in this study. You will have a study visit every month. If you have any health problems between visits, please contact the study staff. If you have a medical emergency that requires immediate care, [insert site-specific instructions]. [*Site-specific: insert institutional policy:*] If you are injured as a result of being in this study, the [institution] will give you immediate necessary treatment for your injuries. You [will/will not] have to pay for this treatment. You will be told where you can get additional treatment for your injuries. There is no program for monetary compensation or other forms of compensation for such injuries either through this institution or the U.S. National Institutes of Health. You do not give up any legal rights by signing this consent form.	Changed for clarity per FDA, and RCC/DAIDS comment.

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Appendix V: Index Case and Partner Screening: Full Study				
INTRODUCTION	Deletion	The screening tests for the study include interview questions and at least one blood test. You may also have another blood test, a physical exam, and a pregnancy test (if you are female.	None	Deleted because unnecessary information or repeated elsewhere.
INTRODUCTION	Deletion	After the screening tests, you will find out if you are eligible for the research study. If you are eligible, the study staff will fully explain the research study to you and answer any questions you have. After the research study has been fully explained to you and if you decide to participate, you will be asked to sign another consent form.	None	Deleted because unnecessary information or repeated elsewhere.
DESCRIPTION, sentence added to first paragraph	Addition	None	The drugs being used in the study are approved by the United States Food and Drug Administration (U.S.FDA) for the treatment of HIV, but not approved for the prevention of HIV.	RCC/DAIDS request.
PURPOSE OF THE SCREENING TESTS, second paragraph	Addition	None	If you agree to be screened for the study you will have at least two visits over the course of several weeks, and each visit will last approximately one or two hours. You will be told the results of all of your screening tests as soon as they are available.	RCC/DAIDS request.
CONFIDENTIALITY, first paragraph	Addition	None	Ethics Committee (EC)	RCC/DAIDS request.

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Appendix V: Index Case and Partner Screening: Full Study (continued)				
CONFIDENTIALITY, fourth paragraph	Addition	None	Having a Certificate of Confidentiality does not prevent you from releasing information about yourself and your participation in the study.	RCC/DAIDS request.
RESEARCH-RELATED INJURY:	Change	[*Site-specific: insert institutional policy*] If you are injured as a result of these screening tests, the study clinic will give you immediate necessary treatment for your injuries. You will then be told where you may receive additional treatment for your injuries. The cost of this treatment may be charged to you. There is no program to pay for the treatment of such injuries. You do not give up any legal rights by signing this consent form.	[*Site-specific: insert institutional policy*] It is unlikely that you will be injured as a result of having the screening tests. If you are injured, the [institution] will give you immediate necessary treatment for your injuries. You [will/will not] have to pay for this treatment. You will be told where you can get additional treatment for your injuries. There is no program for monetary compensation or other forms of compensation for such injuries either through this institution or the U.S. National Institutes of Health. You do not give up any legal rights by signing this consent form.	FDA, and RCC/DAIDS request.
Appendix V: Index Case Enrollment: Full Study				
INTRODUCTION: second paragraph, add as third, fourth, and fifth sentences	Addition	None	About 1750 couples will participate in the full study (about 245 couples at your clinic). The couples participating in this study will come from Asia, Africa, South America, and North America. Each couple will be in the study for at least 5 years.	Information was inadvertently left out.
PURPOSE OF THE STUDY: sentence added to first paragraph	Addition	None	The drugs being used in the study are approved by the United States Food and Drug Administration (U.S.FDA) for the treatment of HIV, but not approved for the prevention of HIV.	RCC/DAIDS request.

