Final

March 28, 2022

Clarification Memo 1

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

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

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.

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

We have corrected Appendix G provided in Letter of Amendment 1 dated February 24, 2022, for consistency with the protocol text in section 9.3, which indicates that CBC/differential and Chemistry panel safety labs are performed at study product administration visits. Specifically, 5 mL blood collections for CBC/differential and Chemistry panel have been added to visit 2 as shown below. Added text is shown in **bold underline.**

					Visit:	1	2	3	4	5	6	7	8[16]	9	10	11
					Day:	Screening visit[3]	D0	D3	D6	D28	D56	D112	D116	D168	D224	D280
					Week:		W0			W4	W8	W16		W24	W32	W40
							Study Product Administration #1					**Study Product Administration #2**				
Procedure	**Ship to[1]**	**Assay location[2]**	**Tube Type[4]**	**Tube size (vol. capacity)[4]**			**PGDM1400LS + VRC07-523LS + PGT121.414.LS**					**PGDM1400LS + VRC07-523LS + PGT121.414.LS**				
BLOOD COLLECTION																
Screening/Diagnostic																
Screening HIV test	Local lab	Local lab	EDTA	5mL		5	—	—	—	—	—	—	—	—	—	—
HBsAg/anti-HCV	Local lab	Local lab	SST	5mL		5	—	—	—	—	—	—	—	—	—	—
Syphilis[9]	Local lab	Local lab	SST	5mL		5	—	—	—	—	—	—	—	—	—	—
HIV diagnostics[7]	UW-VSL / HSML-NICD	UW-VSL / HSML-NICD	EDTA	10mL		—	—	—	—	—	—	10	—	—	—	10
Safety labs[10]																
CBC/ Differential	Local lab	Local lab	EDTA	5mL		5	**5**	—	—	—	5	5	—	5	—	5
Chemistry Panel[6]	Local lab	Local lab	SST	5mL		5	**5**	—	—	—	5	5	—	5	—	5

The corrected Appendix G is shown on the next page.

					Visit:	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**[16]	**9**	**10**	**11**
					Day:	Screening visit[3]	D0	D3	D6	D28	D56	D112	D116	D168	D224	D280
					Week:		W0			W4	W8	W16		W24	W32	W40
							Study Product Administration #1					**Study Product Administration #2**				
Procedure	**Ship to**[1]	**Assay location**[2]	**Tube Type**[4]	**Tube size (vol. capacity)**[4]			**PGDM1400LS + VRC07-523LS + PGT121.414.LS**					**PGDM1400LS + VRC07-523LS + PGT121.414.LS**				
BLOOD COLLECTION																
Screening/Diagnostic																
Screening HIV test	Local lab	Local lab	EDTA	5mL		5	—	—	—	—	—	—	—	—	—	—
HBsAg/anti-HCV	Local lab	Local lab	SST	5mL		5	—	—	—	—	—	—	—	—	—	—
Syphilis[9]	Local lab	Local lab	SST	5mL		5	—	—	—	—	—	—	—	—	—	—
HIV diagnostics[7]	UW-VSL / HSML-NICD	UW-VSL / HSML-NICD	EDTA	10mL		—	—	—	—	—	—	10	—	—	—	10
Safety labs[10]																
CBC/ Differential	Local lab	Local lab	EDTA	5mL		5	5	—	—	—	5	5	—	5	—	5
Chemistry Panel[5]	Local lab	Local lab	SST	5mL		5	5	—	—	—	5	5	—	5	—	5
Drug concentrations/detection																
PGDM1400LS, VRC07-523LS, PGT121.414.LS concentrations	CSR	HVTN Labs	SST	8.5mL		—	y	y	y	y	y	y	—	y	y	y
Humoral assays																
HIV-1 neutralizing Ab	CSR	HVTN Labs	SST	8.5mL		—	y	y	y	y	y	y	—	y	y	y
Non-neutralizing antiviral assays	CSR	HVTN Labs	SST	8.5mL		—	y	y	y	y	y	y	—	y	y	y
Anti-Drug Antibody (ADA)																
ADA detection assays (screening, confirmatory, titration)	CSR	HVTN Labs	SST	8.5mL		—	y	—	—	—	—	y	—	—	—	y
ADA functional assay	CSR	HVTN Labs	SST	8.5mL		—	y	—	—	—	—	y	—	—	—	y
Ab Reaction[11]																
Tryptase / C3 and C4 Complement / Cytokines	CSR	ARUP	SST	8.5mL		—	See footnote 12	—	—	See footnote 12			—	See footnote 12		
ADA detection assays (screening, confirmatory, titration)	CSR	HVTN Labs	SST	8.5mL		—	See footnote y	—	—	—	—	See footnote y	—	—	—	—
ADA functional assay	CSR	HVTN Labs	SST	8.5mL		—	See footnote y	—	—	—	—	See footnote y	—	—	—	—
STORAGE																
Serum	CSR	—	SST	8.5mL		—	76.5[14]	42.5	42.5	42.5	42.5	51[14]	—	42.5	42.5	42.5
Visit total						**25**	**86.5**	**42.5**	**42.5**	**42.5**	**52.5**	**71**	**0**	**52.5**	**42.5**	**62.5**
56-Day total[13]						**25**	**112**	**154**	**197**	**239**	**292**	**71**	**71**	**124**	**95**	**105**
URINE COLLECTION[10]																
Urine dipstick[8]	Local lab	Local lab				X	—	—	—	—	X	—	—	X	—	X
Pregnancy test[6]	Local lab	Local lab				X	X[15]	—	—	—	—	X	—	—	—	X

