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LETTER OF AMENDMENT

DATE: 12 July 2021

TO: ACTG CTU Principal Investigators, CRS Leaders, and CTU/CRS Coordinators

FROM: A5404 Protocol Team

SUBJECT: Letter of Amendment #1 for Protocol A5404

The following information affects the A5404 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 also affects 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. Sites are still required to submit an LOA registration packet to the DAIDS Protocol Registration Office (PRO) at the Regulatory Support Center along with a Protocol Signature Page, which has been appended to this document. 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 reasons for all of the changes in this LOA are shown in the bulleted list below. Descriptions of the changes themselves begin on page 4 of this document.

- The team revised language requiring participants of ACTIV-2/A5401 to be "at selected sites" to ensure participating A5404 sites can enroll ACTIV-2/A5401 participants from any ACTIV-2/A5401 site.
- The team revised the window for receipt of the mRNA-based COVID-19 vaccine for ACTIV-2/A5401 from 60-240 days to 30-240 days after the last dose of a select ACTIV-2/A5401 investigational therapy.
- The team added the option for participants to enroll after receipt of the first and second doses of community-provided mRNA COVID-19 vaccine.
- The team changed the outcome measures to reflect the time points that will be available for participants who enroll after the second dose of vaccine.
- The team revised the inclusion criterion for participants who received camostat or the active comparator/placebo for camostat in ACTIV-2/A5401 to allow enrollment if at least 50% of the doses were received.

- The team decided to update Study Product Formulation and Preparation in line with the information available in the most recent package insert for the Moderna mRNA-1273 vaccine.
- The team revised the screening window to 28 days before study entry to allow sites more time to schedule multiple participants to receive study-provided vaccine on a single day.
- The team made a minor revision to Section 6.1 Schedule of Evaluations (Table 6.1-2).
- The team updated the Protocol Team Roster.
- The team made modifications to the SIC based on the aforementioned protocol modifications and as requested by the Advarra IRB. The changes described below have been made and a revised SIC is provided as an attachment.

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The following are changes (noted in bold or strikethrough) to A5404, Version 2.0, 07May2021, titled "SARS-CoV-2 Immune Responses after COVID-19 Therapy and Subsequent Vaccine." These changes will be included in the next version of the A5404 protocol if it is amended at a future date.

1. "At selected sites" was removed from the following sections:

    a. Schema
        I. Design section: "Participants of ACTIV-2/A5401 ~~at selected sites~~ who received an investigational therapy or its comparator (placebo or active comparator)."
        II. Final paragraph of the Sample Size section: "If up to 70 Phase II participants in the A5401/ACTIV-2 trial from each therapy group ~~at selected sites~~ are not able to be enrolled, then Phase III participants in the A5401/ACTIV-2 trial from that select therapy group ~~at selected sites~~ can be enrolled until full enrollment is achieved. However, Phase II participants are preferred."
        III. Population section: "ACTIV-2/A5401 trial participants ~~at selected sites~~ who received an investigational therapy or its active comparator/placebo."

    b. Study Design
        I. First bullet of first paragraph: "Participants of ACTIV-2/A5401 who received selected investigational therapy or its comparator (active or placebo) ~~at select sites~~."
        II. Fourth paragraph: "If sufficient Phase II participants in the A5401/ACTIV-2 trial from a select therapy group ~~at selected sites~~ are not able to be enrolled, then Phase III participants in the A5401/ACTIV-2 trial from that select therapy group ~~at selected sites~~ can be enrolled until full enrollment is achieved. However, Phase II participants are preferred."

    c. Section 4.1.3: "For participants who are in, or who have completed, the ACTIV-2/A5401 trial: Receipt of all selected investigational therapy or active comparator/placebo for that therapy ~~at selected sites~~."

2. Window for receipt of mRNA-based COVID-19 vaccine for ACTIV-2/A5401 participants

    The window for receipt of the mRNA-based COVID-19 vaccine for ACTIV-2/A5401 participants was changed from 60-240 days to **30**-240 days after their last dose of a select ACTIV-2/A5401 investigational therapy. This change is reflected in the following sections:

    a. Schema, Design Section
    The second sentence of the third paragraph: "Participants in ACTIV-2/A5401 will receive their mRNA-based COVID-19 vaccine ~~60~~**30**-240 days after receiving their last dose of a select ACTIV-2/A5401 investigational therapy, or its comparator."

    b. Section 2.2 Rationale, sub-section Reinfection
    The third sentence of the second paragraph: "The optimal timing of a vaccination to boost such waning immunity is unknown and is the rationale for the ~~60~~**30**-240-day window after receiving their last dose of ACTIV-2/A5401 select therapy (i.e., post-infection) for vaccination in the proposed study."

c. Section 3.0 Study Design

I. The second sentence of the second paragraph, "ACTIV-2/A5401 participants will be offered the Moderna mRNA-1273 COVID-19 vaccine or receive an mRNA-based COVID-19 vaccine in the community ~~60~~**30**-240 days after receiving their last dose of ACTIV-2/A5401 select therapy (investigational agent or active comparator or placebo)."