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Appendix V: Index Case Enrollment: Full Study (continued)				
PROCEDURES: First Study Visit (Enrollment), sentence changed and added to fourth paragraph	Change	We will draw a blood sample (no more than 35 mL, which is about 7 teaspoons *[can be changed to local equivalent]*).	We will draw a blood sample (no more than 45 mL, which is about 9 teaspoons *[can be changed to local equivalent]*). **[*NOTE: US site only – state that participant will receive PPD first, and if > 5mm induration then chest x-ray is obtained*.]**	45 mL is equivalent to 9 teaspoons, not 7 teaspoons. Sentence inadvertently omitted.
PROCEDURES: First Study Visit (Enrollment), last paragraph	Change	You must understand that we do not know if anti-HIV drugs will prevent your partner from getting HIV from you, so you should avoid activities that may spread HIV.	You cannot count on anti-HIV drugs to prevent you from passing HIV to your partner, so you should avoid all activities where you could pass your HIV infection, even if you are taking the anti-HIV drugs.	FDA request.
PROCEDURES: Additional Visits: first paragraph	Deletion	If you become sick during the study, you may be asked to return to the clinic more often than every month. We will let you know if this is necessary and help you schedule any additional visits. If your pills are no longer working against HIV, we will try to give you different drugs that will work. We may have to draw your blood (no more than 20 mL, which is about 4 teaspoons [*can be changed to local equivalent*]) to figure out how well your drugs are working against the virus. Some of this blood may be stored for future HIV-related testing.	If you become sick during the study, you may be asked to return to the clinic more often than every month. We will let you know if this is necessary and help you schedule any additional visits.	Information moved to RISKS and/or DISCOMFORTS: Anti-HIV Drugs:

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Appendix V: Index Case Enrollment: Full Study (continued)				
IF YOUR PARTNER BECOMES INFECTED WITH HIV WHILE PARTICIPATING IN THIS STUDY: second paragraph	Change	We will draw blood (no more than 20 mL, which is about 4 teaspoons *[change to local equivalent])*.	We will draw blood (no more than 30 mL, which is about 6 teaspoons *[change to local equivalent])*.	Corrected to reflect appropriate blood draw amount.
IF YOUR PARTNER BECOMES INFECTED WITH HIV WHILE PARTICIPATING IN THIS STUDY: added as third paragraph	Addition	None	The anti-HIV pills may stop working against HIV. If that happens, we will try to give you different drugs that will work. We may have to draw your blood (no more than 30 mL, which is about 6 teaspoons [*can be changed to local equivalent*]) to figure out how well your drugs are working against the virus. Some of this blood may be stored for future HIV-related testing.	Information moved here from PROCEDURES, Addition Visits and the amount of blood was corrected.
RISKS and/or DISCOMFORTS: Anti-HIV Drugs: fourth paragraph	Deletion	Suddenly stopping your treatment can cause an increase in the amount of HIV in your blood, and the virus can become resistant to HIV, which means that the drugs will no longer work.	Suddenly stopping your treatment can cause an increase in the amount of HIV in your blood, and the virus can become resistant, which means that the drugs will no longer work.	Changed to reflect correct meaning.
RISKS and/or DISCOMFORTS: Anti-HIV Drugs: last paragraph	Addition	None	*[Place information here regarding what the current recommendation is at your local site for initiation of antiretroviral therapy. If neviraprine is not recommended as first line therapy for treatment-naïve individuals, please state it here]*	FDA request.

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Appendix V: Index Case Enrollment: Full Study (continued)				
RISKS and/or DISCOMFORTS: Pregnancy and Breastfeeding, number 1	Addition	Birth control drugs that prevent pregnancy given by pills, shots or placed under the skin (some birth control drugs will not work if you are taking certain anti-HIV drugs, your doctor will tell you if this is a problem for you);	Birth control drugs that prevent pregnancy given by pills, shots, the "patch", or placed on or under the skin (some birth control drugs will not work if you are taking certain anti-HIV drugs, your doctor will tell you if this is a problem for you);	RCC/DAIDS request.
RISKS and/or DISCOMFORTS: Pregnancy and Breastfeeding, third paragraph.	Deletion	If you become pregnant <u>while taking study medication</u>, you must notify the study doctor immediately.	If you become pregnant, you must notify the study doctor immediately.	The study doctor should be informed of all pregnancies as soon as possible.
Other Risks Associated with HIV Transmission	Addition	None	• There are other risks involved with HIV transmission that you should know about. These risks are additional reasons why you and your partner must always wear a condom when having any kind of sex: • If the HIV in your body is at a high level (called "viral load") it may make it easier to pass HIV to your partner. • If you or your partner has an ulcer on your penis or vagina, it may make it easier to pass HIV to your partner. • If you and your partner practice unprotected oral sex, it may make it easier to pass HIV infection to your partner. • Not being circumcised may make it easier to get HIV.	FDA request.
CONFIDENTIALITY, first paragraph	Addition	None	Ethics Committee (EC)	RCC/DAIDS request.