Footnotes for Appendix G

[1]CSR = central specimen repository; UW-VSL = University of Washington Virology Specialty Laboratory (Seattle, Washington, USA); HSML-NICD = HIV Sero-Molecular Laboratory-National Institute for Communicable Diseases (Johannesburg, South Africa)

[2]HVTN Laboratories include: Duke University Medical Center (Durham, North Carolina, USA); South African Immunology Laboratory-National Institute for Communicable Diseases (SAIL-NICD, Johannesburg, South Africa); Dartmouth College (Hanover, New Hampshire, USA). Non-HVTN laboratories: ARUP Laboratories (Salt Lake City, Utah, USA)

[3]Screening may occur over the course of several contacts/visits up to and including day 0 prior to study product administration.

[4]Local labs may assign appropriate alternative specimen type or tube types for locally performed tests.

[5]Chemistry panels are defined in Section 9.2 (pre-enrollment), and Sections 9.3 and 9.4 (enrollment and follow-up).

[6]For participants assigned female sex at birth, pregnancy test must be performed on urine or blood specimens on the day of study product administration with negative results received prior to administration. Persons who are NOT of reproductive potential due to having undergone hysterectomy or bilateral oophorectomy (verified by medical records), are not required to undergo pregnancy testing.

[7]At an early termination visit for a withdrawn or terminated participant who is not HIV-infected (see Section 9.10), blood should be drawn for HIV diagnostic testing, as shown for visit 11 above. If a participant has a confirmed diagnosis of HIV infection, do not collect blood for HIV diagnostic testing (see Section 9.12).

[8]And microscopy if needed.

[9]Syphilis testing will be done by serology.

[10]For participants with confirmed diagnosis of HIV infection, only specimens required for protocol-specified safety laboratory tests, urinalysis and pregnancy tests will be collected.

[11]To investigate Ab administration-related clinical reactions, assays may be performed on serum samples taken prior to the study product administration associated with the reaction and collected after the onset of reaction. Refer to the SSP for more information.

[12]SST blood will be collected at specific time points after the onset of any Ab reaction. Refer to the SSP for more information.

[13]The 56-day total blood volume does not include up to 51mL SST blood collected for any Ab reaction; however, the 56-day limit is not exceeded at any visit by the possible collection of SST blood for an Ab reaction.

[14]Of this volume, 8.5mL of SST blood will be **collected post study product administration (**see SSP for details).

[15]Pregnancy test at enrollment does not need to be performed if negative results are received from screening pregnancy test conducted within 48 hours prior to study product administration .

[16]Phone contact only. No specimen collection at this visit.

y = SST blood collected for serum storage will also cover specimen needs for drug concentrations, HIV-1 neutralizing Ab assays, non-neutralizing antiviral assays, and ADA detection and functional assays (including for any Ab reactions); no separate blood draw is needed.

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: 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, 2020

Protocol version: 1.0
Protocol modification: not applicable

Original protocol