II. Figure 3.0-1 was replaced with the figure below:

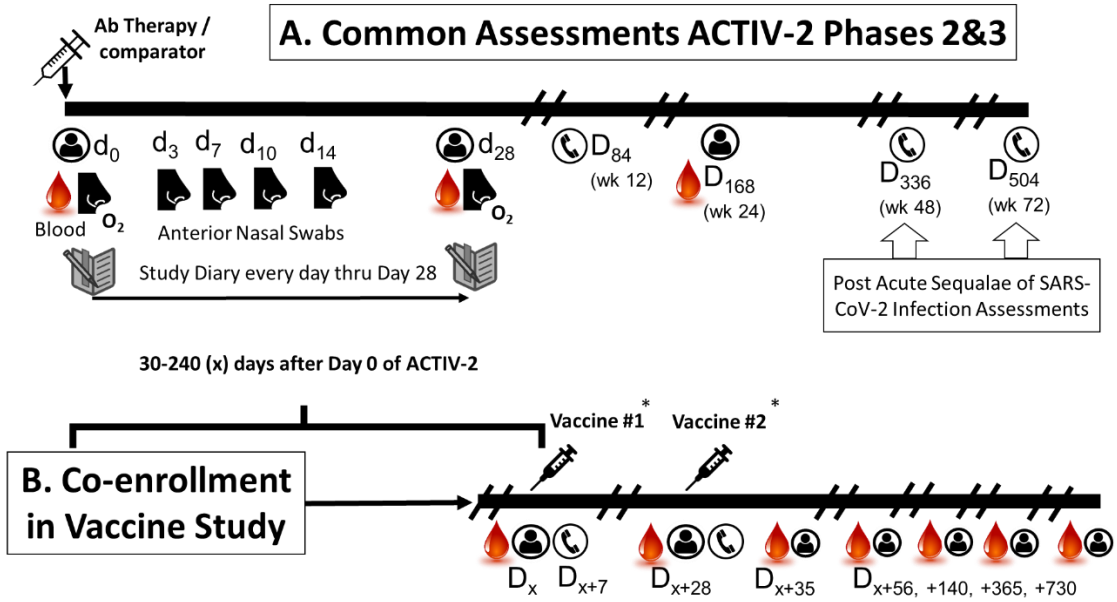

Figure 3.0-1: This schema includes common assessments for ACTIV-2/A5401 participants in both phases 2 and 3 (panel A). If possible, blood will be collected before each vaccine dose is administered and 56, 140, 365, and 730 days after **their first vaccine dose** (panel B). If possible, participants will be contacted 7 days after each vaccine dose to grade vaccine-associated symptoms.

d. Section 4.1 Inclusion Criteria

I. Section 4.1.4: "For participants who are in, or who have completed, the ACTIV-2/A5401 trial and will be receiving study-provided Moderna mRNA-1273 COVID-19 vaccine: Receipt of the last dose of investigational therapy or active comparator/placebo for that therapy ≥**30** ~~60~~ days and ≤240 days prior to study entry."

II. Section 4.1.5 (with an additional revision to clarify that this applies to participants who have already received one or both vaccine doses): "For participants who are in, or who have completed, the ACTIV-2/A5401 trial and **have received or** will be receiving community-provided mRNA-based COVID-19 vaccine: Receipt of the last dose of investigational therapy or active comparator/placebo for that therapy ≥**30** and ≤240 days prior to **receipt or** planned receipt of the first dose of community-provided vaccine."

e. Section 6.2.2 Entry Evaluations

The fourth paragraph of this section was revised to, "ACTIV-2/A5401 participants are expected to receive the first dose of study vaccine **30**~~60~~-240 days after receiving the last dose of an investigational therapy or corresponding active comparator/placebo in ACTIV-2/A5401."

3. Participants will be able to enroll after receiving both doses of their mRNA-based COVID-19 vaccine in the community. The following sections have been revised accordingly:

a. Schema, Design Section

The fourth paragraph of this section was revised as follows: "All participants will have blood collected and immune responses measured before first vaccine dose (if feasible), at second dose of vaccine (e.g., 28 days later**; if feasible**), and at 56 **(if feasible)**, 140, 365, and 730 days after **their first vaccine dose**."

b. Schema, Regimen

ACTIV-2/A5401 participants
Participants will receive the following study-provided regimen: Moderna mRNA-1273 COVID-19 vaccine, 100 µg **(0.5 mL) to be administered** intramuscularly **(IM) at Entry and Day 28**.
Or
Participants will receive a two-dose series of a community-provided mRNA-based COVID-19 vaccine that has received FDA EUA or FDA approval (e.g., Moderna or Pfizer). **Vaccine will not be provided by the study.**
NOTE: These participants may enter the study before their first vaccine dose, after their first vaccine dose, or after their second vaccine dose.
Or
Participants will receive their first Moderna mRNA-1273 COVID-19 vaccine dose in the community. Their second Moderna mRNA-1273 dose will be provided by the study (100 µg **[0.5 mL] to be administered IM 28 days after their first dose).**
NOTE: These participants may enter the study before or after their first vaccine dose.

Participants without prior history of SARS-CoV-2 infection
Participants will receive the following study-provided regimen: Moderna mRNA-1273 COVID-19 vaccine, 100 µg (0.5 mL) to be administered IM at Entry and Day 28.

c. Section 3.0 Study Design

The last sentence of the second paragraph: "Participants will have blood collected and immune responses measured before the first vaccine dose (if feasible), and before the second dose of vaccine (e.g., 28 days later for Moderna vaccine and 21 days later for Pfizer vaccine if given in the community) **(if feasible)**, and 56 **(if feasible)**, 140, 365, and 730 days after **their first vaccine dose** (Figure 3.0-1)."

d. Section 4.2 Exclusion Criterion 4.2.2

This criterion was revised as follows: “For participants who are in, or who have completed, the ACTIV-2/A5401 trial: Self-report of receipt of the ~~second~~ **first** dose of an mRNA-based COVID-19 vaccine **140 days or more before A5404 enrollment**.”

