Clinical Considerations

Review

Clinical Procedures

- Medical History
- Medication History- Concomitant Medications
- Physical Exams
- Rectal Exams
- STI/RTI Management
- Clinical Management of Lab Test Results
- Product use Management

Medical History

Medical History: Timing and Purpose

- When:
  - Obtained and documented at Screening
  - Reviewed/updated at Enrollment, prior to randomization
- Purpose:
  - To establish eligibility and document relevant baseline medical history and conditions, for comparison during follow-up
- History should also be obtained at interim visits, as clinically indicated

What information should be collected?

Assess past problems, including those where medication was taken for an extended period of time

Evaluate all current symptoms, illnesses, allergies

Document previous surgeries and chronic and acute conditions

Baseline Medical History Questions Sheet

- Form provided to assist in obtaining a complete, accurate, and relevant participant self-reported medical history
- Use each item to probe participant's medical conditions as well as any conditions s/he is currently experiencing at the time of the Screening and Enrollment visits

PTID:_____ Staff Initials/Date:_____

MTN-017 Baseline Medical History Questions Sheet

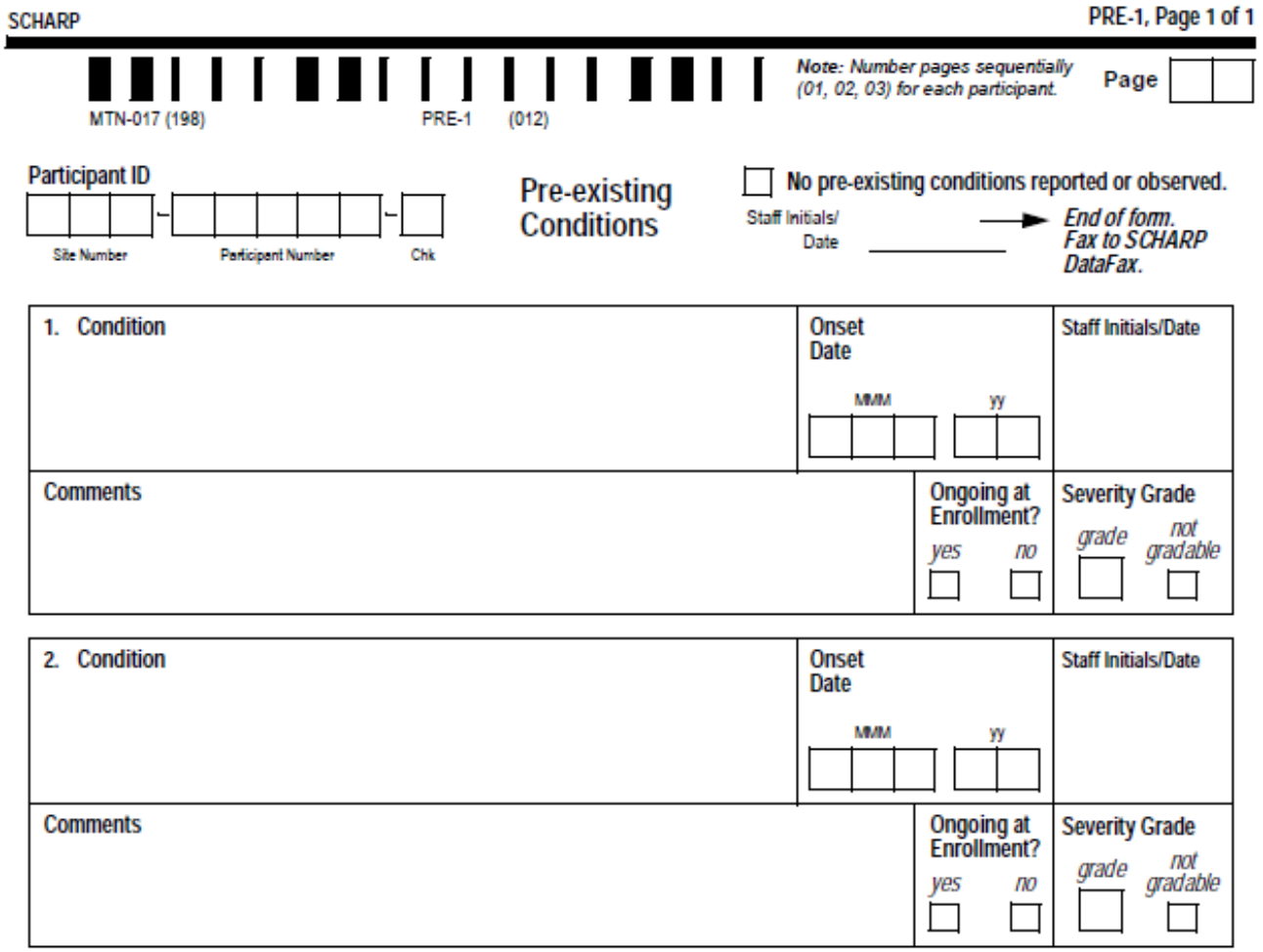
Complete at the Screening Visit. Record relevant baseline conditions on the Pre-existing Conditions CRF. Relevant conditions include (but is not limited to): hospitalizations; surgeries; allergies; conditions requiring prescription or chronic medication (lasting for more than 2 weeks); and any conditions currently experienced by the participant.

