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

DAIDS DOCUMENT ID 38458

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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

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