e. Section 5.1.1 Regimen and Duration

Participants will receive the following study-provided regimen: Moderna mRNA-1273 COVID-19 vaccine, 100 µg (0.5 mL) to be administered intramuscularly (IM) at **Entry** and Day 28.
Or
Participants will receive a two-dose series of a community-provided mRNA-based COVID-19 vaccine that has received FDA EUA or FDA approval.
NOTE: Participants who receive a community-provided mRNA-based COVID-19 vaccine may receive their first **and second** COVID-19 vaccine dose**(s)** before study entry.
Or
Participants will receive (or have recently received) a community-provided Moderna mRNA-1273 COVID-19 vaccine at (or before) **Entry** and study-provided Moderna mRNA-1273 COVID-19 vaccine, 100 µg (0.5 mL) to be administered intramuscularly (IM) at ~~at~~ least 28 days apart.

f. Section 6.1, Table 6.1-3

The title of this section was changed to, “~~Community-Provided mRNA-based COVID-19 Vaccine~~ Schedule of Evaluations for ACTIV-2/A5401 Participants **who Received First Dose of a Community-Provided mRNA-based COVID-19 Vaccine Before Entry or Will Receive First Dose After Entry”**

g. Section 6.1, Table 6.1-4 was added:

Table 6.1-4. Schedule of Evaluations for ACTIV-2/A5401 Participants Who Received First and Second Doses of a Community-Provided mRNA-based COVID-19 Vaccine before Entry

Evaluation	Screening See section 6.2.1	Study Entry See section 6.2.2	56 Days Post-Vaccination #1 See section 6.2.3	140 Days Post-Vaccination #1 See section 6.2.3	365 Days (1 Year) Post-Vaccination #1	730 Days (2 Years) Post-Vaccination #1	Premature Study D/C	Event-Driven Evaluation: SARS-CoV-2 Infection
Visit Window (days)	-28		+7	±7	±28			+14
Visit Type (P: In Person, R: Remote)	R/P	P	P	P	P	P	P	P
Documentation of ACTIV-2/A5401 participation and receipt of investigational therapy or active comparator/placebo for investigational therapy	X							
Medical/Medication History	X	X						
Clinical Assessments	X	X	X	X	X	X	X	X
Pregnancy Testing		X	If pregnancy suspected				X	X
Documentation of Community-Provided COVID-19 Vaccination (see section 6.3.7)		X						
Vaccine Symptom Screen (see section 6.3.8)		X						
Stored Plasma		X	X	X	X	X	X	X
Stored Serum		X	X	X	X	X	X	X
Stored PBMCs		X	X	X	X	X	X	X
Stored PAXgene RNA Tube		X						
Documentation of New Active SARS-CoV-2 Infection by Antigen or Nucleic Acid Test								X
Nasopharyngeal (NP) Swab Collection (See section 6.3.11)								X
ACTIV-2/A5401 Investigational Therapy or Active Comparator/Placebo Questionnaire		X						

h. Section 6.2.1 Screening Evaluations

I. The second paragraph has been revised to, "If the participant is receiving community-provided mRNA COVID-19 vaccine**,** ~~then screening evaluations must occur prior to the participant receiving their second dose of vaccine; however,~~ it is preferred for these participants to have their screening evaluations before their first **or their second** vaccine dose, if feasible."

i. Section 6.2.2 Entry Evaluations

I. The header for the last paragraph was revised to, "Entry Evaluations for **ACTIV-2/A5401** Participants **who Received First Dose of a Community-Provided mRNA-based COVID-19 Vaccine Before Entry or Will Receive First Dose After Entry**"

j. Section 6.2.3 Post-Entry Evaluations

I. The header, Community-Provided Vaccine: Day of Second Dose of Vaccine sub-section was revised to include the following as the first paragraph: "**This visit will only be performed if the participant enters the study before their second vaccine dose."**

II. The following sub-section was added after the Community-Provided Vaccine: Day of Second Dose of Vaccine sub-section.

56 and 140 Days Post-Vaccination #1 for ACTIV-2/A5401 Participants Who Received First and Second Doses of a Community-Provided mRNA-based COVID-19 Vaccine before Entry

- **56 days post-vaccination #1 timepoint:**
  - **This visit will not be conducted if the participant enrolls more than 56 days after their first vaccine dose.**
  - **This visit may be combined with the Entry visit if the participant enrolls between 56 and 63 days after their first mRNA COVID-19 vaccine dose. Evaluations indicated at both timepoints will be conducted only once.**
- **140 days post-vaccination #1 timepoint: This visit may be combined with the Entry visit if the participant enrolls between 133 and 147 days after their first mRNA COVID-19 vaccine dose. Evaluations indicated at both timepoints will be conducted only once.**

k. Section 6.3.7 Vaccine Administration
The first sub-section title was changed to, "**Documentation of** Community-Provided COVID-19 Vaccination"

l. Section 6.3.8 Vaccine Symptom Screen
The first sentence has been revised to, "For participants who receive community-provided mRNA-based COVID-19 vaccine: If the participant enrolls >14 days after the first **or second** dose of their vaccine, then a Vaccine Symptom Screen is not collected **for the doses provided prior to enrollment**."

4. Section 4.1, Inclusion Criterion 4.1.3:

The following note was added.