	Have you ever experienced any significant medical problems involving the following organ system/disease?	Yes	No
1	Head, eyes, ears, nose, or throat	☐	☐
2	Prostate	☐	☐
3	Lymphatic	☐	☐
4	Cardiovascular	☐	☐
5	Respiratory	☐	☐
6	Liver	☐	☐
7	Renal (including urinary symptoms)	☐	☐
8	Gastrointestinal	☐	☐
9	Musculoskeletal (including bone fractures)	☐	☐
10	Neurologic	☐	☐
11	Skin	☐	☐
12	Endocrine/Metabolic	☐	☐
13	Hematologic	☐	☐
14	Cancer	☐	☐
15	Drug Allergy	☐	☐
16	Other Allergy	☐	☐
17	Mental Illness	☐	☐
18	Have you ever experienced or are currently experiencing any of the following anogenital symptoms/diagnoses?	Yes	No
	18a Anal or genital sores or ulcers	☐	☐
	18b Urethral discharge	☐	☐
	18c Dysuria or urethral burning	☐	☐
	18f Anal pain	☐	☐

Pre-Existing Conditions Case Report Form

- Serves as the “starting point” or baseline from which a study clinician must determine whether conditions identified during follow-up are adverse events
- Provides a “snapshot” of a participant’s medical status at point of randomization
- Information on the Baseline Medical History Questions Sheet lend to what is documented on the Pre-Existing Conditions CRF

Pre-Existing Conditions Case Report Form



SCHARP

PRE-1, Page 1 of 1

MTN-017 (198) PRE-1 (012)

Note: Number pages sequentially (01, 02, 03) for each participant.

Page

Participant ID

Site Number | Participant Number | Chk

Pre-existing Conditions

☐ No pre-existing conditions reported or observed.

Staff Initials/ Date _____ → *End of form. Fax to SCHARP DataFax.*

1. Condition	Onset Date MMM yy	Staff Initials/Date
Comments	Ongoing at Enrollment? yes ☐ no ☐	Severity Grade grade ☐ not gradable ☐

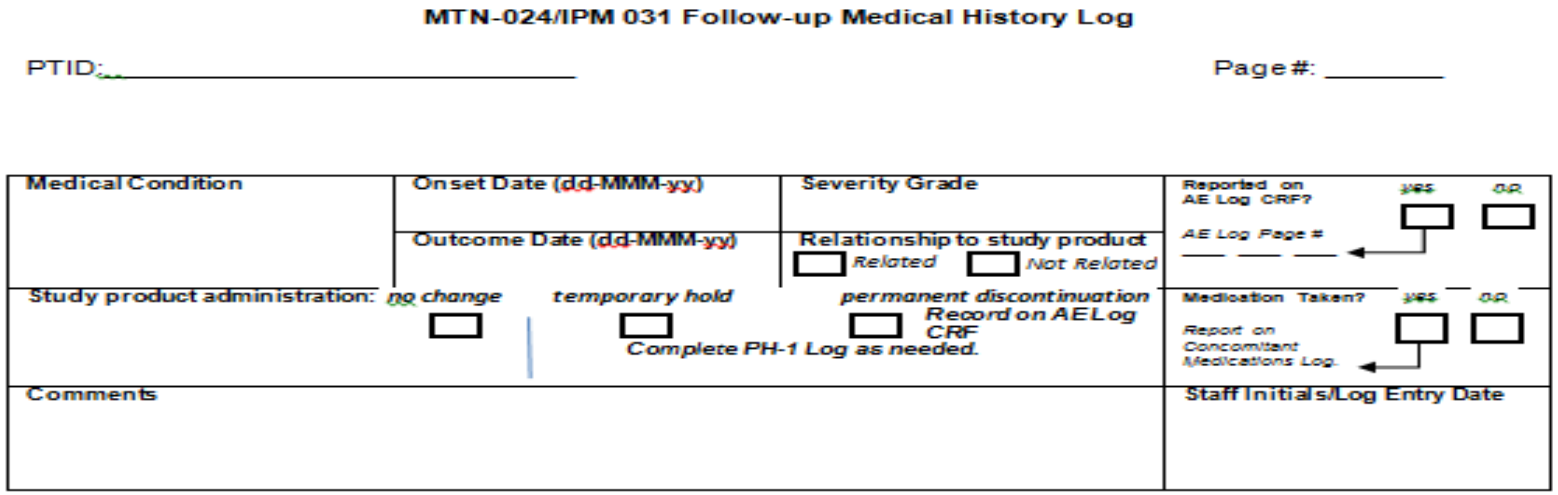
2. Condition	Onset Date MMM yy	Staff Initials/Date
Comments	Ongoing at Enrollment? yes ☐ no ☐	Severity Grade grade ☐ not gradable ☐

Follow Up Medical History Log

- Once a participant is enrolled and before his/her first follow-up visit, site staff should transcribe all entries on the Pre-Existing Conditions CRF that are marked as “ongoing” at Enrollment onto a new Follow-up Medical History Log designated for use for that participant.

