February 22, 2016

Clarification Memo 1

Protocol

Version 1.0

HVTN 703/HPTN 081

A phase 2b study to evaluate the safety and efficacy of VRC01 broadly neutralizing monoclonal antibody in reducing acquisition of HIV-1 infection

DAIDS-ES ID 12045

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 Appendices G, H, J, and K: Visit numbering 1

The changes described herein will be incorporated in the next version of Protocol HVTN 703/HPTN 081 if it undergoes full protocol amendment at a later time.

Item 1 Corrected in Appendices G, H, J, and K: Visit numbering

The visit numbers in Appendices G, H, J, and K have been corrected to remove impediments to SDMC database programming. This is a technical correction that has no effect on study design, study procedures, or participant experience or safety.

The cited tables with corrected visit numbers are attached.

Appendix G Schedule 2—Laboratory procedures for HIV-infected participants

				Visit:	#.X[5]	39	40	41	42	43	44	45	46	
				Days after diagnosis:	D0	D7	D14	D21	D35	D49	D77	D105	D161	
				Weeks after diagnosis:	W0	W1	W2	W3	W5	W7	W11	W15	W23	
Procedure	**Ship to[1,2]**	**Assay location[2]**	**Tube Type[3]**	**Tube size (vol. capacity)[3]**										**Total**
BLOOD COLLECTION														
Screening or diagnostic assays														
HIV diagnostics	UW-VSL/HSML-NICD	UW-VSL/HSML-NICD	EDTA	10mL	10	—	—	—	—	—	—	—	—	**10**
HIV PCR viral load	UW-VSL/HSML-NICD	UW-VSL/HSML-NICD	EDTA	10mL	—	10	10	10	10	10	10	10	10	**80**
CD4+T cell count	Local Lab	Local Lab	EDTA	5mL	5	5	5	5	5	5	5	5	5	**45**
Safety lab														
Hemoglobin	Local Lab	Local Lab	EDTA	5mL	—	—	—	—	—	5	—	5	—	**10**
Drug levels														
VRC01 Ab levels	CSR	NVITAL	SST	8.5mL	8.5	8.5	8.5	8.5	8.5	8.5	8.5	8.5	8.5	**76.5**
Immunogenicity & Virologic Assays														
Functional humoral assays[6]	CSR	Duke/SAIL-NICD	SST	8.5mL	17	17	17	17	17	17	17	17	17	**153**
Viral isolation/sequencing	CSR	TBD	EDTA	10mL	10	10	10	10	10	10	10	10	10	**90**
Storage														
Serum	CSR		SST	8.5mL	25.5	17	17	17	17	17	17	17	17	**161.5**
Plasma	CSR		EDTA	5mL	5	5	5	5	5	5	5	5	5	**45**
PBMC	CSR		ACD	8.5mL	34	—	—	—	—	—	34	—	34	**102**
Visit total					**115**	**72.5**	**72.5**	**72.5**	**72.5**	**77.5**	**106.5**	**77.5**	**106.5**	**773**
56-Day total					**115**	**188**	**260**	**333**	**405**	**483**	**329**	**262**	**184**	
URINE COLLECTION														
Pregnancy Test[4]	Local Lab	Local Lab			X	—	—	—	—	—	X	—	—	

[1] CSR = central specimen repository

[2] HVTN Laboratory Program includes laboratories at UW-VSL, Duke, NVITAL, HSML-NICD, and SAIL-NICD. UW-VSL = University of Washington Virology Specialty Laboratory (Seattle, Washington, USA); Duke- Duke = Duke University Medical Center (Durham, North Carolina, USA); NVITAL = NIAID Vaccine Immune T-Cell Antibody Laboratory (Gaithersburg, Maryland, USA); HSML-NICD = HIV Sero-Molecular Laboratory, National Institute for Communicable Diseases (Johannesburg, South Africa); SAIL-NICD = South African Immunology, Laboratory-National Institute for Communicable Diseases (Johannesburg, South Africa).

[3] Local labs may assign appropriate alternative tube types for locally performed tests.

[4] Pregnancy test may be performed on blood specimens.

[5] Confirmatory draw for HIV diagnostics will be collected at this visit.