NOTE**S**:

- Selected investigational therapies will be posted on the A5404 PSWP.
- **For participants who received camostat or the active comparator/placebo for camostat: Receipt of ≥50% of the doses indicated in ACTIV-2/A5401.**

5. Section 5.2, Study Product Formulation and Preparation

   a. In section 5.2.1 Formulation and Storage, the following modifications have been made:

      The Moderna mRNA-1273 COVID-19 vaccine is supplied as a frozen suspension, stored between ~~-25~~ **-50**° to -15°C, in multi-dose vials, and does not contain a preservative. ~~Store in the original carton to p~~ **Protect** from light. Do not store on dry ice or below ~~-40~~ **-50**°C. The Moderna mRNA-1273 COVID-19 vaccine is white to off-white suspension. It may contain white or translucent product-related particulates.

      The Moderna mRNA-1273 COVID-19 vaccine must be thawed prior to administration. After thawing, a maximum of 10-11 doses (0.5 mL each) can be withdrawn from each vial, dependent on the syringes and needles used. Vials can be stored refrigerated between 2° to 8°C for up to 30 days prior to first use. Do not refreeze once thawed. Unpunctured vials may be stored between 8° to 25°C for up to ~~12~~ **24** hours. Do not refreeze. After the first dose has been withdrawn, the vial should be held between 2° to 25°C and discarded after ~~6~~ **12** hours. Do not refreeze.

   b. In section 5.2.2 Preparation, the following modifications have been made:

      1. Remove one vial of the Moderna mRNA-1273 COVID-19 vaccine from the freezer and thaw either in the refrigerator or at room temperature. If thawed in the refrigerator, the vial must be kept between 2°C and 8°C for two hours and 30 minutes. If thawed at room temperature, the vial must be kept between 15°C and 25°C for one hour. Once thawed, the vial may be kept between 8°C and 25 °C for up to ~~12~~ **24** hours. Do NOT refreeze.
      2. With the vial upright, gently swirl the vaccine. Do NOT shake. Do NOT dilute the vaccine.
      3. Examine the vaccine. It should be white to off-white in color and may contain white or translucent product-related particulates. Do not use if liquid contains other particulate matter or is discolored.
      4. Withdraw 0.5 mL of vaccine into an appropriately sized syringe. When the stopper of the vial is punctured to start preparation, record this as the vaccine preparation time. Assign a ~~6~~ **12** hour beyond use date and time from the preparation time.

      The prepared vaccine should be administered immediately. If immediate administration is not possible, the **prepared** vaccine may be stored **refrigerated at** ~~between~~ 2°C **to 8°C or left at ambient room temperature at 15°C to** ~~and~~ 25°C for up to ~~6~~ **12** hours. **Keep out of direct sunlight.**

6. Section 6.1 Schedule of Evaluations:

   The windows for screening for the following groups have been changed to 28 days before study entry. Day 0 has been removed from the Study Entry header for clarity and

consistency. Tables 6.1-1, 6.1-2, and 6.1-3 have been revised accordingly. Additionally, Table 6.1-2 was updated to indicate that stored PBMCs for 35 total SARS-CoV-2-naïve participants are to be collected at the Event-Driven Evaluation: SARS-CoV-2 Infection visit. The changes are shown below.

Table 6.1-1. Study-Provided Moderna COVID-19 Vaccine Schedule of Evaluations for ACTIV-2/A5401 Participants

Evaluation	Screening	Study Entry/~~Day 0~~ See section 6.2.2	Post-Vaccination #1 Follow-up/Day 7	Day 28	Post-Vaccination #2 Follow-up/Day 35	Day 56	Day 140	Day 365 (1 Year)	Day 730 (2 Years)	Premature Study D/C	Event-Driven Evaluation: SARS-CoV-2 Infection
Visit Window (days)	**-28**		7-14 days post-vaccine	+7	7-14 days post-vaccine	+7	±7	±28			+14

Table 6.1-2. Study-Provided Moderna COVID-19 Vaccine Schedule of Evaluations for Participants without Prior History of SARS-CoV-2 Infection

Evaluation	Screening	Study Entry/~~Day 0~~ See section 6.2.2	Post-Vaccination #1 Follow-up/Day 7	Day 28	Post-Vaccination #2 Follow-up/Day 35	Day 56	Day 140	Day 365 (1 Year)	Day 730 (2 Years)	Premature Study D/C	Event-Driven Evaluation: SARS-CoV-2 Infection
Visit Window (days)	**-28**		7-14 days post-vaccine	+7	7-14 days post-vaccine	+7	±7	±28			+14
Visit Type (P: In Person, R: Remote)	R/P	P	R	P	R	P	P	P	P	P	P
Stored PBMCs for 35 total SARS-CoV-2-naïve participants (See section 6.3.9)		X				X		X	X		**X**

Table 6.1-3. ~~Community-Provided mRNA-based COVID-19 Vaccine~~ Schedule of Evaluations for ACTIV-2/A5401 Participants **who Received First Dose of a Community-Provided mRNA-based COVID-19 Vaccine Before Entry or Will Receive First Dose After Entry**

Evaluation	Screening See section 6.2.1	Study Entry/~~Day 0~~ See section 6.2.2	Post-Vaccination #1 Follow-up See section 6.2.3	Day of 2nd dose of ~~vaccine~~	Post-Vaccination #2 Follow-up	56 Days Post-Vaccination #1	140 Days Post-Vaccination #1	365 Days (1 Year) Post-Vaccination #1	730 Days (2 Years) Post-Vaccination #1	Premature Study D/C	Event-Driven Evaluation: SARS-CoV-2 Infection
Visit Window (days)	**-28**		7-14 days post-1st dose of vaccine	-3	7-14 days post-2nd dose of vaccine	+7	±7	±28			+14

7. Section 6.2 Timing of Evaluations, has been revised to reflect that the windows for screening for all groups has been changed to 28 days before study entry.

   a. The third and fourth paragraphs of section 6.2.1, Screening Evaluations have been changed as follows.