Follow Up Medical History Log

- Form used to track the participants' medical conditions during follow-up



MTN-024/IPM 031 Follow-up Medical History Log

PTID:_____ Page #: _____

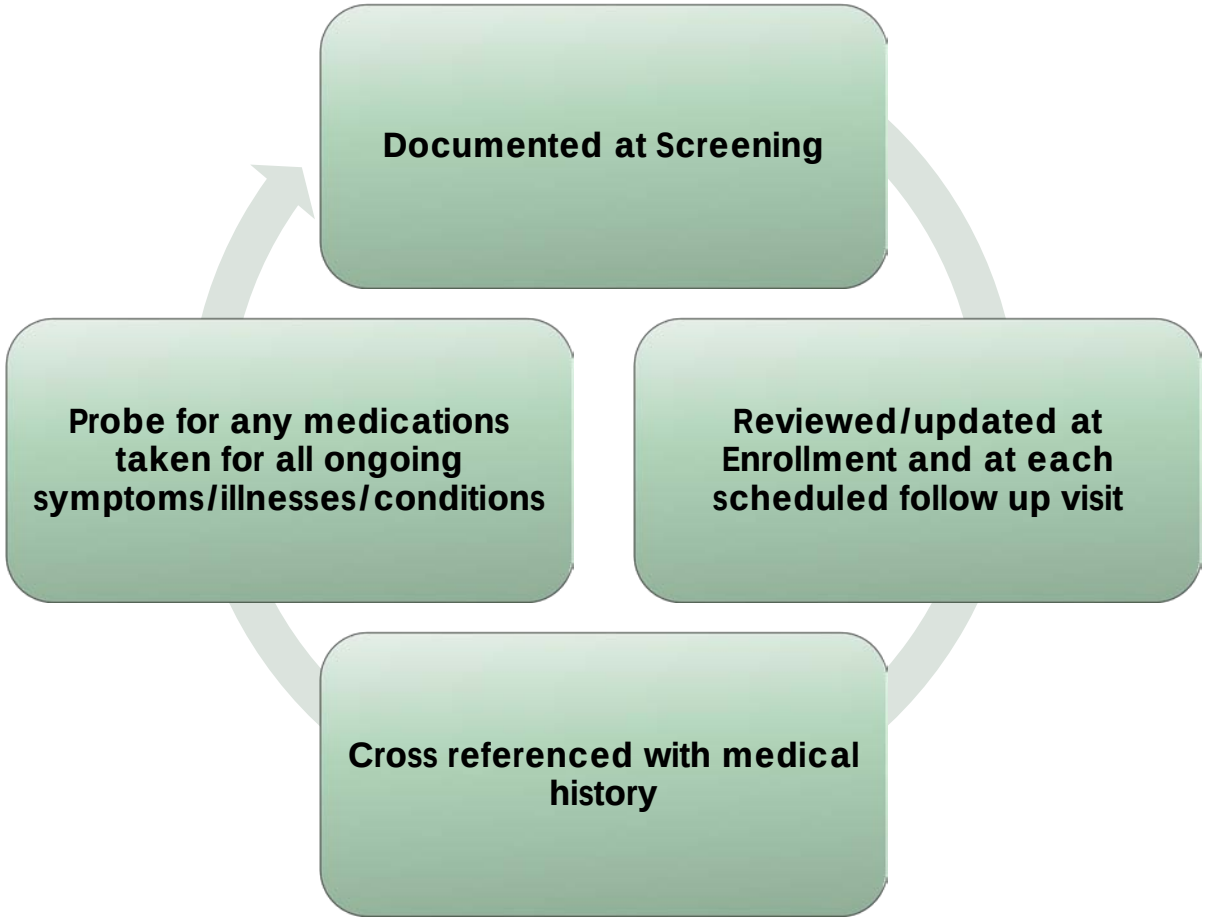
Medical Condition	Onset Date (dd-MMM-yy)	Severity Grade	Reported on AE Log CRF? YES ☐ OR ☐
	Outcome Date (dd-MMM-yy)	Relationship to study product ☐ Related ☐ Not Related	AE Log Page # ___ ___ ___
Study product administration: no change ☐ temporary hold ☐ permanent discontinuation ☐ Record on AE Log CRF. Complete PH-1 Log as needed.			Medication Taken? YES ☐ OR ☐ Report on Concomitant Medications Log.
Comments			Staff Initials/Log Entry Date

Medication History

What is a Concomitant Medication?

