HPTN 084 Study-Specific Procedures Manual Overview and Version Control

Section Number	Section Title	Current Version Number	Current Version Date	Updates and Comments
1	Introduction	4.0	02Mar2023	Updates for Version 4.0 • Editorial changes throughout • Added Molly Dyer and removed Priyanka Agarwal from Table 1-1 (Contacts). • Clarified there are no LOC activation requirements for Protocol V4.0. • Section 1.5.2: Added a clarification: o The ICF for the original, double-blinded portion of the study is irrelevant to the open-label protocol amendments. Sites should implement the ICFs associated with the amendments.
2	Protocol	4.0	02Mar2023	Updates for Version 4.0 • Added CM#2 to V3.0; V4.0 and CM#1 to V4.0
3	Document Requirements	4.0	02Mar2023	Updates for Version 4.0 • In table 3-1b, updated listing to match current CRFs. • Removed reference to a protocol deviation alias; the process of emailing the protocol deviation alias was removed in a prior version of the SSP.
4	Continuation in Protocol Version 3.0 (OLE)	4.1	02Mar2023	Updates for Version 4.1 • Section 4.2.1: Added a clarification: o Participants do not need to be re-consented with the ICF contained in the main body of the original protocol. That part of the study has concluded and the information in it is not representative of the trial or participant activities. The executed form specific to amendment v4.0 will document the participant's continued participation in the study. o Table 4-1: Assessment of understanding example revised for the V4.0 protocol Updates for Version 4.0, 21Nov2022 (Version distributed to the Gaborone CRS only for their IRB) • Revised assessment of understanding example; added reference to V4.0 protocol.
5	Study Procedures Overview	4.0	02Mar2023	Updates for Version 4.0 • Added reference to Protocol V4.0 and Step 6 • Removed language around HIV testing and split visits; referred to the lab SSP section.
6	Visit Checklists	4.0	02Mar2023	Updates for Version 4.0 • Removed a duplicate row 'review/update locator information' from Step 5. • Added Step 6 Visits
7	Participant Retention	4.0	02Mar2023	Updates for Version 4.0 • Added reference to OLE 2/Amendment 4.

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8	Study Product Considerations	4.0	2Mar2023	Updates for Version 4.0 • Correction to Appendix 8a, Sections 8.1.2, 8.1.4 and 8.1.5, bullet labeled (1) should read retrieve oral active CAB bottle with two part label from Step 1 supply. • Appendix 8b: Added reference to Step 6.
9	Clinical Considerations	4.0	02Mar2023	Updates for Version 4.0 • Editorial changes throughout • Moved CMC section to the front of this section (9.2) and renumbered sections. • Added reference to Step 6 throughout. • Added flowcharts for OLE 1 & 2. • Section 9.3 (Participant-Reported Medical History during Follow up): o Added a clarification- For split visits excluding HIV confirmatory visits, the HIV viral load does not need to be repeated if the split visit occurs less than 7 days from the initial visit. See SSP, Section 11.3.2 for further procedures. • Section 9.5.1 (Adverse Events): o Added a clarification- See Section 10.7.3 for managing any AEs noted while performing testing under v3.0 that is not required by the version 4.0 protocol. • Section 9.5.4.1 (Precautionary and Prohibited Medications): o Added a note to always refer to the latest IB for more detailed information; removed immunomodulators from list. • Section 9.6.3 (Missed or Late Injections): o Several clarifications added to this section around missed or late injections. • Section 9.7 (Specimen Collection): o Updated text around creatine clearance assessment for participants who initiated the trial under HPTN 084-01. • Section 9.8.1: Updated header to 'suspected hepatoxicity' from liver toxicities/damage • Section 9.9 (HIV Considerations During Study Conduct): o Sites should email the 084HIV@hptn.org alias in cases of reactive or "indeterminate" results regardless of the site interpretation (false positive, discordant, discrepant) or with questions about the HIV test algorithm. When emailing this group, make sure to attach the template for documenting of all HIV results for the participant." o Participants who are determined not to be infected (i.e. false positive) may resume study products ONLY after CMC consultation. o Added section on the management of participants with discrepant HIV results.

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				• Section 9.12 (Pregnancy): o Added a graphic showing the different options for participants consenting to the pregnancy sub-study. o Added steps around the transitions related to pregnancy, including what to do if a participant in Step 4d experiences pregnancy loss prior to 40 weeks gestational age. o Added paragraph on ultrasound during pregnancy in all participants. o Added several tools to assist with infant assessments. • Added Appendix 9b: HPTN 084 Cheat Sheet for PPT transitions from V3.0 to V4.0. • Added Appendix 9c: Added example SOP for the management of pregnancy
10	Adverse Event Reporting and Safety Monitoring	V4.0	02Mar2023	Updates for Version 4.0 • Added reference to OLE 2. • Added clarifying language in Section 10.7.3 including: o AEs must be followed to resolution even after a site transitions to a newer protocol version and the new version does not specify testing in the SOE. o Reminder to check the Toxicity Management section in the currently approved protocol version.
11	Laboratory and Specimen Management Procedures	V4.0	02Mar2023	Updates for Version 4.0 • Editorial changes throughout Table 11-13: SOE- Step 6: • Added SOE for Step 6- Participants on Maintenance Doses of CAB LA weeks 49-96 Section 11.3.2: • Minor editorial changes • During the open-label part of this study, in addition to the HIV alias, also copy the CMC alias lists immediately about any HIV reactive or positive. Figure 11.3: • Updated HIV testing algorithm for follow-up (Fig. 11.3, page 34) to include consulting the seroconversion committee.
12	Counseling Considerations	V4.0	02Mar2023	Updates for Version 4.0 • Throughout added text around counseling for discordant results, including example talking points. • Appendix 12A: Added text around choice to start ART following discordant results.

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13	Data Management	V4.0	02Mar2023	Updates for V4.0 • Updates to table listing HPTN 084 SDMC staff. • Updates to Table 13-2 HPTN OLE Visit Codes, Target Days, and Visit Windows • Updates to Appendix 13A: HPTN084 Schedule of Forms
14	CASI	V4.0	02Mar2023	Updates for V4.0 • Only the footer was updated. No other edits were made. • No changes to the CASI PDF (14A)
15	Reporting Plan	V4.0	02Mar2023	Updates for V4.0 • Only the footer was updated. No other edits were made.
16	Data Communiqués	V4.0	02Mar2023	Updates for V4.0 • Only the footer was updated. No other edits were made.
17	COVID-19 Measures	V4.0	02Mar2023	Updates for V4.0 • Editorial changes • Section 17.1- Removed list of COVID resources.
Appx I	Guidance for the management of discordant/ discrepant HIV test results	V2.2	07Feb2023	This document has its own version # Key changes to the guidelines document include: • New requirements for pre-approval for HIV DNA testing (this testing is not available/performed in the OLE) • Guidance for repeat HIV RNA testing • Guidance for HIV discriminatory/confirmatory testing • Guidance for stopping CAB based on HIV RNA screening test results (OLE only) • Guidance for starting ART based on HIV RNA screening test results (OLE only)