      For **all** participants ~~receiving study-provided vaccine~~, screening evaluations to determine eligibility must be completed within **28** days prior to study entry unless otherwise specified.

      ~~For participants receiving community-provided vaccine, screening evaluations to determine eligibility must be completed within 14 days prior to study entry unless otherwise specified.~~

   b. The first and second paragraphs of section 6.2.2, Entry Evaluations have been changed as follows.

      For **all** participants ~~receiving study-provided vaccine~~, entry evaluations must occur ≤**28** days after screening evaluations unless otherwise specified.

      ~~For participants receiving community-provided vaccine, entry evaluations must occur ≤14 days after screening evaluations unless otherwise specified.~~

8. Section 7.4 Study Monitoring. The second sentence of the third paragraph was revised as follows.

   The first interim review will occur when 10 participants have enrolled to one select therapy group**, received their first dose of vaccine after study entry,** and their data through study Day 7 (7 days after the first vaccine dose) are available, or 3 months after the first

participant enrolls, whichever occurs first.

9. Section 10.0 Statistical Considerations was revised as follows.

   a. Section 10.2.1.1 (Primary Outcome Measure)
   "Neutralizing antibody (NAb) level at least **140** days after the first dose of the study- or community-provided vaccine."

   b. Section 10.2.2.2 (Secondary Outcome Measure)
   "New Grade 3 or higher AE, or SAE, or AE leading to change or discontinuation in vaccine receipt from first dose of the mRNA-based COVID-19 vaccine and through **140** days after the first dose of vaccine."

   c. Section 10.2.2.6 (Secondary Outcome Measure)
   "Flow cytometry of PBMC for markers of exhaustion on B and T cells at study entry/Day 0, 56 **and 140** days after the first vaccine dose."

   d. Section 10.4 Sample Size. The first sentence of the third paragraph was revised.

      For the primary outcome measure of NAb levels ~~56~~ **140** days after the first vaccine dose, we will calculate the ratio of geometric mean responses (GMRs) for participants with prior select investigational therapy exposure versus participants who received placebo.

   e. Section 10.6 Analyses.

      I. The first sentence of the fifth paragraph was revised.

         The primary analysis population will include all participants who received at least one vaccine dose and provided NAb responses at least ~~56~~ **140** days after the first vaccine dose.

      II. The first sentence of the sixth paragraph was revised.

         The analysis population for the secondary outcome measure exploring change in NAb levels from pre- to post-vaccine will include all participants who received at least one vaccine dose and provided NAb responses within 7 days prior to the first dose of the vaccine and at least ~~56~~ **140** days after the first vaccine dose.

10. The Protocol Team Roster has been updated as follows.

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NOTE: Changes to the INFORMED CONSENT **FORM** have been made as requested by the Advarra IRB and to reflect that participants will be able to enroll after receiving both doses of their mRNA-based COVID-19 vaccine. Additional modifications add missing information or improve the clarity.

11. SAMPLE INFORMED CONSENT FORM title

    As requested by Advarra, the section title has been changed to, ~~APPENDIX I: ACTG SAMPLE~~ INFORMED CONSENT **FORM**.

    a. This change is also reflected in the first sentence of section 13.1: "This protocol and the informed consent document (~~APPENDIX I: ACTG SAMPLE~~ INFORMED CONSENT **FORM**) and any subsequent modifications will be reviewed and approved by the IRB or EC responsible for oversight of the study."

12. The Summary, Required Activities section has been revised:
    a. As requested by Advarra, "vaccination" has replaced "vaccine" in the first paragraph.
    b. Changes were made to reflect that participants will be able to enroll after receiving both doses of their mRNA-based COVID-19 vaccine.

       If you enter the study before you have the first **vaccination**, you will have blood drawn from a vein in your arm before your first **and second** mRNA COVID-19 **vaccination**. **If you enter the study before you have the second vaccination, you** will have blood drawn again before your second mRNA COVID-19 **vaccination**. **If you enter the study after you have two doses of vaccine, you will have blood drawn on the day you enroll in the study.** This blood will be used to measure immune and genetic (determined by inherited factors) responses to your initial SARS-CoV-2 (the virus that causes COVID-19) infection and to the mRNA COVID-19 vaccine.

    If you are receiving study-provided Moderna mRNA-1273 COVID-19 vaccine, the study vaccine will be given by needle into the muscle of your arm on study days 0 and 28.

    Phone Visits 7 to 14 Days after Vaccinations
    If you enter the study before your first or second mRNA COVID-19 vaccination, between 7 and 14 days after **the** vaccine**(s)**, you will be contacted by phone by the study

team to see whether or not you have had any new symptoms or medical events. If you **enter the study** more than 14 days after your first **vaccination**, then you will only be contacted after the second vaccine. **If you enter the study more than 14 days after your second vaccination, then you will not be contacted.**

Study Visits 2 Months, 5 Months, 1 Year, and 2 Years After Your First mRNA COVID-19 Vaccine
You will have blood drawn. This blood will be used to measure immune responses to your study-provided or community-provided mRNA COVID-19 vaccine.

13. "Summary," "Risks"

    As requested by Advarra, the "Summary," "Risks," first subsection title has been revised to:

    If You Are Receiving **the** Study-Provided Moderna mRNA-1273 COVID-19 Vaccine.

14. "WHAT DO I HAVE TO DO IF I AM IN THIS STUDY?," "Location of Study Visits"

    As requested by Advarra, section, "WHAT DO I HAVE TO DO IF I AM IN THIS STUDY?," "Location of Study Visits" has been revised to:

    Your study visits will take place in person or remotely. You and the study staff at your study site will discuss the location for each visit.
    - In-person visits will take place at the clinic, at your home, or at another non-clinic location.
    - Remote visits will take place over the phone or via telemedicine systems approved for use at your **study** site.