- A concomitant medication (con-med) is a drug or product, other than a study drug, taken by a participant during a clinical research study

Concomitant Medications



Examples of Acceptable Con Meds

- Prescription and “over-the counter” medications and preparations
- Pre-exposure Prophylaxis(PrEP)*
- Vaccinations (including Hep B if offered)
- Lubricants (except study provided lubricant)
- Douches and/or enemas
- Vitamins and other nutritional supplements
- Herbal, naturopathic, and traditional preparations

*if local standard of care for HIV prevention

Examples of Prohibited Con Meds

- Any investigational products
- Systemic immunomodulatory medications (e.g. corticosteroids)
- Warfarin or heparin
- Rectally-administered medications or products, containing N-9 or corticosteroids (including over-the-counter preparations)

Examinations

Physical Exam

- **When:**
  - Required at Screening, Enrollment and Period 3 end visit
  - Additional clinical assessments may be performed at any time at the discretion of the examining clinician in response to symptoms or illnesses present
- **Documentation:**
  - Abbreviated Physical Exam CRF is recommended source document
  - Transcribe medically-relevant abnormal findings at Screening or Enrollment onto PRE CRF
  - During follow-up, transcribe abnormalities onto AE CRF as needed
  - All visits – cross-reference with Con Meds Log

Abbreviated Physical Exam CRF

Participant ID ☐☐☐-☐☐☐☐☐-☐ (Site Number – Participant Number – Chk)

Abbreviated Physical Exam

Visit Date ☐☐ dd ☐☐☐ MMM ☐☐ yy

VITAL SIGNS

1. Weight	☐☐☐ kg	4. Pulse	☐☐☐ beats per minute
2. Body Temp	☐☐.☐ °C	5. Respirations	☐☐ breaths per minute
3. Blood Pressure (BP)	☐☐☐ / ☐☐☐ mmHg	6. Height	☐☐☐ cm OR ☐ not done → Required at Screening only.

SYMPTOM-DIRECTED FINDINGS *Items 7 and 8 are required. Assess items 9—18 only if clinically indicated.*

	not done	normal	abnormal	Notes:
7. General appearance	☐	☐	☐	
8. Abdomen/ Gastrointestinal	☐	☐	☐	Notes:
9. Neck	☐	☐	☐	Notes:
10. Lymph Nodes	☐	☐	☐	Notes:
11. Heart/Cardiovascular	☐	☐	☐	Notes:
12. Lungs/Respiratory	☐	☐	☐	Notes:
13. Extremities	☐	☐	☐	Notes:

Physical Exam

- Required components of the physical exam are:
  - Height (required only at Screening)
  - Weight (must be repeated with each physical exam)
  - Vital Signs (temperature, pulse, blood pressure)
  - General appearance
  - Abdomen
- Other exam components can be added as indicated by participant symptoms (medical history form can help drive further examination)

Rectal Exam

- **When:**
  - Required at every scheduled study visit
  - Additionally when clinically indicated to evaluate anorectal symptoms
- **Documentation:**
  - Anorectal Exam (ARE-1) CRF is recommended source document
  - Transcribe abnormal non-exclusionary findings at Screening or Enrollment onto PRE CRF
  - During follow-up, transcribe abnormalities onto AE CRF as needed
  - Unexpected discomfort should also be noted on the ARE CRF
  - All visits – cross-reference with Con Meds Log

Participant ID ☐☐☐-☐☐☐☐☐-☐ (Site Number / Participant Number / Chk)

Anorectal Exam

Exam Date ☐☐ dd ☐☐☐ MMM ☐☐ yy

PERIANAL EXAMINATION

1. Findings from the perianal examination: ☐ *no abnormal findings* ☐ *abnormal findings* ☐ *not done*
   - *not done* → *If not done, specify reason(s) in Comments. Go to item 2.*
   - *no abnormal findings* → *If no abnormal findings, go to item 2.*

1a. Abnormal findings. *Mark all that apply.*

☐ Warts	☐ Leukoplakia	☐ Erythema
☐ Fissure	☐ Fistula	☐ Bleeding
☐ Ulceration	☐ Petechiae (< 3 mm)	☐ Other abnormal findings specify: _____
☐ Pigmentation	☐ Purpura (0.3–1 cm)	_____
☐ Hemorrhoids	☐ Ecchymosis (> 1 cm)	
☐ Skin tags	☐ Discharge	

DIGITAL RECTAL EXAMINATION

2. Findings from the digital rectal examination: ☐ *no abnormal findings* ☐ *abnormal findings* ☐ *not done*
   - *not done* → *If not done, specify reason(s) in Comments. Go to item 3.*
   - *no abnormal findings* → *If no abnormal findings, go to item 3.*

2a. Abnormal findings, specify: _____

ANOSCOPY

3. Was an anoscopy performed at this visit? ☐ *yes* ☐ *not required* ☐ *no, specify:* _____
   - *not required* / *no, specify:* → *If not required or no, end of form.*

Rectal Exam

- Required components of the rectal exam are:
  - Perianal Examination
  - Digital Rectal Examination (DRE)
  - Anoscopy
  - Specimen Collection

STI/RTI Management

- Clinical and laboratory evaluations are performed to diagnose the following STIs and RTIs:
  - Neisseria gonorrhea (GC)/Chlamydia trachomatis (CT)
  - Herpes simplex virus (HSV1/2)
  - Human papillomavirus (anal HPV)
  - Syphilis
  - Hepatitis B and C

STI/RTI Management

- STI/RTIs will be treated in accordance with current World Health Organization (WHO) guidelines which can be accessed at: http://www.who.int/reproductivehealth/topics/rtis/evidence/en/index.html.

