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LETTER OF AMENDMENT

DATE: June 26, 2020

TO: ACTG CTU Principal Investigators, CRS Leaders, and CTU/CRS Coordinators at A5369 Protocol-Specific Sites

FROM: A5369 Protocol Team

SUBJECT: Letter of Amendment #3 for Protocol A5369, Version 1.0, 03/09/18, entitled "HIV-1-Gag Conserved-Element DNA Vaccine (p24CE) as Therapeutic Vaccination in HIV-Infected Persons with Viral Suppression on Antiretroviral Therapy"

The following information affects the A5369 study and must be forwarded to your institutional review board (IRB)/ethics committee (EC) as soon as possible for their information and review. This Letter of Amendment (LOA) must be approved by your IRB/EC before implementation.

The following information may also affect the Sample Informed Consent. Your IRB/EC is responsible for determining the process of informing participants of the contents of this LOA.

Upon receiving final IRB/EC and any other applicable regulatory entity approvals for this LOA, sites should implement the LOA immediately. Sites are still required to submit an LOA registration packet to the Division of AIDS (DAIDS) Protocol Registration Office (PRO) at the Regulatory Support Center. Sites will receive a registration notification for the LOA once the DAIDS PRO verifies that all required LOA registration documents have been received and are complete. An LOA registration notification from the DAIDS PRO is not required prior to implementing the LOA. A copy of the LOA registration notification, along with this letter and any IRB/EC correspondence, should be retained in the site's regulatory file.

The main reason for this LOA is to provide guidance for the study visit window in follow-up to the COVID-19-related Clarification Memo (CM) #2, dated 04/08/20. The LOA is being implemented to further broaden the visit window in light of the feasibility at sites due to COVID-19 situations.

Only new text from this LOA appears in **bold**. Deletions are shown in ~~strikethrough~~.

1. The Title Page has been updated as follows:

   DAIDS Clinical Representative: **Pablo Belaunzaran Zamudio, MD, DTM&H, MSc**
   ~~Karin L. Klingman, MD~~

2. The Protocol Team Roster has been updated as follows:

   DAIDS Clinical Representatives
   ~~Karin L. Klingman, MD~~
   ~~HIV Research Branch~~
   ~~TRP, DAIDS, NIAID, NIH~~
   ~~5601 Fishers Lane, Rm 9E40A, MSC 9830~~
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3. Section 6.2.3, Post-Entry Evaluations, is being updated as shown below.

   6.2.3 Post-Entry Evaluations

   Post-entry evaluations occur after the study entry visit and vaccination #1 administration at week 0. Study visits are scheduled as indicated in the SOE.

   The visit window for the post-entry evaluations is ±14 days.

   Due to the feasibility challenges posed by the COVID-19 situation, starting 03/16/20, the visit window is broadened from ±14 days to -14 days to +60 days. The broadened visit window is applicable to visits scheduled to occur before 04/30/20. This will be reviewed again at a later date to see if the 04/30/20 date should be extended (to include visits occurring after 04/30/20), and/or if the visit windows themselves need to be extended further. **See the update below.**

   Upon further review, the visit window is broadened from ±14 days to -14 days to +180 days for visits that were planned to occur before 07/15/20. While +180 days is allowed, sites are encouraged to schedule the applicable visits within +90 days.

   The week 24 and week 26 visits should remain separate and coordinated to be as close to 2 weeks apart as feasible, but can be up to 60 days apart. Thus, if the week 26 visit has to be delayed, it is better to postpone the week 24 visit until the week 26 visit can occur 2 weeks later, or as close to that interval as possible.

NOTE A: The deferred study vaccinations #2, #3, and #4 should be performed within 14 days from the time of the previously scheduled week 4, week 12, and week 24 visits, respectively (see section 6.3.10).

NOTE B: After study entry, administration of non-HIV vaccines must occur more than 2 weeks prior to the scheduled study vaccination #2 (week 4), #3 (week 12), and #4 (week 24) injections.

Study Completion Evaluations
The week 48 evaluations will be completed as the participant's final on study visit.

For week 48 visits after 03/16/20, the visit can be a "hybrid" visit, with safety data (AEs) and clinical assessment data per section 6.3.4 (Clinical Assessments, Concomitant Medications/ARV Medications) collected remotely, and the actual clinic visit being dedicated to the lab draw.

4. Protocol Signature Page

   Per a regulatory requirement by the DAIDS, a Protocol Signature Page (PSP) is appended for submission to the DAIDS Protocol Registration System (DPRS) as part of the LOA registration packet.

HIV-1-Gag Conserved-Element DNA Vaccine (p24CE) as Therapeutic Vaccination in HIV-Infected Persons with Viral Suppression on Antiretroviral Therapy

SIGNATURE PAGE

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 (e.g., US National Institutes of Health, Division of AIDS) and institutional policies.

Principal Investigator: _____
Print/Type

Signed: _____Date: _____
Name/Title