Final

February 24, 2023

Clarification Memo 03

Protocol

Version 1.0

HVTN 140 / HPTN 101

A phase 1 dose-escalation clinical trial to evaluate the safety, tolerability, and pharmacokinetics of PGDM1400LS alone and in combination with VRC07-523LS and PGT121.414.LS in healthy, HIV-uninfected adult participants

DAIDS-ES ID 38723

IND #154188—HELD BY DAIDS

HIV Vaccine Trials Network (HVTN) and HIV Prevention Trials Network (HPTN) 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 (CMs).

List of changes

The changes described herein will be incorporated in the next version of Protocol HVTN 140 / HPTN 101 if it undergoes full protocol amendment at a later time. Added text is shown in **bold underline** and deleted text is shown with ~~strikethrough~~.

Item 1 Deleted in Appendix I, *Procedures at HVTN CRS for Part B*: Checkmarks for "Timing of HIV infection assessment" and "Confirm HIV test results provided to participants" procedures listed at visit 10 and 11 respectively

HIV diagnostics blood collections for Part B participants are performed at visits 7 and 11 as noted in Appendix G, *Laboratory procedures for Part B*. Checkmarks for two associated procedures "Timing of HIV infection assessment" and "Confirm HIV test results provided to participants" were incorrectly added to visit 10 and 11 of Appendix I, *Procedures at HVTN CRS for Part B*, respectively. These have been deleted. An updated Appendix I is appended.

Revision:

Visit	**01[1]**	**02[2]**	**03**	**04**	**05**	**06**	**07**	**08**	**09**	**10**	**11**	**Post**
Day:		D0	D3	D6	D28	D56	D112	D116	D168	D224	D280	
Week:		W0	W0	W0	W4	W8	W16	W16	W24	W32	W40	
Procedure	Scr	Inf 1					Inf 2	Phone contact				
HIV infection assessment[7]	X	—	—	—	—	—	X		—	— ~~X~~	X	—
Confirm HIV test results provided to participant[8]	—	X	—	—	—	—	—		X	—	~~X~~ —	X

Appendix I, Procedures at the HVTN CRS for Part B

Visit	**01**[1]	**02**[2]	**03**	**04**	**05**	**06**	**07**	**08**	**09**	**10**	**11**	**Post**
Day:		D0	D3	D6	D28	D56	D112	D116	D168	D224	D280	
Week:		W0	W0	W0	W4	W8	W16	W16	W24	W32	W40	
Procedure	Scr	Inf 1					Inf 2	Phone contact				
Study procedures												
Signed screening consent (if used)	X	—	—	—	—	—	—		—	—	—	—
Assessment of understanding	X	—	—	—	—	—	—		—	—	—	—
Signed protocol consent	X	—	—	—	—	—	—		—	—	—	—
Medical history	X	—	—	—	—	—	—		—	—	—	—
Complete physical exam	X	—	—	—	—	—	—		—	—	X	—
Confirm eligibility, obtain demographics, randomize	X	—	—	—	—	—	—		—	—	—	—
Infusion	—	X	—	—	—	—	X		—	—	—	—
Solicited AE assessment[3]	—	X	X[3]	X[3]	—	—	X[3]	X[3]	X[3]	—	—	—
Abbreviated physical exam	—	X	X	X	X	X	X		X	X	—	—
Risk reduction counseling[4]	X	X	—	—	X	X	X		X	X	X	—
Contraception status assessment[5]	X	X	—	—	X	X	X		X	X	X	—
Social impact assessment	—	X	—	—	X	X	X		X	X	X	—
Behavioral risk assessment questionnaire[6]	X	—	—	—	—	—	—		—	—	X	—
Social impact assessment questionnaire	—	—	—	—	—	X	—		X	—	X	—
Acceptability questionnaire	—	X	—	—	—	—	X		—	—	—	—
Outside testing questionnaire	—	—	—	—	—	—	—		—	—	X	
Concomitant medications	X	X	X	X	X	X	X		X	X	X	—
Intercurrent illness/Unsolicited AE assessment	—	X	X	X	X	X	X		X	X	X	—
HIV infection assessment[7]	X	—	—	—	—	—	X		—	—	X	—
Confirm HIV test results provided to participant	—	X	—	—	—	—	—		X	—	—	X
Specimen collection [8]	X	X	X	X	X	X	X		X	X	X	—

Protocol modification history

Protocol modifications are made via clarification memos, letters of amendment, or full protocol amendments. The version history of, and modifications to, Protocol HVTN 140 / HPTN 101 are described below.

Date: February 24, 2023

Protocol version: Version 1.0
Protocol modification: Clarification Memo 03

Item 1 Deleted in Appendix I, *Procedures at HVTN CRS for Part B*: Checkmarks for "Timing of HIV infection assessment" and "Confirm HIV test results provided to participants" procedures listed at visit 10 and 11 respectively

Date: December 20, 2022

Protocol version: Version 1.0
Protocol modification: Letter of Amendment 3

Item 1 Updated in Section 8.3.2, *VRC07-523LS*: storage conditions for VRC07-523LS vials after thaw and prepared product in IV bags or syringes

Item 2 Updated in Section 1.1, *Protocol Team*: HVTN Protocol Team leader

Date: September 19, 2022

Protocol version: Version 1.0
Protocol modification: Letter of Amendment 2

Item 1 Added in Section 7.2, *Exclusion criteria*; and Section 7.3.1, *Delaying study product administrations for a participant (Part B only)*: considerations for timing of receipt of vaccines for Monkeypox

Date: July 7, 2022

Protocol version: Version 1.0
Protocol modification: Clarification Memo 2

Item 1 Corrected in Letter of Amendment 1 dated February 24, 2022, and Clarification Memo 1 dated March 28, 2022: date of original protocol

Date: March 28, 2022

Protocol version: Version 1.0
Protocol modification: Clarification Memo 1

Item 1 Corrected in Appendix G, *Laboratory procedures for Part B*: CBC/differential and Chemistry panel added to visit 2

Date: February 24, 2022

Protocol version: Version 1.0
Protocol modification: Letter of Amendment 1

Item 1 Added in Section 1, *Overview*: HPTN Leadership and Operations Center

Item 2 Updated in Section 1.1, *Protocol Team*: team members

Item 3 Added in Section 8.3.3.3, *PGT121.414.LS fixed-dose intravenous infusion* preparation: information regarding storage times and temperatures

Item 4 Corrected in Appendix F, *Laboratory procedures for Part A*: Ab reaction maximum blood volume in footnote 13

Item 5 Corrected in Appendix G, *Laboratory procedures for Part B*: formatting

Item 6 Corrected in Appendix F, *Laboratory procedures for Part A* and Appendix G, *Laboratory procedures for Part B*: visit number referenced in footnote 7

Item 7 Corrected in Appendix I, *Procedures at HVTN CRS for Part B*: remote documentation of diary in footnote 3

Item 8 Added in Section 8.4.1, *General considerations for subcutaneous infusion study product administration*: reference to HVTN140/HPTN101 Study-Specific Procedures (SSP) manual) for additional details on anatomic locations for infusions

Item 9 Revised in Section 8.3.1.1, *Thawing instructions*: PGDM1400LS vial storage time conditions

Date: June 23, 2021

Protocol version: 1.0
Protocol modification: not applicable

Original protocol