March 30, 2020

Clarification Memo 2

Version 2.0

HVTN 127/HPTN 087

A multicenter, randomized, partially blinded phase 1 clinical trial to evaluate the safety and serum concentrations of a human monoclonal antibody, VRC-HIVMAB075-00-AB (VRC07-523LS), administered in multiple doses and routes to healthy, HIV-uninfected adults

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Clinical Research Site (CRS) filing instructions

Please distribute this clarification memo to all appropriate staff members, and file with your protocol documents. Consult your local Institutional Review Board (IRB)/Ethics Committee (EC) regarding submission requirements for clarification memos.

List of changes

Item 1 Clarified throughout protocol: “Clinic visits” ................................................................. 2

The changes described herein will be incorporated in the next version of Protocol HVTN 127/HPTN 087 if it undergoes full protocol amendment at a later time.
Item 1  Clarified throughout protocol: “Clinic visits”

In order to address the impact of the current COVID-19 pandemic on clinical site operations and to enhance site flexibility to follow public health guidelines to maximize participant and staff safety, “clinic visits” for data collection and procedures (scheduled and ad hoc) may be conducted by phone, text message, email, or other electronic means. An in-person clinic visit is required only for physical exam, point-of-care testing, collecting biological samples, or administering study agents.
Protocol modification history

Protocol modifications are made to HVTN protocols via clarification memos, letters of amendment, or full protocol amendments. HVTN protocols are modified and distributed according to the standard HVTN procedures as described in the HVTN Manual of Operations (MOP).

The version history of, and modifications to, Protocol HVTN 127/HPTN 087 are described below.

**Date: March 30, 2020**
*Protocol version: Version 2.0*
*Protocol modification: Clarification Memo 2*

Item 1 Clarified throughout protocol: “Clinic visits”

**Date: April 25, 2019**
*Protocol version: Version 2.0*
*Protocol modification: Letter of Amendment 4*

Item 1 Revised in Section 8.3.1.1, Intravenous infusion preparation instructions (T1, T2, and T3): Storage limits for prepared study product

Item 2 Added as Appendix K: Visit windows for all groups

Item 3 Corrected in Section 9.9, Visit windows and missed visits: Visit window source and procedures for documenting out-of-window and missed visits

**Date: March 4, 2019**
*Protocol version: Version 2.0*
*Protocol modification: Letter of Amendment 3*

Item 1 Revised in Section 8.3.1.1, Intravenous infusion preparation instructions (T1, T2, and T3): Storage limits for prepared study product

**Date: December 20, 2018**
*Protocol version: Version 2.0*
*Protocol modification: Letter of Amendment 2*

Item 1 Removed from signature blocks in Appendices A and C: Growing participant cells over time

Item 2 Clarified in Section 6.3, Blinding: Separation of AE assessment/reporting from study product administration
**Date: August 17, 2018**

*Protocol version: Version 2.0*

*Protocol modification: Letter of Amendment 1*

**Item 1** Revised in Sections 7.3., 9.5.1, 9.10, 9.12, and Appendices A, F, and G: Follow-up for participants diagnosed with HIV infection during study participation

**Item 2** Clarified in Section 4.10, *Potential risks of study products and administration*: Serious infusion reactions

**Item 3** Added in Section 7.2, *Exclusion criteria*: Exclusion for prior receipt of VRC01-class anti-HIV antibodies

**Item 4** Deleted in Section 7.3.1, *Delaying study product administration for a participant*: Counseling on glucocorticosteroid receipt

**Item 5** Revised in Sections 8.3.1.2 and 8.3.1.3: Syringe/bag labeling

**Item 6** Revised in Section 8.4.3 and Appendix A: Number of syringes required to administer calculated study product dose

**Item 7** Revised in Section 9.5.1 and Appendix A, Item 20: Study-product related seroreactivity on HIV test kits

**Item 8** Corrected in footnote “c” to Table 11-1: List of subjective solicited AEs

**Item 9** Revised in Appendix F, *Laboratory procedures*, Section 6.1, and Appendix A and C: Blood draws for PBMC storage removed

