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.

Conditions Requiring Hold/Discontinuation

Condition	Temporary Hold	Permanent Discontinuation
Positive HIV Rapid Test Result	X	
Confirmed HIV infection		X
Acquisition of hepatitis B infection (for Truvada group only)		X
Initial result of ≥ Grade 2 creatinine clearance (for Truvada group only)	X	
Confirmation of ≥ Grade 2 creatinine clearance (for Truvada group only)		X
Initial result of ≥ Grade 2 glycosuria or proteinuria (for Truvada group only)	X	
Confirmation of ≥ Grade 2 glycosuria or proteinuria (for Truvada group only).		X
Allergic Reaction to the study product		X
Reported use of PrEP for HIV prevention outside of the study		X
Reported use of PEP for potential HIV exposure		X
Non-therapeutic injection drug use		X
Pregnancy		X
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.	X	
Grade 3 maternal AE Related to Study Product Use	X	
Grade 4 maternal AE (regardless of relationship to study product)	X	
Grade 3 or 4 infant AE (regardless of relationship to study product)	X	
Deep epithelial disruption (ulceration)	X	
Coenrollment (consult PSRT regarding ongoing product use and other potential safety considerations)	X	

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 ≤ Grade 2 within 2 weeks, resume product
  - If not ≤ Grade 2 within 2 weeks, consult PSRT

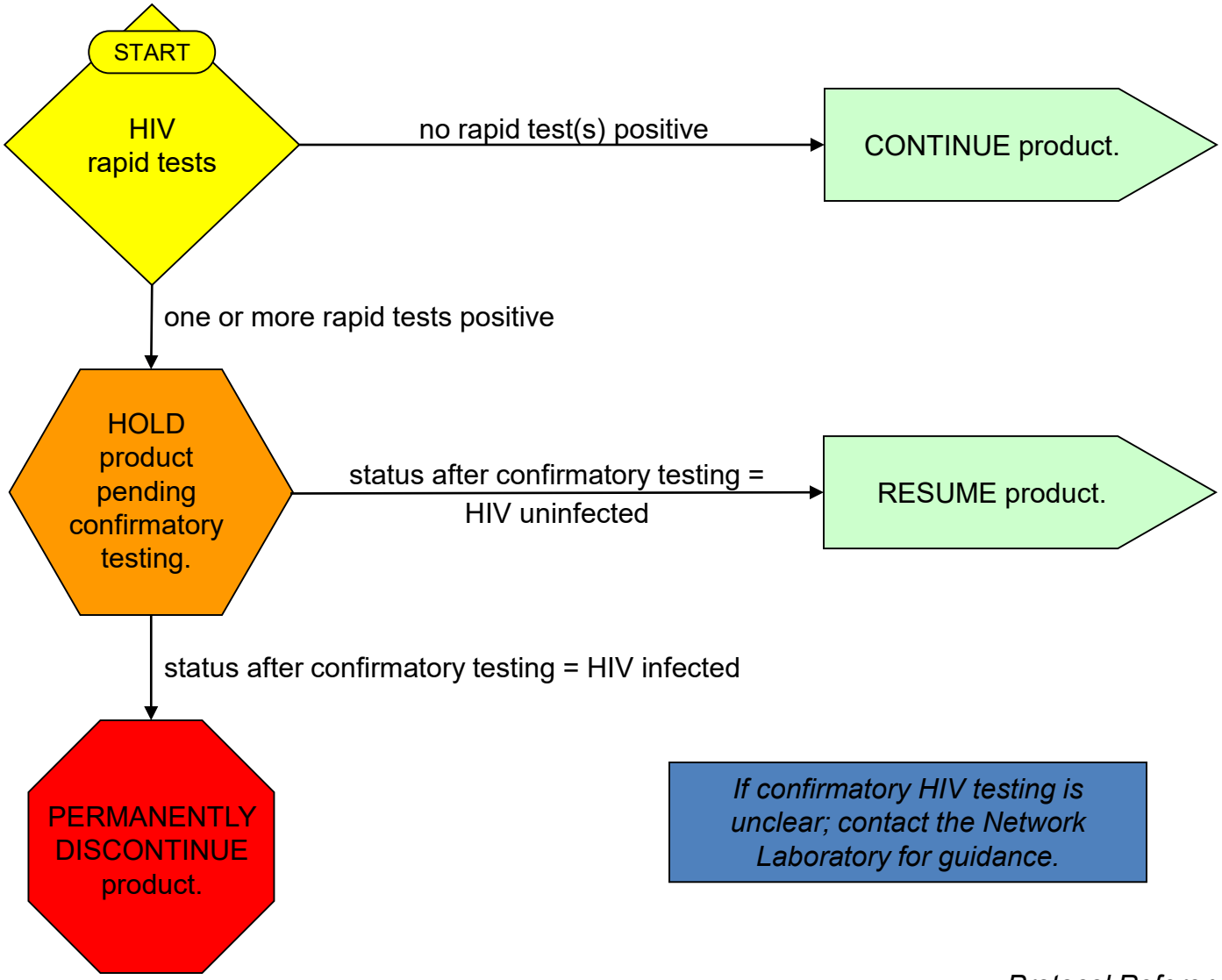
Infants:

- 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

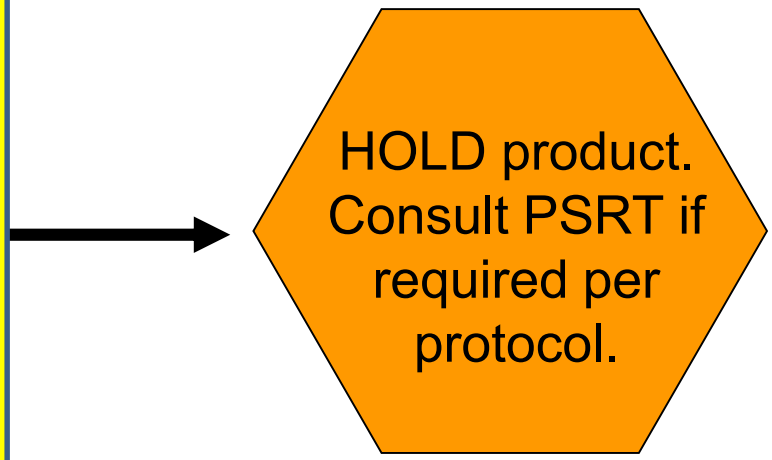
Product Use Management: HIV Infection



Protocol Reference: Section 9.5

Product Use Management:
Additional Conditions Requiring Product Hold

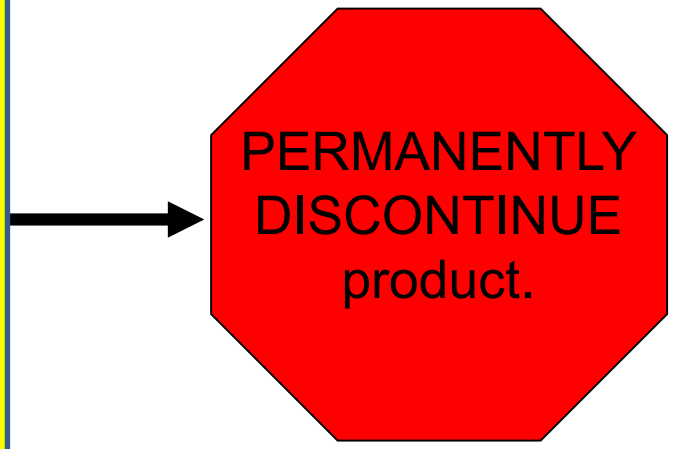
- Unable or unwilling to comply with required study procedures, or otherwise might be put at undue risk to their/their infant's safety and well-being by continuing product use, according to the judgment of the IoR/designee (consult PSRT)
- Initial result of ≥ Grade 2 creatinine clearance (for Truvada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