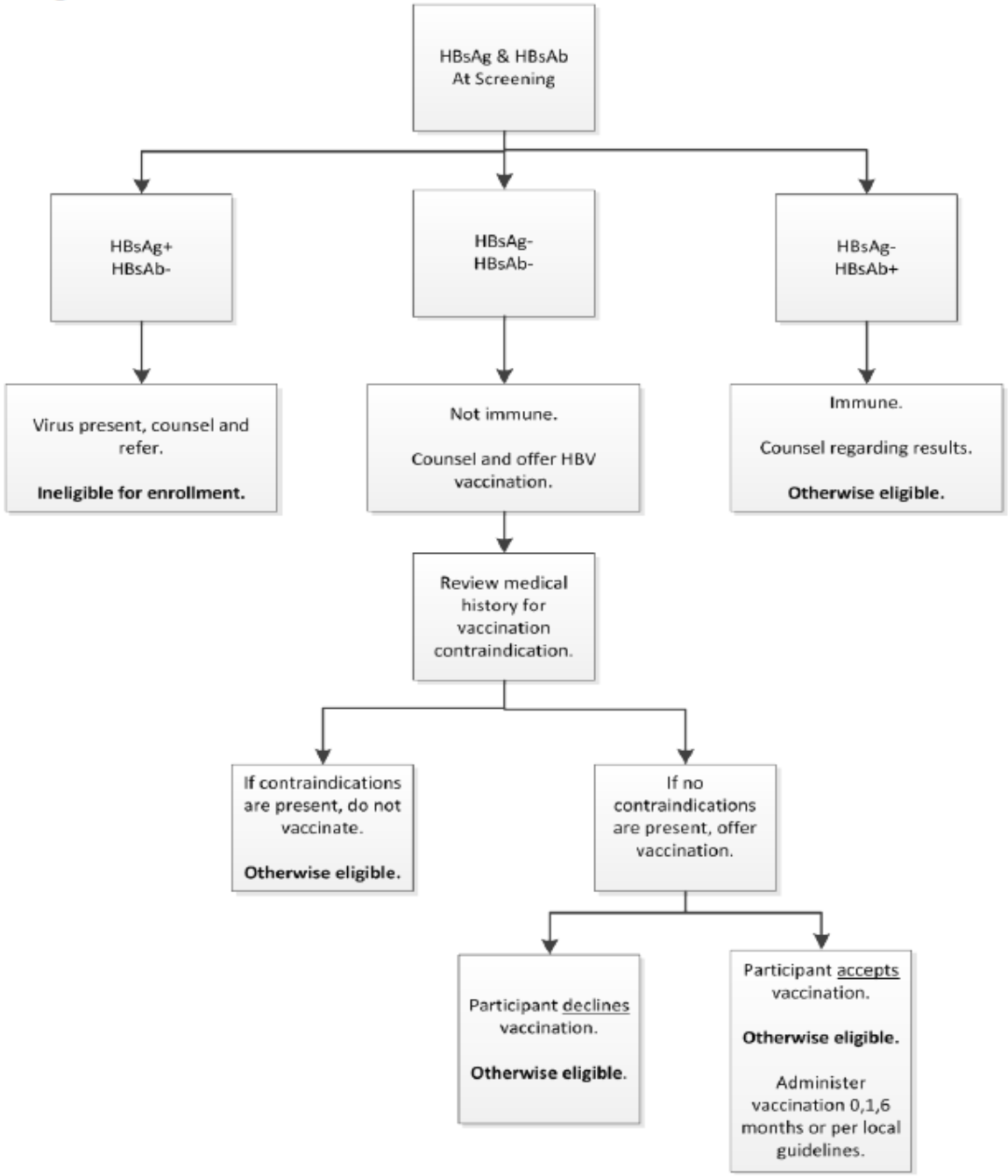
STI/RTI Management

- Potential participants presenting with an active (symptomatic) infection requiring treatment at Screening will be excluded from study participation
  - HSV-1 or HSV-2 seropositive diagnosis with no active lesions is allowed, since treatment is not required
  - In cases of non-anorectal GC/Chlamydia (i.e. urethral) identified at screening, one re-screening no earlier than two months after the screening visit will be allowed