15. "WHAT DO I HAVE TO DO IF I AM IN THIS STUDY?," "Screening Visit," "At this visit"

    As requested by Advarra and to reflect that participants will be able to enroll after receiving both doses of their mRNA-based COVID-19 vaccine, the second and third bullets of Section, "WHAT DO I HAVE TO DO IF I AM IN THIS STUDY?," "Screening Visit," "At this visit" have been revised to:

    - If you will receive **the** study-provided Moderna mRNA-1273 COVID-19 vaccine, then study staff will tell you about that **study** vaccine.
    - If you are receiving **a** community-provided mRNA COVID-19 vaccine, then study staff will ask you which vaccine (for example, Pfizer or Moderna) you are getting and when you received or are scheduled to receive your first **and (if applicable) second** vaccine dose.

16. "WHAT DO I HAVE TO DO IF I AM IN THIS STUDY?," "Entry Visit"

    As requested by Advarra and to reflect that participants will be able to enroll after receiving both doses of their mRNA-based COVID-19 vaccine, the seventh and eighth bullets of Section, "WHAT DO I HAVE TO DO IF I AM IN THIS STUDY?," "Entry Visit," has been revised to:

    - If you are receiving **the** study-provided Moderna mRNA-1273 COVID-19 vaccine, you

will receive the first dose of the vaccine. You will be asked to remain at the clinic for approximately 30 minutes for monitoring after you receive the Moderna mRNA-1273 COVID-19 vaccine.
- If you are receiving community-provided mRNA-based COVID-19 vaccine, you can receive your first **and second** dose**s** before the study Entry Visit.

17. "WHAT DO I HAVE TO DO IF I AM IN THIS STUDY?," "Phone Visits 7 to 14 Days after Vaccinations"

To reflect that participants will be able to enroll after receiving both doses of their mRNA-based COVID-19 vaccine, the first sentence of Section, "WHAT DO I HAVE TO DO IF I AM IN THIS STUDY?," "Phone Visits 7 to 14 Days after Vaccinations" has been revised to:

"**If you enroll into the study before a vaccination, then** you will be contacted by phone by the study team between 7 and 14 days after each mRNA COVID-19 vaccine dose to assess whether you have had any new symptoms or clinical events since your last visit."

18. "WHAT DO I HAVE TO DO IF I AM IN THIS STUDY?," "Study Visit on Day of 2nd Dose of Vaccine"

As requested by Advarra and to reflect that participants will be able to enroll after receiving both doses of their mRNA-based COVID-19 vaccine, section, "WHAT DO I HAVE TO DO IF I AM IN THIS STUDY?," "Study Visit on Day of 2nd Dose of Vaccine" has been revised to:

- If you are receiving **the** study-provided Moderna mRNA-1273 COVID-19 vaccine, you will return to the clinic at least 28 days (about 4 weeks, or 1 month) after your first vaccine dose to receive your second dose. You will be asked to remain at the clinic for approximately 30 minutes for monitoring after you receive the vaccine. If you do not receive the second dose of the vaccine at this time (and you still want to receive it), you may still get the second dose through the study up to 140 days after your first vaccine dose. You will still be contacted by phone 7 to 14 days after you receive the vaccine.
- If you are receiving **the** community-provided mRNA COVID-19 vaccine **and enter the study before receiving your second dose:**
  - You will return to the clinic within 3 days before you receive your second mRNA COVID-19 vaccine dose. If you received the Moderna mRNA-1273 COVID-19 vaccine, this will be about 28 days after your first dose. If you received the Pfizer-BioNTech mRNA COVID-19 vaccine, this will be about 21 days after your first dose. You will be asked to bring your vaccine card to this visit.
  - If you received the Moderna mRNA-1273 COVID-19 vaccine for your first dose, you may be able to get the second dose of the Moderna mRNA-1273 COVID-19 vaccine through the study, if you want to.
- If you do not receive your 2nd dose of **the** vaccine, you may still remain on the study and have the remaining study visits performed.
- **If you enter the study after receiving both doses of mRNA COVID-19 vaccine in the community, then you will not have this visit.**

19. "WHAT DO I HAVE TO DO IF I AM IN THIS STUDY?," "Study Visit 8 Weeks (56 days, or about 2 months) after Your First mRNA COVID-19 Vaccine Dose"

As requested by Advarra, the last sentence of section, "WHAT DO I HAVE TO DO IF I AM

IN THIS STUDY?," "Study Visit 8 Weeks (56 days, or about 2 months) after Your First mRNA COVID-19 Vaccine Dose" has been revised. The sentences below have been added at the end of the paragraph:

If you are receiving **the** community-provided mRNA COVID-19 vaccine, you will be asked to bring your vaccine card to this visit. **If you enroll more than 56 days after your first mRNA COVID-19 vaccine dose, you will not have this visit. If you enroll between 56 and 63 days after your first mRNA COVID-19 vaccine dose, then this study visit may be combined with your entry visit.**

20. "WHAT DO I HAVE TO DO IF I AM IN THIS STUDY?," "Study Visit 20 Weeks (140 days, or about 5 months) after Your First mRNA COVID-19 Vaccine Dose"

    To reflect that participants will be able to enroll after receiving both doses of their mRNA-based COVID-19 vaccine, the sentence below has been added to the end of the section.

    If you enroll between 133 and 147 days after your first mRNA COVID-19 vaccine dose, then this study visit may be combined with your entry visit.