Protocol Reference: Section 9.3

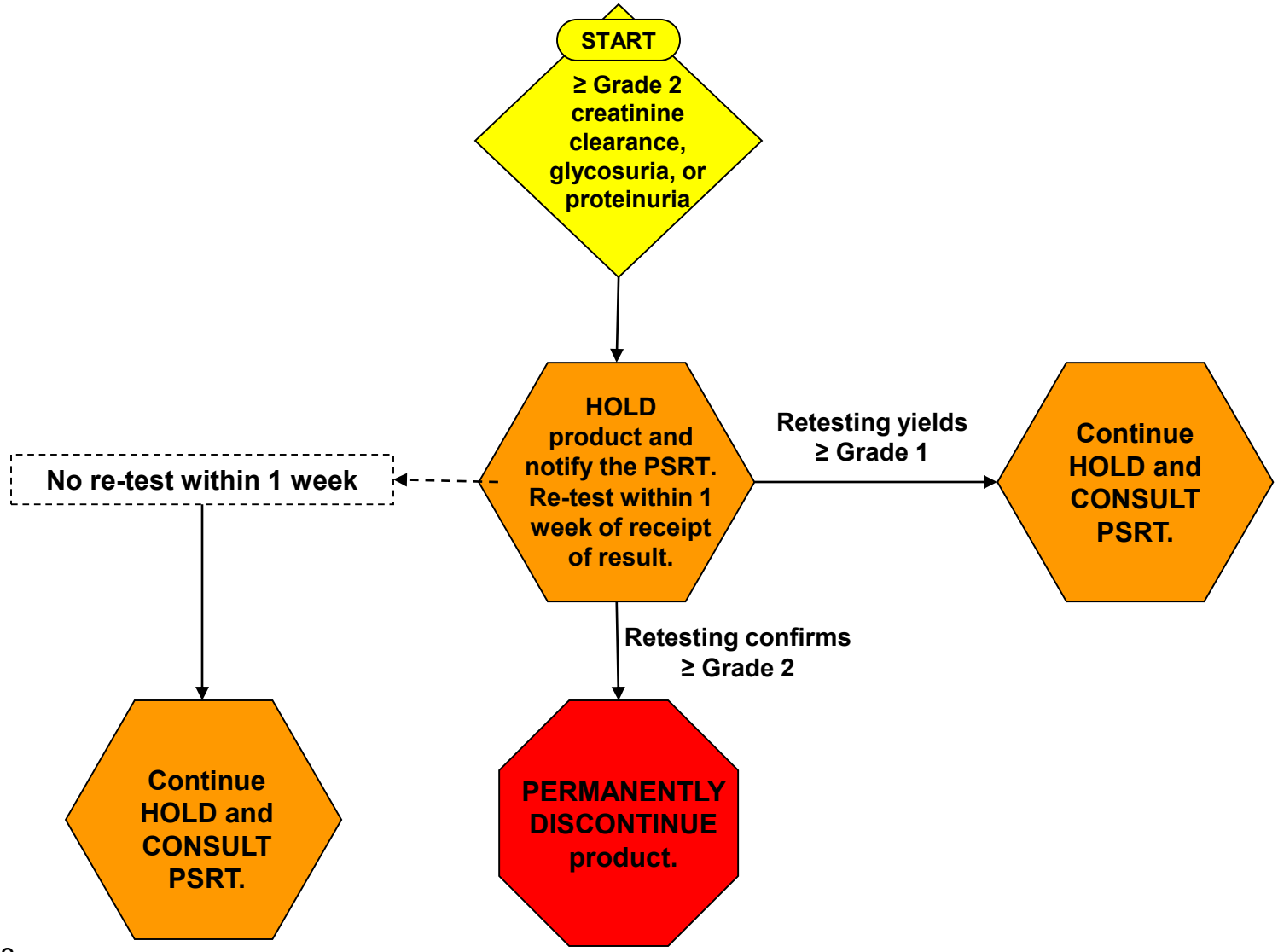
Product Use Management:
Additional Conditions Requiring Permanent Discontinuation

