CLARIFICATION MEMO #01 TO:

MATRIX-002

Trial to Assess Acceptability and Safety of Two Placebo Prototype Vaginal Films

Cooperative Agreement #7200AA22CA00002

A Non-IND Study

Version 1.0 / May 24, 2023

Clarification Memo Date: July 8, 2024

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-002 Protocol Co-Chairs, and MATRIX-002 Product Developer (PD) 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-002 documentation and is effective immediately. A copy of this CM must be retained in the PD's and in each study site's Essential Documents file for MATRIX-002. No changes in the sample informed consent form or schedule of visits/procedures are included in this CM.

This document clarifies that study participants are considered evaluable participants once data collection for the first product use period is completed, which occurs at Visit 6. Insertion of the second film, which also occurs at Visit 6, is not needed to consider study participants as evaluable.

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.

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1. The following clarification applies to Section 10.6.2 (Primary Analysis[es]), which states that "All participants randomized into the study who complete Visit 6 will be included in the primary analysis":

Randomized study participants are considered evaluable participants once data collection for the first product use period is completed, which occurs at Visit 6. Insertion of the second film, which also occurs at Visit 6, is not needed to consider study participants as evaluable.

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