Clarification Memorandum #2 for:

IMPAACT 2008
Phase I/II Multisite, Randomized, Controlled Study of Monoclonal Antibody VRC01 with Combination Antiretroviral Therapy to Promote Clearance of HIV-1-Infected Cells in Infants

Version 2.0, dated 29 May 2017

DAIDS ES # 20735
IND # 133,017 Held By DAIDS

Clarification Memorandum Date: 01 April 2020

Summary of Clarifications

This Clarification Memorandum (CM) is being issued to safeguard the health and well-being of IMPAACT 2008 study participants in the context of circulating severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the associated coronavirus disease (COVID-19) pandemic.

As the study Sponsor, the Division of AIDS (DAIDS) has determined that this CM should be implemented immediately upon issuance. Consistent with United States Food and Drug Administration guidance, institutional review board/ethics committee (IRB/EC) approval of this CM is not required by the Division of AIDS prior to implementation. However, given the context of the COVID-19 pandemic and the importance of the guidance provided in this CM, sites should submit this CM to IRBs/ECs for their information or, if required by the IRBs/ECs, for their review and approval.

The purpose of this CM is to provide operational flexibility for conducting study visits and procedures when needed to ensure ongoing contact with participants and to prioritize the conduct of clinically and scientifically important evaluations when possible.

Implementation of this CM is expected to be time-limited in relation to the COVID-19 pandemic. In consultation with IMPAACT Network leadership and the study Sponsor, the IMPAACT 2008 Protocol Team will determine when, in the future, the guidance provided in this CM is no longer applicable. When such a determination is made, study sites will be formally notified and instructed to inform their IRBs/ECs.

Please file this CM and any applicable IRB/EC correspondence in your essential document files for IMPAACT 2008.

Implementation

This CM provides operational guidance to study sites from the IMPAACT 2008 Protocol Team. The Protocol Team acknowledges that the extent to which site operations may be disrupted by the COVID-19 pandemic may vary across sites and over time. **All sites should follow applicable government, health authority, and institutional policies with respect to conduct of study visits and procedures, with utmost importance placed on the health and well-being of study participants and study staff.** Site investigators should continue to follow current protocol specifications for communication with the Protocol Team and/or Clinical Management Committee and should contact the Clinical Management Committee (impaact.2008cmc@fstrf.org) with any questions or concerns regarding this CM or management of study participants.

Visit Scheduling

- Sites that anticipate operational disruptions or closures in the near future are advised to conduct study visits early in the allowable visit window. Visits conducted prior to opening of the allowable window would also be preferred to completely missing a visit at a later date.
- Sites that are currently experiencing operational disruptions or closures are advised to conduct study visits late in the allowable visit window. Visits conducted after closing of the allowable window would also be preferred to completely missed visits.
- Effective with the issuance of this CM, the allowable window for the Week 24 and Week 36 visits is broadened to ±6 weeks; the allowable visit window for the Week 48 visit is broadened to -6 to +12 weeks.
- In the event that any scheduled visits or procedures are missed, all participants should remain on-study for the full duration of follow-up (i.e., through the Week 48 visit) if possible.

Prioritization of Study Visit Procedures

- Sites with full capacity to conduct study visits in-person at the study clinic should continue to do so in full compliance with the protocol.
- Sites may also conduct study visits — in full or in part — off-site if permitted by applicable government, health authority, and institutional policies. Where this option is permitted, site staff should communicate with participants' caregivers to determine in advance where and when such visits will take place, with adequate protections for safety, privacy, and confidentiality. Off-site visit procedures should be conducted by site staff who are adequately qualified and trained to conduct the procedures, as determined by the site Investigator of Record (IoR), with attention paid to occupational health, biohazard containment, and specimen and data chain of custody. These staff should also be adequately qualified and trained to immediately assess and/or manage any adverse events or social impacts that may occur during the visits. If adverse events requiring further evaluation or management are identified during an off-site visit, staff conducting the visit should arrange for appropriate clinical management, in consultation with the IoR or designee as needed.
- Sites with limited capacity to conduct study visits should prioritize the visits outlined below for participants in <u>both study arms</u>. When applicable, specimen collection should be prioritized per protocol Section 6.17.1.
  - First priority visits:
    - Weeks 2, 6, and 10: These visits include VRC01 administration (for Arm 1 participants) and specimen collection (for all participants). **VRC01 administration must be performed on-site** with personnel and supplies available in case of an immediate hypersensitivity reaction. If these visits cannot be conducted on-site, procedures other than VRC01 administration may be performed off-site if the requirements listed above, particularly the requirements pertaining to specimen collection and transport, can be met. If specimen collection cannot be

performed off-site, other visit procedures (e.g., history taking, cART adherence assessment) may be performed remotely rather than in-person.
    - Week 14: These visits include specimen collection for assessment of primary study outcome measures. These visits may be conducted off-site if the requirements listed above, particularly the requirements pertaining to specimen collection and transport, can be met. If specimen collection cannot be performed off-site, other visit procedures (e.g., history taking, cART adherence assessment) may be performed remotely rather than in-person.
    - Weeks 3, 7, and 11: These visits should be conducted in-person (on-site or off-site) whenever possible. If in-person visits are not possible, reactogenicity assessments and history taking may be performed remotely.
- Second priority visits:
    - +3-Day Contacts after Weeks 2, 6, and 10: Per protocol Section 6.16, these contacts may be conducted remotely.
    - Weeks 24, 36, and 48: These visits involve specimen collection and may be conducted off-site if the requirements listed above can be met. If specimen collection cannot be performed off-site, other visit procedures (e.g., history taking, cART adherence assessment) may be performed remotely rather than in-person.
- Third priority visits:
    - Weeks 16 and 20: These visits are of lowest priority. They involve specimen collection and may be conducted off-site if the requirements listed above can be met. If specimen collection cannot be performed off-site, other visit procedures (e.g., history taking, cART adherence assessment) may be performed remotely rather than in-person.

Study Drug Supply

- No changes in procedures for preparing, dispensing, or administering study product (VRC01) are permitted. These procedures must be performed on-site to ensure adherence to product temperature requirements. In addition, study product must be administered in a clinical setting to ensure appropriate management in the rare event of an acute hypersensitivity reaction.

Documentation

- Site-specific contingency plans, and the implementation thereof, should be documented in essential document files for IMPAACT 2008.
- Documentation should be entered in participant study charts in real-time should any of the following occur:
    - Missed visits
    - Out-of-window visits
    - Off-site visits (document the location of the visit)
    - Incomplete or partial visits (document which procedures were performed and which were not)
    - Remote contacts performed in lieu of in-person visits (document method used to complete the contact and which procedures were performed)
    - Any other participant contacts
- In consultation with the Division of AIDS, the IMPAACT Network is developing comprehensive guidance for documenting and/or reporting protocol deviations that may occur due to limited site capacity to conduct study visits or procedures during the COVID-19 pandemic. Once this Network-level guidance is available, it will be provided in a separate communication to all sites.