- 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



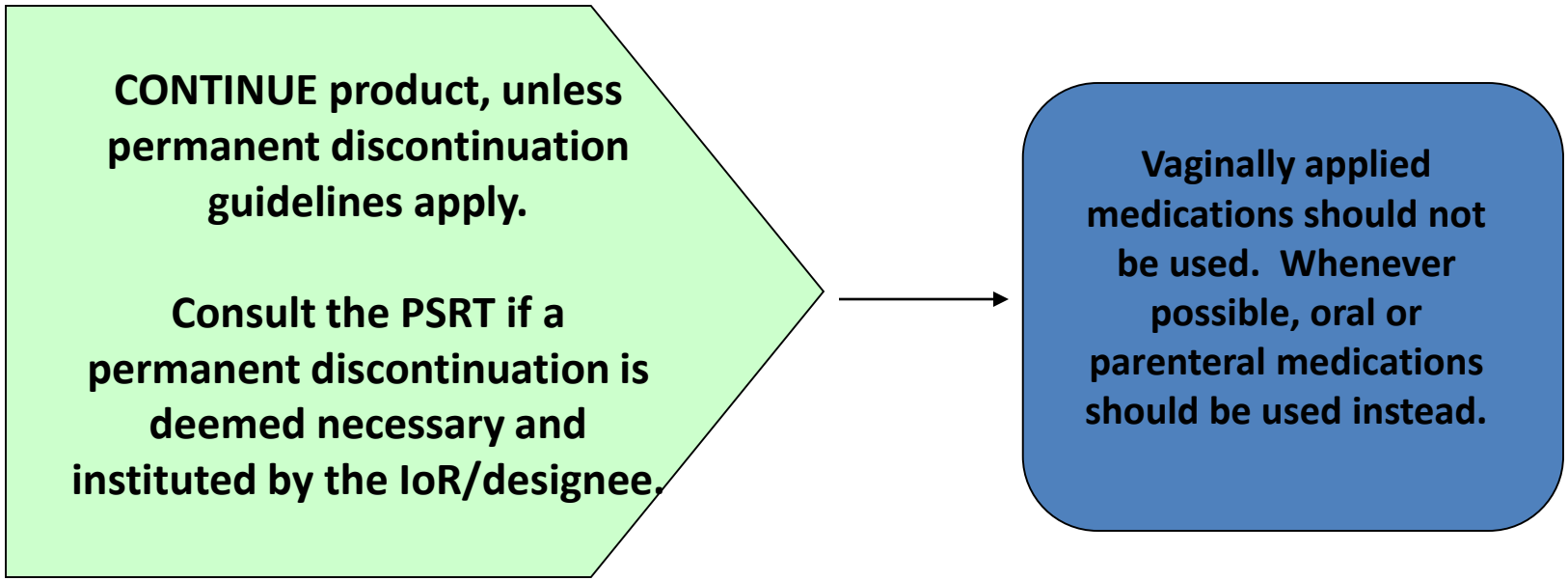
Protocol Reference: Section 9.3

Product Use Management for ORAL Study Product:
≥ Grade 2 Creatinine Clearance, glycosuria, or proteinuria



