HIV VACCINE
TRIALS NETWORK

FINAL

November 16, 2022

Letter of Amendment 2

Protocol

Version 1.0

HVTN 139

A phase 1 clinical trial to evaluate the safety and immunogenicity of HIV-1 vaccines based on chimpanzee serotypes of adenovirus expressing clade C gp140 and a CH505TF gp120 protein boost in healthy, HIV- uninfected adult participants

DAIDS-ES ID 12052

A non-IND study

HIV Vaccine Trials Network (HVTN) Clinical Research Site (CRS) filing instructions

The following information impacts the HVTN 139 study and must be forwarded to your Institutional Review Board (IRB)/Ethics Committee (EC) and any other applicable Regulatory Entity (RE) as soon as possible for their information and review. Their approval is required before implementation.

Upon receiving final IRB/EC and any other RE approval(s) for this Letter of Amendment (LOA), CRSs must implement the LOA immediately.

Upon receiving final IRB/EC and any other applicable RE approval(s), CRSs are required to submit LOA registration documents to the DAIDS Protocol Registration Office (PRO) at the Regulatory Support Center (RSC). CRSs will receive an LOA Registration Notification once the DAIDS PRO verifies that all the required LOA registration documents have been received and are complete. A Registration Notification from the DAIDS PRO is not required prior to implementing the LOA. A copy of the LOA Registration Notification, along with this LOA and any IRB/EC and RE correspondence, should be retained in the CRS's regulatory files.

For additional information on the registration process and specific documents required for LOA registration, refer to the current version of the DAIDS Protocol Registration Manual.

The following information does not affect the sample informed consent. The CRS's IRB/EC is responsible for determining the process of informing study participants of the contents of this LOA.

List of changes

The changes described herein will be incorporated in the next version of Protocol HVTN 139 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 Revised in Section 5, *Objectives and endpoints*: secondary objective 4 moved to exploratory objective 5

The secondary objective 4 has been moved to exploratory objective 5 since the assay data is not being used for clinical management of the participant. It will be used for research purposes only. Results may be used to identify pre-existing immunity that may interfere with other key immunology assessments.

Tracked revised text in section 5.2: Secondary objectives and endpoints

~~*Secondary objective 4:*~~

~~To evaluate vector-specific antibodies both before and after vaccination.~~

~~*Secondary endpoint 4:*~~

~~Magnitude of serum antibody neutralization of AdC6 and AdC7 vectors as assessed by adenovirus neutralization assay at baseline (Parts A and B), 4 weeks after the first vaccination (Parts A and B), and 4 weeks after the second vaccination (Part B)~~

Tracked revised text in section 5.3: Exploratory objectives

Exploratory objective 5:

To assess the magnitude of serum antibody neutralization of AdC6 and AdC7 vector both before and after vaccination.

Item 2 Updated in Section 1.1, *Protocol Team*: Team membership, contact information, and roles

The Protocol Team list has been updated in Section 1.1, *Protocol Team*. Tracked revised text is shown below. Updated protocol team list is appended.

Tracked revised text under *Protocol leadership:*

Protocol Team leader
~~William Hahn~~ **Manuel Villaran**
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~~whahn@fredhutch.org~~
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Tracked revised text under *other contributors to the original protocol*:

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Clinical trials manager
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~~Hua Zheng~~ **Xue Han**
HVTN SDMC, Fred Hutch

Laboratory Center Representative
~~Lisa Sanders~~ **Jen Hanke**
HVTN Laboratory Center, Fred Hutch

Associate Director of *Regulatory affairs* ~~*associate*~~
Megan Brandon
HVTN LOC, Fred Hutch

Protocol development managers
Rufi Dalvi
Kajari Mondal
~~Daciana Margineantu~~
HVTN LOC, Fred Hutch

Project coordinator
Anders McConachie
~~Haven Wilvich~~
HVTN LOC, Fred Hutch

1.1 Protocol Team

Protocol leadership

Chair	Ameena Goga HIV Prevention Research Unit, South African Medical Research Council Ameena.Goga@mrc.ac.za +2712 339 8524 +2782 302 3168	*Statistician*	Youyi Fong HVTN SDMC, Fred Hutch 206-667-1093 yfong@fredhutch.org
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Protocol Team leader	Manuel Villaran HVTN LOC, Fred Hutch 206-667-6757 mvillar2@fredhutch.org	*Laboratory lead*	Stephen De Rosa HVTN Laboratory Center 206-667-1681 sderosa@fredhutch.org