[6] Functional humoral assays include nAb, ADCC, virion capture, and phagocytosis assays.

Appendix H Schedule 3—Laboratory procedures for participants discovered to have been HIV infected at enrollment

					Visit:	**#.X**	**47**	**48**	
					Days after diagnosis:	**D1**	**D14**	**D168**	
					Weeks after diagnosis:	W0	W2	W24	
Procedure	**Ship to[1,2]**	**Assay location[2]**	**Tube Type[3]**	**Tube size (vol. capacity)[3]**					**Total**
BLOOD COLLECTION									
Screening or diagnostic assays									
HIV diagnostics	UW-VSL/HSML-NICD	UW-VSL/HSML-NICD	EDTA	10mL		10	—	—	**10**
HIV PCR viral load	UW-VSL/HSML-NICD	UW-VSL/HSML-NICD	EDTA	10mL		—	10	10	**20**
CD4+T cell count	Local Lab	Local Lab	EDTA	5mL		5	5	5	**15**
Storage									
Serum	CSR		SST	8.5mL		17	17	17	**51**
Visit total						**32**	**32**	**32**	**96**
56-Day total						**32**	**64**	**32**	
URINE COLLECTION									
Pregnancy Test[4]	Local Lab	Local Lab				X	—	—	

[1] CSR = central specimen repository

[2] HVTN Laboratory Program includes laboratories at UW-VSL and HSML-NICD. 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).

[3] Local labs may assign appropriate alternative tube types for locally performed tests.

[4] Pregnancy test may be performed on blood specimens.

Appendix J Schedule 2—Procedures at HVTN CRS for HIV-infected participants

Visit Number:	#.X[a]	39	40	41	42	43	44	45	46
Days after diagnosis	D0	D7	D14	D21	D35	D49	D77	D105	D161
Weeks after diagnosis:	0	1	2	3	5	7	11	15	23
Study procedures[b]									
Counseling on HIV-1 testing/diagnosis	X	X	—	—	—	—	—	—	—
Abbreviated physical exam	X	X	X	X	X	X	X	X	—
Complete physical exam[c]	—	—	—	—	—	—	—	—	X
ART assessment	X	X	X	X	X	X	X	X	X
Concomitant medications	—	X	X	X	X	X	X	X	X
Intercurrent illness/adverse experience	—	X	X	X	X	X	X	X	X
Transmission risk reduction counseling	X	X	X	X	X	X	X	X	X
Behavioral risk assessment questionnaire	—	—	—	—	—	—	—	—	X
Social impact assessment	X	X	X	X	X	X	X	X	X
Social impact assessment questionnaire	—	—	—	—	—	—	—	—	X

[a] Visit #.X = interim visit for the purpose of drawing samples for confirmatory HIV testing

[b] For specimen collection requirements, see Appendix G.

[c] Includes assessment of HIV/AIDS-related conditions.

Appendix K Schedule 3—Procedures at HVTN CRS for participants discovered to have been HIV infected at enrollment

Visit Number:	#.X[a]	47	48
Days after diagnosis	D0	D14	D168
Weeks after diagnosis:	0	2	24
Study procedures[b]			
Counseling on HIV-1 testing/diagnosis	X	X	—
Abbreviated physical exam[c]	X	X	—
Complete physical exam	—	—	X
ART assessment	X	X	X
Concomitant medications	—	X	X
Intercurrent illness/adverse experience	—	X	X
Transmission risk reduction counseling	X	X	X
Behavioral risk assessment questionnaire	—	—	X
Social impact assessment	X	X	X
Social impact assessment questionnaire	—	—	X

[a] Visit #.X = interim visit for the purpose of drawing samples for confirmatory HIV testing

[b] For specimen collection requirements, see Appendix H.

[c] Includes assessment of HIV/AIDS-related conditions.

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 703/HPTN 081 are described below.

Date: February 22, 2016

Protocol version: Version 1.0
Protocol modification: Clarification Memo 1

Item 1 Corrected in Appendices G, H, J, and K: Visit numbering

Date: August 11, 2015

Protocol version: Version 1.0
Protocol modification: Original protocol