

Section 2. Protocol

This section contains a complete reference copy of the current version of the HPTN 046 protocol and any protocol Clarification Memos (CM) and Letters of Amendment (LOA) for the current version of the protocol. To ensure that this manual continues to reflect current protocol specifications:

- Upon receipt of any protocol CM, place a copy of the memo in this section.
- Upon receipt of any protocol LOA, place a copy of the letter in this section.
- Upon receipt of any full protocol amendment, replace the protocol in this section with the amended version.

At the time of this printing, the following are the current protocol specifications:

- Protocol Version 3.0, dated 26 September 2007
- Letter of Amendment #1 for Protocol Version 3.0, dated XX April 2008

Following are brief descriptions of Clarification Memos, Letters of Amendment, and Full Protocol Amendments. More information can be found in the HPTN Manual of Operations.

Clarifications Memos typically are short documents prepared to provide further explanation or more detailed information related to current protocol specifications. The content of a CM should have no impact on participant safety, the risk to benefit ratio of study participation, or the study informed consent forms. CMs must be reviewed and approved by the DAIDS Medical Officer prior to finalization. Once finalized, CMs are distributed to all Protocol Team members and study sites by the CORE; **IRB approval of Clarification Memos is not required by DAIDS**; however sites may submit CMs to their IRBs/ECs for their information.

Letters of Amendment typically are short documents prepared to specify changes to a protocol that have minimal impact on participant safety and the risk-to-benefit ratio of study participation and involve relatively minor modifications of study informed consent forms, if any. LOAs must be reviewed and approved by the DAIDS Regulatory Affairs Branch prior to finalization. Once finalized, LOAs are distributed to all Protocol Team members and study sites by the CORE; **IRB/EC approval of Letters of Amendment is required prior to implementation**. LOAs do not result in a change of the protocol version number and do not require Protocol Registration through the DAIDS RCC. However, if a Letter of Amendment requires a modification of study site informed consent forms, revised forms should be submitted to the DAIDS Protocol Registration Office (via the CORE) for informational purposes.

Full Protocol Amendments are prepared to incorporate significant changes — involving more than minimal impact on participant safety and risk-to-benefit ratio of study participation — and result in the generation of a new protocol version with a new version number. Full protocol amendments must be approved by the DAIDS Regulatory Affairs Branch. Once finalized, protocol amendments are distributed to all Protocol Team members and study sites by the CORE. **IRB/EC approval for both the amended protocol and informed consent forms must be obtained, and DAIDS Protocol Registration procedures must be completed for the new version of the protocol and consents prior to implementation** (within 90 days of issuance of the new protocol version).