April 4, 2018

Clarification Memo 1

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-ES ID 38458

[IND #137719—HELD BY DAIDS]

HIV Vaccine Trials Network (HVTN) 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  Corrected in Appendix G, Procedures at CRS: Visit 20 day ................................. 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  Corrected in Appendix G, Procedures at CRS: Visit 20 day

The Day number for Visit 20 in Appendix G in Version 2.0 of protocol HVTN 127/HPTN 087 has been corrected as shown below (deletion shown by strikethrough; added text in **bold underline**). The corrected Appendix G, Procedures at CRS is attached.

Revised:

<table>
<thead>
<tr>
<th>Visit</th>
<th>01</th>
<th>02</th>
<th>03</th>
<th>04</th>
<th>05</th>
<th>06</th>
<th>07</th>
<th>08</th>
<th>09</th>
<th>10</th>
<th>11</th>
<th>12</th>
<th>13</th>
<th>14</th>
<th>15</th>
<th>16</th>
<th>17</th>
<th>18</th>
<th>19</th>
<th>20</th>
<th>Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day</td>
<td>D0</td>
<td>D3</td>
<td>D6</td>
<td>D9</td>
<td>D12</td>
<td>D14</td>
<td>D18</td>
<td>D24</td>
<td>D36</td>
<td>D48</td>
<td>D60</td>
<td>D72</td>
<td>D84</td>
<td>D96</td>
<td>D112</td>
<td>D124</td>
<td>D136</td>
<td>D148</td>
<td>D160</td>
<td>D172</td>
<td>D184</td>
</tr>
</tbody>
</table>
## Appendix G  Procedures at CRS

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Scr.</th>
<th>Inf/Inj1</th>
<th>Inf/Inj2</th>
<th>Inf/Inj3</th>
<th>Inf/Inj4</th>
<th>Inf/Inj5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Signed screening consent (if used)</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Assessment of understanding</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Signed protocol consent</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medical history</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete physical exam</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Confirm eligibility, obtain demographics, randomize</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abbreviated physical exam</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risk reduction counseling</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contraception assessment&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Behavioral risk assessment questionnaire</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social impact assessment</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Social impact assessment questionnaire</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Acceptability questionnaire</td>
<td></td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Belief questionnaire&lt;sup&gt;3&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concomitant medications</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Intercurrent illness/U/solicited adverse experience</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AESI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV infection assessment&lt;sup&gt;4&lt;/sup&gt;</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Confirm HIV test results provided to participant</td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

### Study product administration

- Infusion/Injection<sup>2</sup>
- Solicited AE assessment<sup>8</sup>

### Local lab assessments

- Screening HIV test
- Hepatitis B, Hepatitis C
- Syphilis
- CBC, differential
- Chemistry panel<sup>7</sup>
- Urine dipstick<sup>10</sup>
- Pregnancy (urine or serum HCG)<sup>11</sup>

### Poststudy

- Unblind participant

---

<sup>1</sup> Week:
- Scr: 01
- W0: 02
- W4: 03
- W8: 04
- W12: 05
- W16: 06
- W20: 07
- W24: 08
- W28: 09
- W32: 10
- W36: 11
- W40: 12
- W44: 13
- W48: 14
- W52: 15
- W56: 16
- W60: 17
- W64: 18
- W68: 19
- W72: 20
- W80: Post

<sup>2</sup> Infusion/Injection:
- Inj1: 01
- Inj2: 02
- Inj3: 03
- Inj4: 04
- Inj5: 05

<sup>3</sup> Belief questionnaire:
- D28: 06
- D56: 07
- D84: 08
- D112: 09

<sup>4</sup> HIV infection assessment:
- D28: 10
- D56: 11
- D84: 12
- D112: 13

<sup>5</sup> Pregnancy (urine or serum HCG):
- D28: 14
- D56: 15
- D84: 16
- D112: 17

---

HVTN127-HPTN087_v2.0_cm1_FINAL.docx  Page 3 of 7
1 Screening may occur over the course of several contacts/visits up to and including day 0 prior to study product administration.
2 Specimens collected at Day 0 may be obtained within the 14 days prior to study product administration, except for a pregnancy test which must be performed on urine or blood specimens within 24 hours prior to study product administration with negative results received prior to study product administration.
3 For specimen collection requirements, see Appendix F.
4 Pregnancy prevention (contraception) assessment is required only for participants who were assigned female at birth and who are capable of becoming pregnant. For such participants, use of effective contraception is required from 21 days prior to the first study product administration until the last scheduled clinic visit.
5 Group 6 participants only.
6 Includes pre-test counseling and HIV testing. A subsequent follow-up contact is conducted to provide post-test counseling and to report results to participant.
7 Blood draws required at study product administration visit must be performed prior to administration of study product; however, it is not necessary to have results prior to administration, except for results of a serum pregnancy test, if indicated. Lab tests may be drawn with the 3 days prior to study product administration.
8 Solicited AE assessments performed daily for at least 3 days following study product administration (see Section 9.8).
9 Chemistry panels are defined in Section 9.2.
10 And microscopy if needed.
11 For a participant who was assigned female sex at birth, pregnancy test must be performed on urine or blood specimens within 24 hours prior to study product infusion/injection with negative results received prior to infusion/injection. Persons who have undergone total hysterectomy or bilateral oophorectomy (verified by medical records), are not required to undergo pregnancy testing.
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: 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