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Appendix V: Index Case Enrollment: Full Study (continued)				
CONFIDENTIALITY, fourth paragraph	Addition	None	Having a Certificate of Confidentiality does not prevent you from releasing information about yourself and your participation in the study.	RCC/DAIDS request.
RESEARCH-RELATED INJURY:	Addition	None	The study staff will monitor your health closely while you are in this study. You will have a study visit every month. If you have any health problems between visits, please contact the study staff. If you have a medical emergency that requires immediate care, [insert site-specific instructions].	FDA, RCC/DAIDS request.
RESEARCH-RELATED INJURY:	Change	[*Site-specific: insert institutional policy*] If you are injured as a result of being in this study, the study clinic will give you immediate necessary treatment for your injuries. You will then be told where you may receive additional treatment for your injuries. The cost of this treatment may be charged to you. There is no program to pay for the treatment of such injuries. You do not give up any legal rights by signing this consent form.	[Sites to specify institutional policy:] If you are injured as a result of being in this study, the [institution] will give you immediate necessary treatment for your injuries. You [will/will not] have to pay for this treatment. You will be told where you can get additional treatment for your injuries. There is no program for monetary compensation or other forms of compensation for such injuries either through this institution or the U.S. National Institutes of Health. You do not give up any legal rights by signing this consent form.	FDA, RCC/DAIDS request.
Risk Table	Changes/ Additions	Refer to Version 1.0	Refer to Version 2.0	The risks for ZDV, EFV, NVP, TDF, d4T, ddI, and ATZ were updated or added according to the newest DAIDS' risk lists.

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Appendix V: Partner Enrollment: Full Study				
PURPOSE OF THE STUDY, sentence added to first paragraph	Addition	None.	The drugs being used in the study are approved by the United States Food and Drug Administration (U.S.FDA) for the treatment of HIV, but not approved for the prevention of HIV.	RCC/DAIDS request.
PROCEDURES: First Study Visit (Enrollment): last paragraph	Change	You must understand that we do not know if anti-HIV drugs will keep you from getting HIV from your partner, so you should avoid all activities where the HIV infection can pass to you, even if your partner is taking the anti-HIV drugs.	You cannot count on anti-HIV drugs to prevent you from passing HIV to your partner, so you should avoid all activities where you could pass your HIV infection, even if you are taking the anti-HIV drugs.	FDA request.
Other Risks Associated with HIV Transmission:	Addition	None	• There are other risks involved with HIV transmission that you should know about. These risks are additional reasons why you and your partner must always wear a condom when having any kind of sex: • If the HIV in your partner's body is at a high level (called "viral load") it may make it easier to pass HIV to you. • If you or your partner has an ulcer on your penis or vagina, it may make it easier to pass HIV to you. • If you and your partner practice unprotected oral sex, it may make it easier to pass HIV infection to you. • **Not being circumcised may make it easier to get HIV.**	FDA request.
POTENTIAL BENEFITS, fourth paragraph	Addition	Because your partner will be treated for HIV, your chance of getting HIV from your partner may be reduced.	Because your partner will be treated for HIV, your chance of getting HIV from your partner may be reduced, but no guarantee can be made.	RCC/DAIDS request.

