MTN-043 Clinical Flow Sheets
General Guidance

Guidelines for clinical management and temporary product hold/permanent discontinuation of study product are outlined in protocol section 9.

• In general, the IoR/designee has the discretion to hold study product temporarily at any time if s/he feels that continued product use would be harmful to the participant or interfere with treatment deemed clinically necessary.

• Unless otherwise specified in protocol section 9, the IoR/designee should immediately consult the PSRT for further guidance on resuming study product, continuing the hold temporarily, or progressing to permanent discontinuation of study product.

• The IoR/designee will document all temporary product holds and permanent discontinuations on applicable CRFs.

• Syndromic management of genital symptoms is acceptable while awaiting laboratory results if such practice is in line with the local standards of care.

• Observed single dose treatment should be provided whenever possible, per clinician discretion.

• When clinically appropriate, investigators should use oral or parenteral (in the case of syphilis, for example) medications when at all possible.
<table>
<thead>
<tr>
<th>Condition</th>
<th>Temporary Hold</th>
<th>Permanent Discontinuation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive HIV Rapid Test Result</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Confirmed HIV infection</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Acquisition of hepatitis B infection (for Truvada group only)</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Initial result of ≥ Grade 2 creatinine clearance (for Truvada group only)</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Confirmation of ≥ Grade 2 creatinine clearance (for Truvada group only)</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Initial result of ≥ Grade 2 glycosuria or proteinuria (for Truvada group only)</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Confirmation of ≥ Grade 2 glycosuria or proteinuria (for Truvada group only)</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Allergic Reaction to the study product</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Reported use of PrEP for HIV prevention outside of the study</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Reported use of PEP for potential HIV exposure</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Non-therapeutic injection drug use</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Pregnancy</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Unable or unwilling to comply with required study procedures, or otherwise might be put at undue risk to their/their infant’s safety and well-being by continuing product use, according to the judgment of the IoR/designee.</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Grade 3 maternal AE Related to Study Product Use</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Grade 4 maternal AE (regardless of relationship to study product)</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Grade 3 or 4 infant AE (regardless of relationship to study product)</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Deep epithelial disruption (ulceration)</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Coenrollment (consult PSRT regarding ongoing product use and other potential safety considerations)</td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>
Product Use by Grade

If not specifically addressed in protocol section 9.3:

**Grade 1 or 2:**
*Mothers or Infants*: Regardless of relatedness to study product, may continue product use

**Grade 3:***
*Mothers:*
  - If judged to be *not related*, continue product use
  - If judged to be *related*
    - Temporarily hold product
    - Reassess weekly x 2 weeks
    - If $\leq$ Grade 2 within 2 weeks, resume product
    - If not $\leq$ Grade 2 within 2 weeks, consult PSRT

*Infants:*
  - Grade 3, regardless of relationship to study product, hold mother’s study product, consult PSRT

**Grade 4:**
*Mothers or Infants*: Regardless of relationship, temporarily hold, consult PSRT
Product Use Management:  HIV Infection

START
HIV rapid tests

no rapid test(s) positive
CONTINUE product.

one or more rapid tests positive

HOLD product pending confirmatory testing.

status after confirmatory testing = HIV uninfected
RESUME product.

status after confirmatory testing = HIV infected
PERMANENTLY DISCONTINUE product.

If confirmatory HIV testing is unclear; contact the Network Laboratory for guidance.
Product Use Management:
Additional Conditions Requiring Product Hold

- Unable or unwilling to comply with required study procedures, or otherwise might be put at undue risk to their/their infant’s safety and well-being by continuing product use, according to the judgment of the IoR/designee (consult PSRT)
- Initial result of ≥ Grade 2 creatinine clearance (for Truvada group only)
- Initial result of ≥ Grade 2 glycosuria or proteinuria (Truvada group only)
- Deep epithelial disruption
- Co-enrollment (consult PSRT)

HOLD product. Consult PSRT if required per protocol.
Product Use Management:
Additional Conditions Requiring Permanent Discontinuation

- Acquisition of hepatitis B infection (for Truvada group only)
- Confirmation of ≥ Grade 2 creatinine clearance (for Truvada group only).
- Confirmation of ≥ Grade 2 glycosuria or proteinuria (for Truvada group only).
- Allergic Reaction to the Study Product
- Reported use of PrEP for HIV prevention
- Reported use of PEP for potential HIV exposure
- Non-therapeutic injection drug use
- Pregnancy

PERMANENTLY DISCONTINUE product.
Product Use Management for **ORAL** Study Product:

≥ Grade 2 Creatinine Clearance, glycosuria, or proteinuria

- **START**
  - ≥ Grade 2 creatinine clearance, glycosuria, or proteinuria

- **HOLD** product and notify the PSRT.
- Re-test within 1 week of receipt of result.
  - Retesting yields ≥ Grade 1
    - Continue HOLD and CONSULT PSRT.
  - Retesting confirms ≥ Grade 2
    - PERMANENTLY DISCONTINUE product.
  - No re-test within 1 week

Reference: SSP Table 7-3
Product Use Management: Sexually Transmitted Infections and Reproductive Tract Infections

CONTINUE product, unless permanent discontinuation guidelines apply.

Consult the PSRT if a permanent discontinuation is deemed necessary and instituted by the IoR/designee.

Vaginally applied medications should not be used. Whenever possible, oral or parenteral medications should be used instead.

*Treat per local or current WHO guidelines, using observed single dose regimens whenever possible.
Product Use Management:
Deep epithelial disruption (ulceration)

If confirmed by investigator, HOLD Product

Re-evaluate by speculum exam in 3-5 days. Has it resolved?
Yes
RESUME product.

No

Re-evaluate by speculum exam in 2-3 days. Has it resolved?
Yes
RESUME product.

No

CONTINUE HOLD consult the PSRT re: discontinuation

If reoccurrence with no identified etiology, hold product and consult the PSRT regarding permanent discontinuation

Protocol Reference: Section 9.4