CLARIFICATION MEMO #01 TO:

MATRIX-001

A Phase I Randomized, Placebo-Controlled, Double-Blind Study to Assess Safety, Pharmacokinetics, and Modeled Pharmacodynamics of a Vaginal Insert Containing Tenofovir Alafenamide and Elvitegravir

Cooperative Agreement #7200AA22CA00002

IND # 141,295

Version 1.0 / May 4, 2023

Clarification Memo Date: August 22, 2023

Section 1: Summary of Clarifications and Rationale

The procedures clarified in this Clarification Memorandum (CM) have been approved by the MATRIX Prime-Clinical Trials Hub, MATRIX-001 Protocol Co-Chairs, and MATRIX-001 Product Developer (PD)/Sponsor and are to be implemented immediately upon issuance. IRB/IEC approval of this CM is not required by MATRIX prior to implementation; however, investigators may submit the CM to the IRB/IEC overseeing the study at their site for the IRB/IEC's notification. This CM is official MATRIX-001 documentation and is effective immediately. A copy of this CM must be retained in the PD/Sponsor's and in each study site's Essential Documents file for MATRIX-001. No changes in the sample informed consent form or schedule of visits/procedures are included in this CM.

This document clarifies that the US-based clinical research site, Eastern Virginia Medical School (EVMS), may conduct the protocol-specified HIV testing procedures using HIV rapid saliva tests under CLIA certification instead of HIV blood tests. This document also corrects a typo in Section 6.3, clarifies Section 10.7 language regarding unblinding of study participants, and updates the Protocol Team Roster.

Section 2: Implementation

With the exception of updates to the protocol team roster, text to be deleted is noted below with a ~~strikethrough~~, text to be added is in **bold**, and text in ***bold italics*** is not to be added, but to serve as a clarification of the implementation item in question. This information will be included in the protocol the next time the protocol is updated.

---

1. The following clarification applies to Section 7 (Study Procedures) and Appendices I (Schedule of Study Visits and Evaluations), II (Algorithm for HIV Testing – Screening/Enrolling/Follow-up) and IV (Sample Informed Consent Form [Screening, Enrollment, Long-Term Storage and Future Testing):

   The US-based clinical research site, Eastern Virginia Medical School (EVMS), may conduct the protocol-specified HIV testing procedures using HIV rapid saliva tests under CLIA certification instead of HIV blood tests.

2. The following clarification applies to Section 6.3 (Study Product Formulation and Storage), which states that "Inserts will be packaged in 20 cc, round, white, high-density polyethylene (HDPE) bottles":

   The statement has a typo and should instead say that "Inserts will be packaged in 50 cc, round, white, high-density polyethylene (HDPE) bottles".

3. The following clarification applies to Section 10.7 (Blinding), which states that "In case of a severe adverse event and the need to unblind, a pharmacist with access to the randomization code will provide appropriate information":

   "Severe adverse event" defined as a Grade 3 or higher adverse event.

4. Protocol Team Roster – Additions:

   Kent Melchiors, MD
   CONRAD Medical Safety Officer
   601 Colley Ave
   Norfolk, VA 23507
   Email: melchikm@evms.edu

   Homaira Hanif, PhD
   CONRAD Sociobehavioral Scientist
   601 Colley Ave
   Norfolk, VA 23507
   Email: hhanif@conrad.org

   Elizabeth T. Montgomery, PhD
   D2D Hub Pillar 2 MATRIX-001 Sociobehavioral Research (SBR) Lead
   RTI International
   2150 Shattuck Avenue, Suite 800
   Berkeley, CA 94704 USA
   Phone: 1-310-694-7212
   Email: emontgomery@rti.org

Ellen Luecke, MPH
D2D Hub Pillar 2 MATRIX-001 SBR Manager
RTI International
2150 Shattuck Avenue, Suite 800
Berkeley, CA 94704 USA
Phone: 1-919-485-1392
Email: eluecke@rti.org

The above information will be incorporated into the next version of the protocol at a later time if it is amended.