Other contributors to the original protocol

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Study product developer representatives	Hildegund Ertl Wistar Institute Vaccine and Immunotherapy Center Emmanuel (Chip) Walter Duke Human Vaccine Institute Zachary Sagawa Infectious Disease Research Institute	*DAIDS protocol pharmacist*	Oladapo Alli DAIDS, NIAID 240-627-3593
		SDMC Associate director of lab science	April Randhawa HVTN SDMC, Fred Hutch
Laboratory Center Representative	Jen Hanke HVTN Laboratory Center, Fred Hutch	*Clinical trials manager*	Taylor Jones-Bradford Nelisiwe Xaba Michelle Nebergall HVTN LOC, Fred Hutch
Associate Director of Regulatory affairs	Megan Brandon HVTN LOC, Fred Hutch	*Clinical safety specialist*	Maija Anderson HVTN LOC, Fred Hutch
Community engagement unit representative	Baepanye Kagisho HVTN LOC, Fred Hutch	*Regional Medical Liaison*	Azwi Takalani HVTN LOC, Fred Hutch
Community educator/recruiter	Mduduzi Ngubane Isipingo South African Medical Research Council	*Clinic coordinator*	Brodie Daniels Isipingo South African Medical Research Council
Community Advisory Board (CAB) member	Sphelelo Mqadi Isipingo South African Medical Research Council	*Clinical data manager*	Andrea Repetto, HVTN SDMC, Fred Hutch
Protocol development managers	Rufi Dalvi Kajari Mondal HVTN LOC, Fred Hutch	*Statistical research associate*	Xue Han HVTN SDMC, Fred Hutch
		Project coordinator	Anders McConachie HVTN LOC, Fred Hutch

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 139 are described below.

Date: November 16, 2022

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

Item 1 Revised in Section 5, *Objectives and endpoints*: secondary objective 4 moved to exploratory objective 5

Item 2 Updated in Section 1.1, *Protocol Team*: Team membership, contact information, and roles

Date: May 19, 2022

Protocol version: Version 1.0
Protocol modification: Clarification Memo 2

Item 1 Updated in Appendix H, *Laboratory procedures Part B*; Appendix J, *Procedures at HVTN CRS for Part B*; and Appendix L, *HVTN 139 Visit Windows for Part B*: visit numbers for Part B

Date: March 07, 2022

Protocol version: Version 1.0
Protocol modification: Clarification Memo 1

Item 1 Updated in Section 8.3.1, *AdC6-HIVgp140*; Section 8.3.2, *AdC7-HIVgp140*; and 8.3.4, *Placebo for AdC6-HIVgp140 and AdC7-HIVgp140*: label of study products

Date: June 15, 2021

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

Item 1 Revised in Section 4.10.1*, Clinical studies of Chimpanzee Ad vectors targeting diverse pathogens,* Section 4.11*, Potential risks of study products and administration,* Appendices A and B, *Sample Informed Consent Form for Part A and Part B (section 4),* and Appendix N*, Adverse events of special interest:* risks of AdC6 and AdC7 study products

Item 2 Revised in *Appendix A, Sample Informed Consent Form for Part A,* Sections 4 and 17*:* study product developer information

Item 3 Revised in Appendix B*, Sample Informed Consent Form for Part B,* Section 4: study product developer information

Item 4 Revised Section 1.1*, Protocol Team, Protocol Team Leadership:* Co-Chair and member contact information

Item 5 Clarified in Section 9*, Clinic Procedures:* procedures for data entry into the study database and reference to the HVTN HIV testing algorithm

Item 6 Clarified in Section 12*, Protocol conduct:* protocol monitoring

Item 7 Updated Section 14*, Document references (other than literature citations):* the URL for requirements for source documentation

Date: February 23, 2021

Protocol version: Version 1.0
Protocol modification: N/A

Original protocol

Protocol signature page

A phase 1 clinical trial to evaluate the safety and immunogenicity of HIV-1 vaccines based on chimpanzee serotypes of adenovirus expressing clade C gp140 and a CH505TF gp120 protein boost in healthy, HIV- uninfected adult participants.

I will conduct the study in accordance with the provisions of this protocol and all applicable protocol-related documents. I agree to conduct this study in compliance with United States (US) Health and Human Service regulations (45 CFR 46); applicable US Food and Drug Administration regulations; standards of the International Conference on Harmonization Guideline for Good Clinical Practice (E6); Institutional Review Board/Ethics Committee determinations; all applicable in-country, state, and local laws and regulations; and other applicable requirements (eg, US National Institutes of Health, Division of AIDS) and institutional policies.

Investigator of Record Name (print)	Investigator of Record Signature	Date

DAIDS Protocol Number: HVTN 139

DAIDS Protocol Version: Version 1.0

Protocol Date: February 23, 2021