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Appendix V: Partner Enrollment: Full Study (continued)				
CONFIDENTIALITY, first paragraph	Addition	None	Ethics Committee (EC)	RCC/DAIDS request.
CONFIDENTIALITY, fourth paragraph	Addition	None	Having a Certificate of Confidentiality does not prevent you from releasing information about yourself and your participation in the study.	RCC/DAIDS request.
RESEARCH-RELATED INJURY:	Addition	None	The study staff will monitor your health closely while you are in this study. You will have a study visit every month. If you have any health problems between visits, please contact the study staff. If you have a medical emergency that requires immediate care, [insert site-specific instructions].	FDA, RCC/DAIDS request.
RESEARCH-RELATED INJURY:	Change	[*Site-specific: insert institutional policy*] If you are injured as a result of being in this study, the study clinic will give you immediate necessary treatment for your injuries. You will then be told where you may receive additional treatment for your injuries. The cost of this treatment may be charged to you. There is no program to pay for the treatment of such injuries. You do not give up any legal rights by signing this consent form.	[Sites to specify institutional policy:] If you are injured as a result of being in this study, the [institution] will give you immediate necessary treatment for your injuries. You [will/will not] have to pay for this treatment. You will be told where you can get additional treatment for your injuries. There is no program for monetary compensation or other forms of compensation for such injuries either through this institution or the U.S. National Institutes of Health. You do not give up any legal rights by signing this consent form.	FDA, RCC/DAIDS request.

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Appendix V: Specimen Storage				
CONFIDENTIALITY, added as second paragraph	Addition	None	Efforts will be made to keep your study records and test results confidential to the extent permitted by law. However, we cannot guarantee absolute confidentiality. You will be identified by a code, and personal information from your records will not be released without your written permission. You will not be personally identified in any publication about this study. However, your records may be reviewed, under guidelines of the United States Federal Privacy Act *[U.S. sites only]*, by the United States Food and Drug Administration (FDA); the sponsor of the study (United States National Institutes of Health [NIH]), the [*insert name of site*] Institutional Review Board (IRB)/Ethics Committee (EC), study staff, study monitors, the companies that make the drugs used in this study, and (*insert applicable local authorities*].	Verbiage inadvertently left out; RCC/DAIDS request.
CONFIDENTIALITY, third paragraph, last sentence	Addition	None	Having a Certificate of Confidentiality does not prevent you from releasing information about yourself and your participation in the study.	RCC/DAIDS request.
Appendix V: Index Case Pregnancy				
INTRODUCTION, first paragraph, fourth sentence	Addition	You may also talk with your own doctor about what is best for you and your baby and if you should remain on study medicines or choose other anti-HIV drugs.	You may also talk with your own doctor about what is best for you and your baby and if you should remain on study medicines, choose other anti-HIV drugs, or start anti-HIV drugs.	RCC/DAIDS request.

Section Number and Paragraph	Type of Change	Original Text	Added or Revised Text	Justification
Appendix V: Index Case Pregnancy (continued)				
ADDITIONAL INFORMATION FOR PREGNANT PARTICIPANTS, second paragraph	Addition	Tests in pregnant animals do show some risk.	Tests in pregnant animals do show some risk for some anti-HIV drugs.	Clarification.
CONFIDENTIALITY	Addition	None	See Version 2.0	Verbiage inadvertently omitted.
RESEARCH-RELATED INJURY:	Addition	None	The study staff will monitor your health closely while you are in this study. You will have a study visit every month. If you have any health problems between visits, please contact the study staff. If you have a medical emergency that requires immediate care, [insert site-specific instructions]. Sites to specify institutional policy:] If you or your baby are injured as a result of being in this study, the [institution] will give you both immediate necessary treatment for your injuries. You [will/will not] have to pay for this treatment. You will be told where you can get additional treatment for your injuries. There is no program for monetary compensation or other forms of compensation for such injuries either through this institution or the U.S. National Institutes of Health. You do not give up any legal rights by signing this consent form.	FDA request.
RESEARCH-RELATED INJURY:	Change	If your baby or you are injured as a result of being in this study, you will both be given immediate treatment for your injuries. The cost for this treatment will be charged to you or your insurance company. There is no program for compensation either through this institution or the National Institutes of Health (NIH). You will not be giving up any of your legal rights by signing this consent form.		FDA, RCC/DAIDS request.
Appendix VI: Manual for Expedited Reporting of Adverse Events to DAIDS				
This appendix has been added to Version 2.0 – it did not exist in Version 1.0. Refer to Version 2.0 for content.				