Reference: SSP Table 7-3

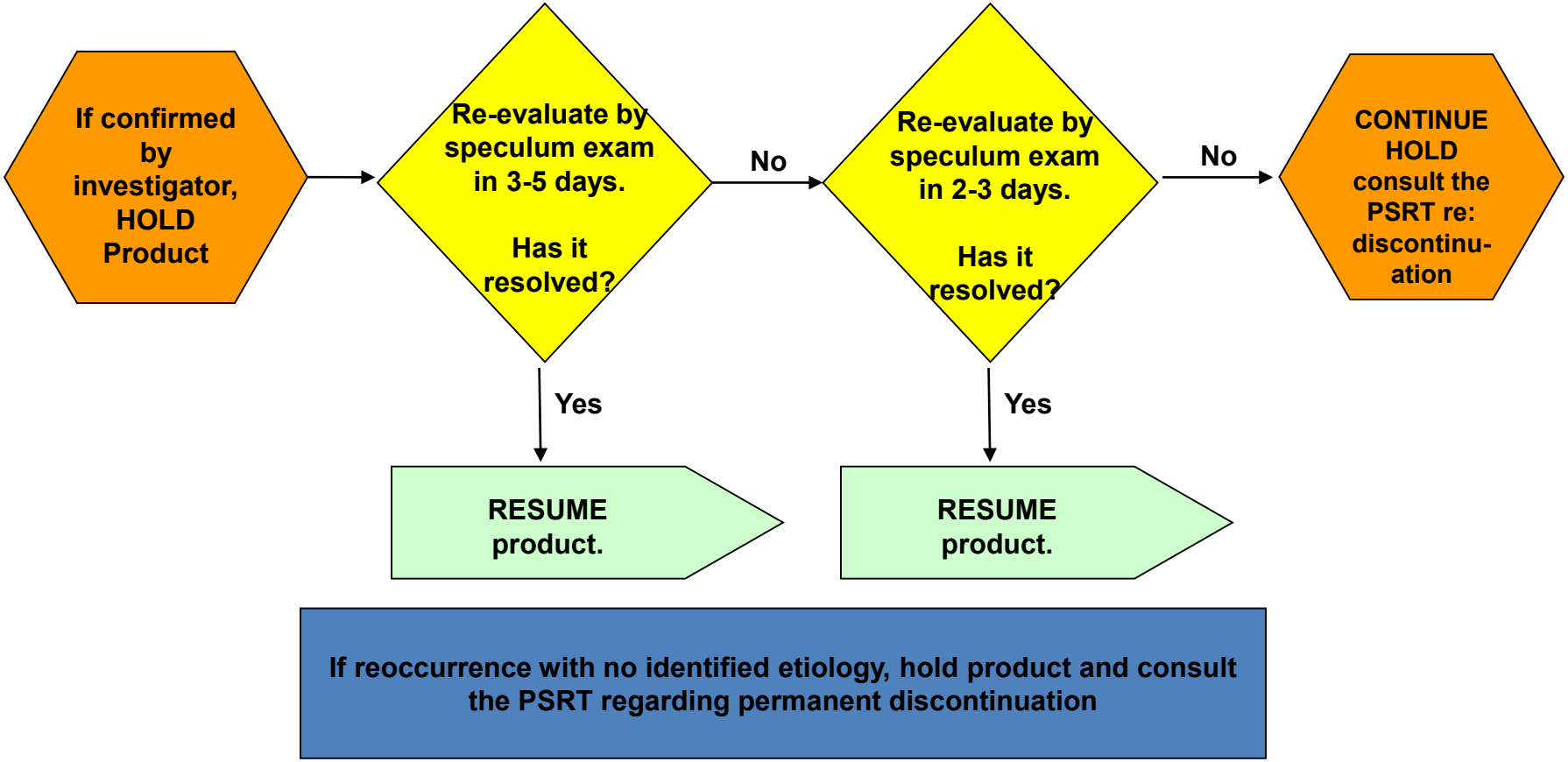
Product Use Management: Sexually Transmitted Infections and Reproductive Tract Infections



***Treat per local or current WHO guidelines, using observed single dose regimens whenever possible.**

Reference: SSP Section 8.5

Product Use Management:
Deep epithelial disruption (ulceration)



Protocol Reference: Section 9.4