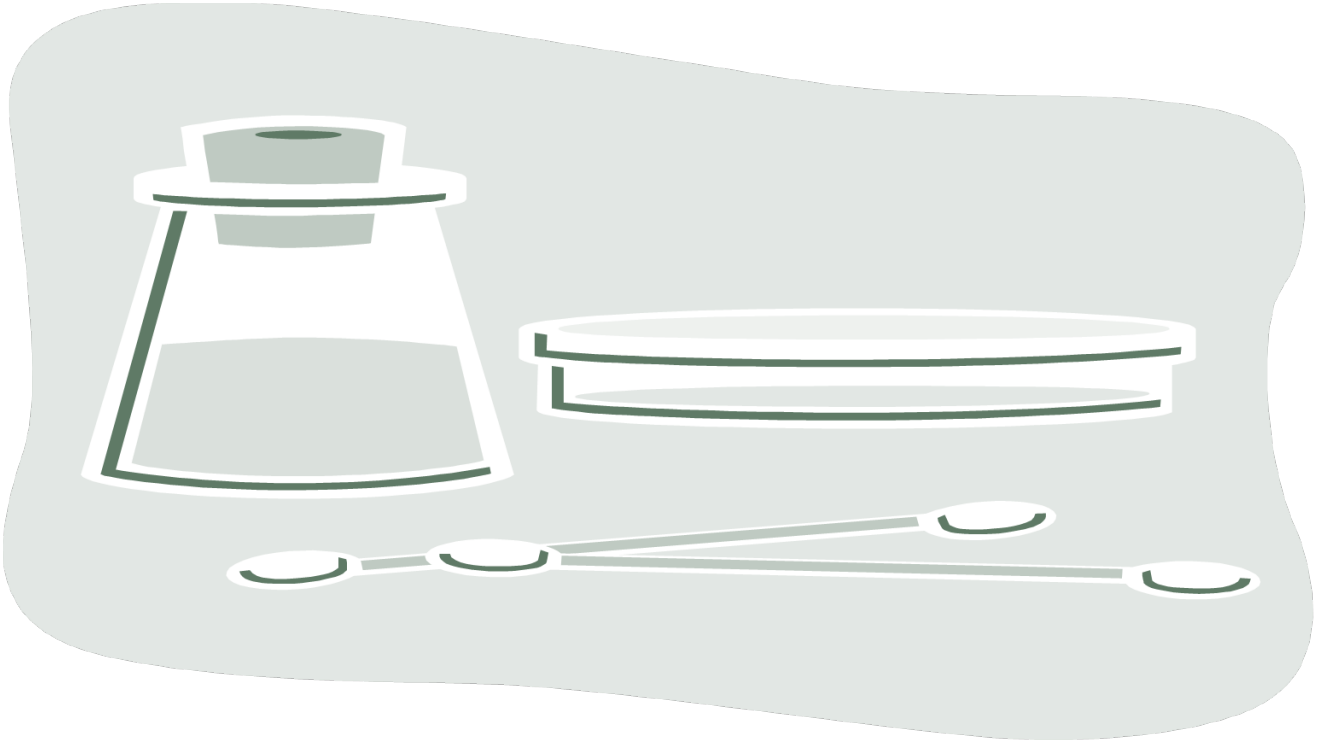
Hepatitis B Testing and Vaccination

- Those with active HBV infection as evidenced by detection of HBsAg:
  - Should receive standardized counseling relevant to natural history and transmission risks of HBV
  - Are excluded from enrollment
- Those who test positive for HBsAb are eligible for enrollment
- Those who test negative for both HBsAg and HBsAb
  - Should offered immunization against HBV and considered eligible for enrollment

Appendix IV: Algorithm For Management of Hepatitis B Serologic Assays Assessed at Screening.



Management of Lab Results



Management of Lab Results

- At each clinic visit results from labs drawn at a previous visit should be discussed with the participant
- All lab results are to be documented fully in the source records and on the CRFs
- Abnormal lab results are to be assessed and reported as an AE if reporting requirements are met
- IoR or designee should routinely review laboratory test results and document review (initials/date) in participant study records or on lab results report