21. "WHAT DO I HAVE TO DO IF I AM IN THIS STUDY?," "Additional Study Visit," "At this visit"

    As requested by Advarra, the third bullet of Section, "WHAT DO I HAVE TO DO IF I AM IN THIS STUDY?," "Additional Study Visit," "At this visit" has been revised to:

    - If you are found to have an active SARS-CoV-2 infection, you may have nasopharyngeal swabs (**for example** ~~i.e.~~, deep nasal swabs) collected by a study staff person as early as possible within 14 days after your symptoms begin. Your current medications will also be reviewed.

22. "CAN I CHOOSE THE TYPES OF RESEARCH THAT MY SAMPLES AND INFORMATION ARE USED FOR?"

    As requested by Advarra, the fourth paragraph of Section, "CAN I CHOOSE THE TYPES OF RESEARCH THAT MY SAMPLES AND INFORMATION ARE USED FOR?" has been revised to:

    Please refer to ~~Attachment A~~ **the separate consent at the end of this document** to consent for use of your samples in other studies.

23. "WHY WOULD THE DOCTOR TAKE ME OFF THIS STUDY EARLY?":

    As requested by Advarra, the second and third paragraphs of Section, "WHY WOULD THE DOCTOR TAKE ME OFF THIS STUDY EARLY?" have been revised to:

    If you received **the** study- or community-provided Moderna mRNA-1273 COVID-19 vaccine for your first dose:
    You may still be able to get the second dose of the Moderna mRNA-1273 COVID-19 vaccine through the study (up to 140 days after your first dose) at the premature study discontinuation visit if you are taken off of the study early.

If you are receiving **the** study-provided Moderna mRNA-1273 COVID-19 vaccine, the study doctor may need to take you off the Moderna mRNA-1273 COVID-19 vaccine without your permission if:

24. "WHAT ARE THE RISKS OF THE STUDY?"

    As requested by Advarra, "WHAT ARE THE RISKS OF THE STUDY?" has been revised as follows.

    a. The third paragraph has been revised to:

       Since we do not fully understand the Moderna mRNA-1273 COVID-19 vaccine's effectiveness in participants who have previously had COVID-19, it is recommended that you continue to take general precautions (**for example** ~~e.g.~~, physical distancing, wearing a mask) to reduce the risk of infection.

    b. The following subsection title has been revised.

       Risks of **the** Study-provided Moderna mRNA-1273 COVID-19 Vaccine

25. "ARE THERE RISKS RELATED TO PREGNANCY AND BREASTFEEDING?"

    As requested by Advarra, "ARE THERE RISKS RELATED TO PREGNANCY AND BREASTFEEDING?" has been revised.

    a. The third paragraph of the "Pregnancy" subsection has been revised to:

       If you have completed the study or choose to discontinue from the study before the end of the pregnancy, then ~~site~~ **study** staff will request permission to contact you regarding pregnancy outcomes at the end of pregnancy.

    b. The following subsection title has been revised:

       If you are receiving **the** study-provided Moderna mRNA-1273 COVID-19 vaccine:

    c. The "Breastfeeding" subsection has been revised to:

       If you are receiving **the** study-provided Moderna mRNA-1273 COVID-19 vaccine: It is not known if the Moderna mRNA-1273 COVID-19 vaccine is safe to use in people who are breastfeeding; however, you are eligible to receive this vaccine if you are breastfeeding.

26. "WHAT ABOUT CONFIDENTIALITY"

    As requested by Advarra, the "WHAT ABOUT CONFIDENTIALITY" section has been revised.

    a. The first paragraph has been revised to:

We will do everything we can to protect your privacy. In addition to the efforts of the study staff to help keep your personal information private, we have gotten a Certificate of Confidentiality from the US Federal Government. This certificate means that researchers cannot be forced to tell people who are not connected with this study, such as the court system, about your participation. Also, any publication of this study will not use your name or identify you personally. **Having a Certificate of Confidentiality does not prevent you from releasing information about yourself and your participation in the study. Even with the Certificate of Confidentiality, if the study staff learns of possible child abuse and/or neglect or a risk of harm to yourself or others, we will be required to tell the proper authorities.**

b. The following paragraph has been inserted after the second paragraph in the section:

All information collected about you as part of the study will be sent securely to the ACTG statistical and data management center in the United States for combining with information from other study participants and statistical analysis of study results. Your name and other personal identifiers will not be sent. Your research site is responsible for sending your information in accordance with the laws, regulations, and policies of your country and research site.

27. "WILL I RECEIVE ANY PAYMENT"

As requested by Advarra, the following language was removed from the section, "WILL I RECEIVE ANY PAYMENT":

For sites in the US
~~«Compensation»~~
You will be paid up to a total of $xx.xx if you complete this study. You will be paid for the visits you complete according to the following schedule:

- $xx.xx for Visits xxx.
- $xx.xx for Visits xxx.
- $xx.xx for Visits xxx.

If you do not complete the study, for any reason, you will be paid for each study visit you do complete.

You will be paid _____ *["following each completed visit," "monthly," "quarterly," "at the end of your participation in the research study," "following each completed visit or at the end of your participation in the research study, whichever you prefer"]*.

If you have any questions regarding your compensation for participation, please contact the study staff.

[OR]

You will not receive any monetary compensation for your participation in this study.
~~*[For sites outside the US: Insert site-specific information on compensation to study participants.]*~~

28. "WHOM TO CONTACT ABOUT THIS STUDY"

As requested by Advarra, all references to “sites outside the US” were removed from the Section “WHOM TO CONTACT ABOUT THIS STUDY.”

