

Letter of Amendment # 2 to:

**HPTN 077: A Phase IIa Study to Evaluate the Safety, Tolerability and Pharmacokinetics of the Investigational Injectable HIV Integrase Inhibitor, GSK1265744, in HIV-uninfected Men and Women
Version 3.0, October 13, 2015
DAIDS Document ID: 11964
IND # 122,744**

Final Version of LoA # 2: July 28, 2016

The following information impacts the HPTN 077 study and must be forwarded to all responsible Institutional Review Boards (IRBs)/Ethics Committees (ECs) as soon as possible for their information and review. This Letter of Amendment (LoA) must be approved by all responsible IRBs/ECs, as well as other regulatory entities as applicable and per the policies and procedures of the regulatory entities.

The information contained in this LoA impacts the participant letter/information sheet in Appendix XIII of the protocol. Your IRB/EC will be responsible for determining the process of informing participants of the contents of this LoA. The following should be noted: LoA # 1, dated July 6, 2016, included this same update contained in this LoA # 2, but to the sample informed consent form for Cohort 2 only. LoA # 1 inadvertently omitted the update to the participant letter/information sheet for Cohort 1 (both the sample informed consent form for Cohort 2 and the participant letter/information sheet for Cohort 1 are contained in Version 3.0 of the protocol). In processing LoA # 1 for local IRB/EC approval, sites may have already incorporated the new information in to an addendum or a participant letter that does not specify which cohort the new information applies to. In these cases, no additional changes are necessitated by this LoA # 2. Additionally, a site may plan to utilize an addendum or a participant letter to provide this new information. No matter the mechanism used to provide this information to participants in follow-up, as stated above, this LoA must be approved by all IRBs/ECs and other regulatory entities as applicable.

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

If the HPTN 077 protocol is fully amended in the future, this Letter of Amendment will be incorporated into the next version. Text appearing below in highlighted **bold** will be added and text with a highlighted ~~strike through~~ will be deleted.

Summary of the Revision and Rationale

In Letter of Amendment (LoA) # 1, dated July 6, 2016, the sample informed consent form in Appendix XII for Cohort 2 participants enrolled under Version 3.0 of the protocol was updated to include a case of ALT elevation from HPTN 077, which is included in the current Investigator's Brochure (Version 5.0, dated January 6, 2016). This same update needs to be included in Appendix XIII, the participant letter/information sheet for participants enrolled in Cohort 1 under Version 2.0 of the study. While participants in this cohort are no longer receiving injections, those that remain in follow-up should be given this updated information. This update was inadvertently omitted from LoA # 1, dated July 6, 2016, to Version 3.0.

IMPLEMENTATION

APPENDIX XIII: SAMPLE HPTN 077 PARTICIPANT LETTER/INFORMATION SHEET FOR PARTICIPANTS ENROLLED UNDER VERSION 2.0

Note: Only the numbered item in the letter that is impacted by this change is depicted below.

4. We told you when you started the study that there have been some people who were taking this medicine in other studies who have had liver side effects. **All Some** of these people were HIV-infected (HIV positive) and ~~they all had~~ some damage to their liver before taking the GSK 744 study medication. ~~In those studies, w~~While taking the study medication, their blood tests showed that their liver was irritated, although they felt well. The medications were stopped, and the liver blood tests **are returned to** normal. That is why anyone in HPTN 077 will not be able to participate if they have HIV-infection, Hepatitis C (or B), or any liver irritation.