Product use Management

Protocol Reference: Section 9

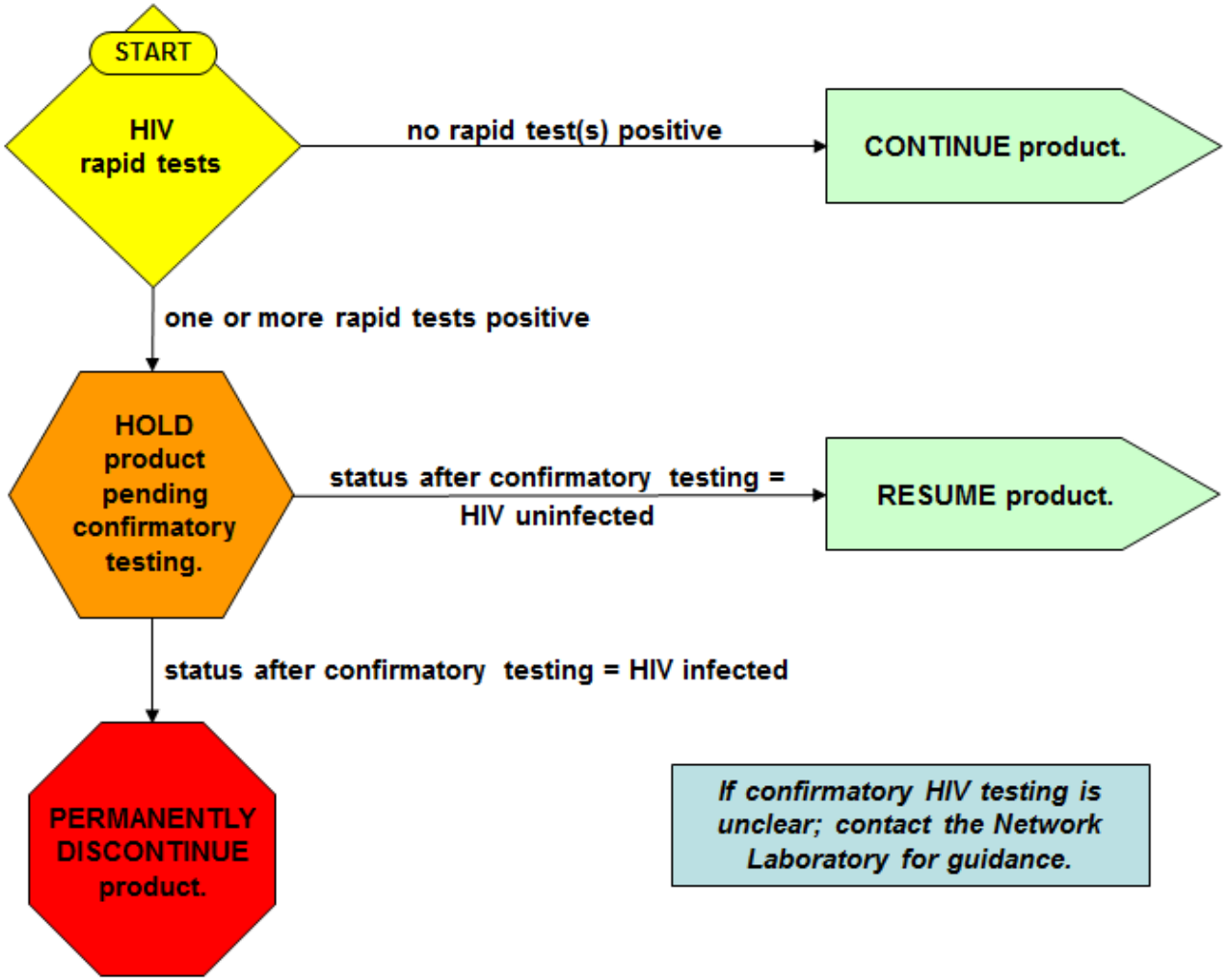
Criteria for Permanent Discontinuation of Study Product

- A participant will be **permanently** discontinued from product use automatically
  - Acquisition of HIV-1 infection (confirmed)
  - Report use of PEP
  - Hepatitis B Infection
  - Participant unable/unwilling to comply with study procedures, or at undue risk by continuing product use (IoR discretion)

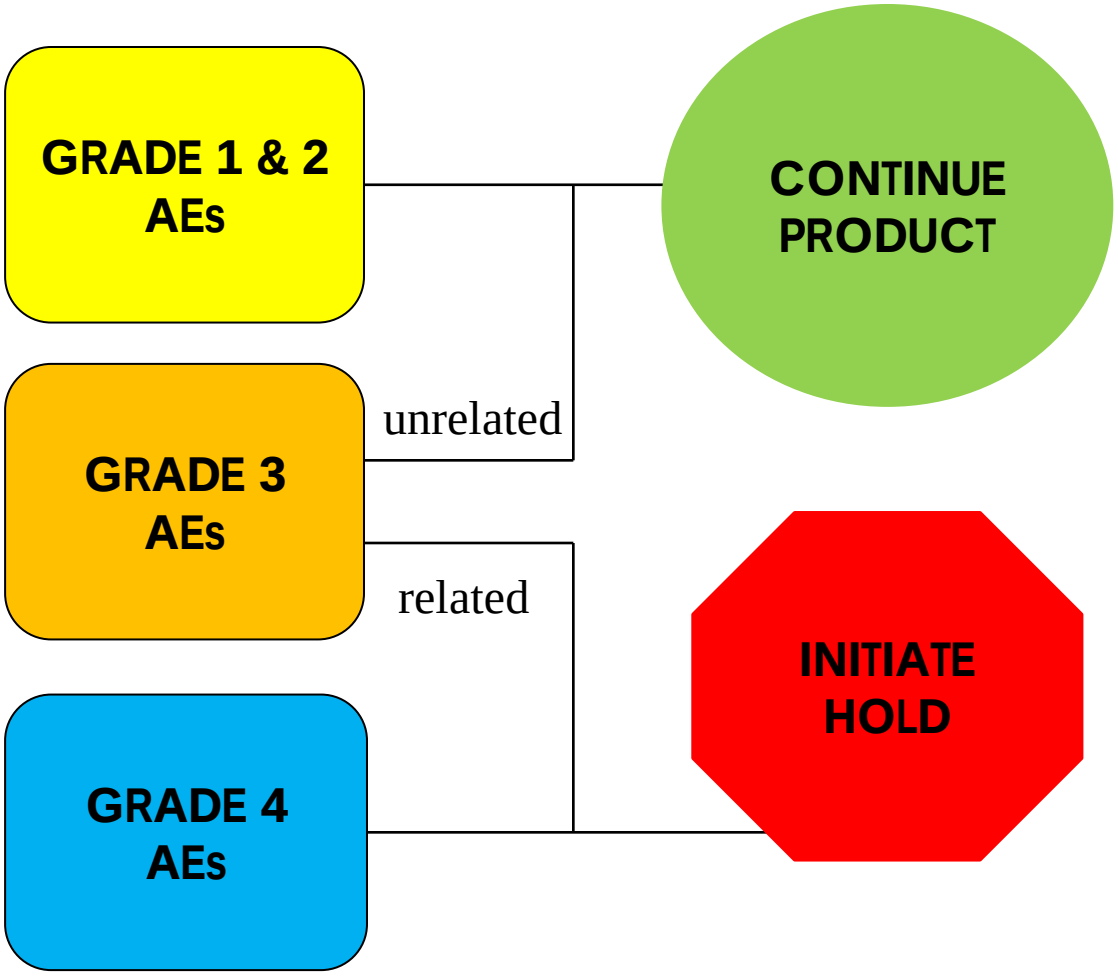
General Criteria for Automatic Product Hold Initiation

