

1. How should the Eligibility Criteria CRF be completed for participants who complete screening procedures and are found to be preliminarily eligible but unable to enroll because targeted enrollment has been reached?

Eligibility is first assessed at Screening and confirmed at Enrollment. When the targeted enrollment is reached, there may be participants in the screening process who will not continue to enrollment. In these cases, follow the forms instructions for item 3 on the Eligibility Criteria CRF. The instruction states to mark 'participant did not return (refused or lost contact)' when a participant begins the screening process and is eligible (up to that point), but does not return to the clinic to complete remaining screening procedures. In addition, for these cases, the participant is considered ineligible because the entire screening process was not completed for eligibility confirmation. Therefore, item 1 will be marked "no."

2. Should a new ring be dispensed anytime the ring is removed for an interim visit?

Unless the site clinician/designee or the participant is not comfortable re-inserting the same ring for any reason, the same ring can be reinserted unless product hold guidelines apply.

3. How should vaginal dryness due to menopausal symptoms be documented at Screening and/or Enrollment?

Menopausal symptoms can be documented on the Screening Menstrual History form under item #9 *[provide additional details as needed to describe the participant's menstrual and menopausal history]* and as a Pre-Existing Condition.

4. What happens if a participant re-inserts a dirty ring? Should the site ask the participant to remove the ring and replace with a clean one, or have them leave it in place?

If a vaginal ring is expelled somewhere dirty, such as the toilet or on the ground, and the participant reinserts the same vaginal ring, she can leave the ring in until her next scheduled visit if she is comfortable doing so. If the participant is not comfortable leaving in the same ring, site staff can request the participant return to the clinic as soon as possible to have her vaginal ring replaced.

5. If a CASI questionnaire is missed due to technical issues, should a split visit be performed or the CASI delayed until the next visit?

If there is a technical issue with the equipment or website and for that reason the participant is not able to complete the CASI questionnaire, the site may conduct the CASI on a different day within the visit window and consider it a Split Visit. However, the entire CASI must be completed on the same day and not split across days.

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6. Clarify with NL which rings should be sent for destruction versus which rings are forwarded to the lab for residual testing (per Clinic Study Product Accountability and Destruction SOP)

All rings should be sent for residual testing with the following exceptions:

- unused rings never inserted into the vagina (they are considered unused and are sent to the pharmacy for quarantine), and;
 - used ring sent for destruction include those vaginal rings that are inserted in the clinic but subsequently removed that same day prior to the participant leaving the clinic for any reason (i.e., the wrong ring has been given or it is determined that a product hold is warranted but not identified prior to ring dispensation and insertion) and sent for destruction.
7. What procedures should be followed if the ring is in >35 days?

It is not recommended that the ring be worn >35 days. The ring should be replaced after 28 days. If this is not possible, every effort should be made to replace the ring within the next 7 days (≤ 35 days). If the ring is used >35 days, attempts should be made to contact the participant and retrieve the study product as soon as possible. Clinician/designee/loR discretion must be used regarding ring use depending on the length of time until this next visit.

If a participant is requested by the clinician/designee to remove the ring to avoid more than 35 days of continual use, site staff should complete a PH-1 form and Vaginal Ring Request Slip to document this requested hold. On the PH-1 form, mark item 2 as "other" and specify that more than 35 days of use as the reason for the requested hold. On the Vaginal Ring Request Slip, mark "hold" and specify the text above. Note that for the next ring dispensation for the participant, mark "resume" on the slip.

8. Should 'partial' ring expulsions be documented on the Ring Adherence CRF (item #2)?

Partial expulsions are NOT recorded on the RA-1 CRF. If the participant felt the ring was partially expelled and was then able to push it back in/adjust it, this partial outage would not be recorded on the RA-1. If the ring was partially expelled and the participant took it out fully (and possibly rinsed it), before reinserting it, this outage should be documented with code '11' on the RA-1 CRF.