**Item 10** Added in Appendix F: ADA detection assay location

**Item 11** Corrected in Appendix G, *Procedures at CRS*: Pregnancy test at Visit 19

**Item 12** Clarified in Appendix H, *Adverse events of special interest (AESIs)*: Updates to AESI list

**Date: April 4, 2018**

*Protocol version: Version 2.0*

*Protocol modification: Clarification Memo 1*

**Item 1** Corrected in Appendix G, *Procedures at CRS*: Visit 20 day

**Date: March 8, 2018**

*Protocol version: Version 2.0*

*Protocol modification: Full Protocol Amendment 1*

**Item 1** Added on Title page: IND number

**Item 2** Revised on Title page and in Section 3, Appendices A, C, and J: Study title

**Item 3** Added: Intramuscular injection (IM) study arm

**Item 4** Revised: Product administration and follow-up visit schedules

**Item 5** Updated in Section 4.9.3: *Clinical studies of VRC07-523LS; VRC 605*
Item 6  “Pharmacokinetics” removed in Section 6.1.2, Sample size calculations for serum levels of VRC07-523LS

Item 7  Updated in Section 6.4.6: Analyses and data sharing prior to end of scheduled follow-up visits

Item 8  Updated in Sections 7, Appendix B, and Appendix D: Use of “sex assigned at birth”

Item 9  Removed in Section 9.1.2, Protocol-specific consent forms: Instruction to follow protocol-specific memo regarding when to start using site-specific consent forms

Item 10  Clarified in Sections 9.3 and 9.4: HIV assessment procedure includes HIV diagnostic testing

Item 11  Clarified in Section 9.8 Assessments of Solicited AEs: CRS clinician assessment

Item 12  Clarified in Section 9.8.1, Assessment of systemic and local symptoms: Thermometry

Item 13  Clarified in Section 9.8.2, Assessment of infusion/injection site: Infusion/injection site reaction measurements

Item 14  Updated in Section 10.1, CRS laboratory procedures: Special instructions and research assays

Item 15  Clarified in Section 11.2.1, Submission of safety forms to SDMC: Submittal deadlines

Item 16  Revised in Section 11.2.2, AE reporting: Unsolicited AE reporting period

Item 17  Clarified in Section 11.2.3, Expedited reporting of AEs to DAIDS: Unblinding procedures

Item 18  Added in Section 11.3, Safety pause and prompt PSRT AE review: Submission of unanticipated problems to IRB/EC

Item 19  Clarified in Section 12.2, Emergency communication with study participants: Circumstances under which communication is allowed prior to IRB/EC approval

Item 20  Clarified in Appendix A, Item 8: Visit intervals

Item 21  Clarified in Appendix A, Item 14: Sample testing

Item 22  Clarified in Appendix A Item 16 and Appendix C: Other research on stored samples

Item 23  Added in Appendix A and in Appendix C: Participants may change their minds regarding use of samples and data in other studies

Item 24  Clarified in footnote to Appendix A and Appendix C signature blocks: Witness requirement

Item 25  Clarified in Appendix B, Approved birth control methods (for sample informed consent form): Condom use for HIV and STI prevention
Item 26  Revised in Appendix D: Table of procedures (for sample informed consent form)
Item 27  Revised in Appendix E: Product administration schedule graphic
Item 28  Revised in Appendix F: Laboratory procedures table
Item 29  Revised in Appendix G: Procedures at CRS table
Item 30  Clarified in Appendix H, Adverse events of special interest (AESI): Update provisions
Item 31  Added as Appendix I: Low risk guidelines for the US and Switzerland
Item 32  Updated and corrected in Section 3.1: Protocol team
Item 33  Updated: Section and appendix numbers and cross-references
Item 34  Corrected: Acronyms, spelling and grammatical errors, page layout, and stylistic inconsistencies

Date: November 28, 2017
Protocol version: Version 1.0
Protocol modification: Original protocol