~~*For sites in the US*~~: During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns, or complaints about the study, please contact the study doctor at the telephone number listed on the first page of this consent document.

If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

29. “WHOM TO CONTACT ABOUT THIS STUDY”

As requested by Advarra, in addition to language that was removed, the language below was added to the Section, “WHOM TO CONTACT ABOUT THIS STUDY,” and other revisions were made:

An institutional review board (IRB) is an independent committee established to help protect the rights of research participants.

[Sites: Select the contact information of your IRB below]

If you have any questions about your rights as a research participant, and/or concerns or complaints regarding this research study, contact:

- By mail:
  Study Subject Adviser
  Advarra IRB
  6100 Merriweather Dr., Suite 600
  Columbia, MD 21044
- or call toll free: 877-992-4724
- or by email: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00050357.

[OR]

~~For sites outside the US~~
If you have ~~For~~ any questions about **your rights as a research participant, and/or concerns or complaints regarding this research study, contact:** this study or a research-related injury, contact:

- **name or title of person on the Institutional Review Board (IRB) or other organization appropriate for the site.**
- ~~name of the investigator or other study staff.~~
- telephone number of above.
- ~~For questions about your rights as a research participant, contact:~~
- ~~name or title of person on the Institutional Review Board (IRB) or other organization appropriate for the site.~~
- ~~telephone number of above.~~

30. INFORMED CONSENT FORM, SIGNATURE PAGE

The INFORMED CONSENT FORM, SIGNATURE PAGE formatting was revised to conform to the CONSENT FOR OPTIONAL USE OF EXTRA SAMPLES IN OTHER STUDIES signature pages.

SIGNATURE PAGE

If you have read this consent form (or had it explained to you), all your questions have been answered, and you agree to take part in this study, please sign your name below and date it.

_____
Printed Name of Participant

_____ _____
Signature of Participant **Date**

_____
Printed Name of Legally Authorized Representative (As Appropriate)

_____ _____
Signature of Legally Authorized Representative **Date**

_____
Printed Name of Study Staff Conducting Consent Discussion

_____ _____
Signature of Study Staff Conducting Consent Discussion **Date**

_____
Printed Name of Witness (As Appropriate)

_____ _____
Signature of Witness **Date**

31. CONSENT FOR USE OF SAMPLES IN OTHER STUDIES

As requested by Advarra, The CONSENT FOR USE OF SAMPLES IN OTHER STUDIES was modified as follows:

CONSENT FOR **OPTIONAL** USE OF **EXTRA** SAMPLES IN OTHER STUDIES

Everything in the main study consent for you signed and dated above still applies to your participation unless otherwise noted below.

When samples are no longer needed for this study, the AIDS CLINICAL TRIALS GROUP (ACTG) may want to use them in other studies and share them with other researchers. These samples are called “extra samples.” The ACTG will only allow your extra samples to be used in other studies if you agree to this. If you have any questions, please ask.

Identifiers will be removed from your samples and from any private information that has been collected about you. This means that no one looking at the labels or at other information will know that the samples or information came from you.

Extra samples are stored in a secure central place called a repository. Your samples will be stored in the ACTG repository located in the United States.

There is no limit on how long your extra samples will be stored. ***[Site: Revise the previous sentence to insert limits if your regulatory authority imposes them.]***

~~*For sites in the US:*~~ When a researcher wants to use your samples and information, their research plan must be approved by the ACTG. Also, the researcher’s **I**nstitutional **R**eview **B**oard (IRB) **or ethics committee (EC) will review their plan.** ***[Site: If review by your institution’s IRB/EC/RE is also required, insert a sentence stating this.]*** IRBs **and ECs** protect the rights and well-being of people in research. If the research plan is approved, the ACTG will send your samples to the researcher’s location. This means that researchers who are not part of the study team may use your samples without asking you again for your consent.

~~*For sites outside the US:* When a researcher wants to use your samples and information, their research plan must be approved by the ACTG. Also, the researcher’s institutional review board (IRB) or ethics committee (EC) will review their plan. *[Site: If review by your institution’s IRB/EC/RE is also required, insert a sentence stating this.]* IRBs/ECs protect the rights and well-being of people in research. If the research plan is approved, the ACTG will send your samples to the researcher’s location. This means that researchers who are not part of the study team may use your samples without asking you again for your consent.~~

You will not be paid for your samples. Also, a researcher may make a new scientific discovery or product based on the use of your samples. If this happens, there is no plan to share any money with you.

Please choose the response that matches what you want by putting your initials in the space provided. Please ask the study staff any questions that you have before you indicate your selection.

Research without Human Genetic Testing

If you agree, your extra samples may be stored (as described above) and used for ACTG-approved research that does not include human genetic testing.

____ (initials) I understand and I agree to this storage and possible use of my samples.

OR

____ (initials) I understand but I do not agree to this storage and possible use of my samples.

SIGNATURE PAGE

If you have read this consent form (or had it explained to you), all your questions have been answered and you agree to take part in this study, please sign your name below and date it.

_____
Printed Name of Participant

_____ _____
Signature of Participant **Date**

_____
Printed Name of Legally Authorized Representative (As Appropriate)

_____ _____
Signature of Legally Authorized Representative **Date**

_____
Printed Name of Study Staff Conducting Consent Discussion

_____ _____
Signature of Study Staff Conducting Consent Discussion **Date**

_____
Printed Name of Witness (As Appropriate)

_____ _____
Signature of Witness **Date**

SARS-CoV-2 Immune Responses after COVID-19 Therapy and Subsequent Vaccine

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