- Reactive rapid HIV test
- Grade 3 AE (Related)
- Grade 4 AE, regardless of relatedness
- Participant is unable or unwilling to comply with required study procedures, or otherwise might be put at undue risk to their safety and well-being by continuing product use, according to the judgment of the IoR/designee*

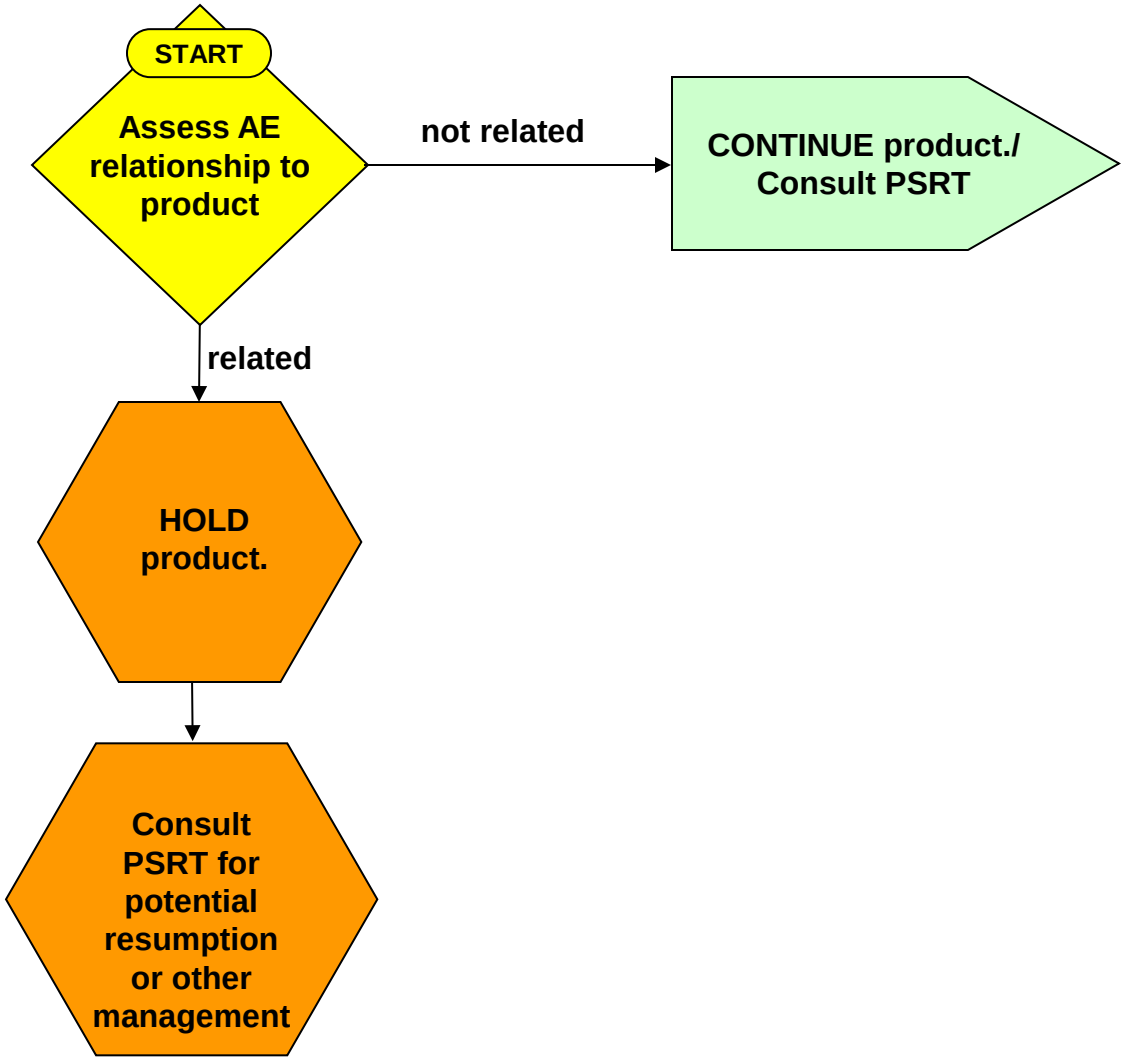
HIV Infection



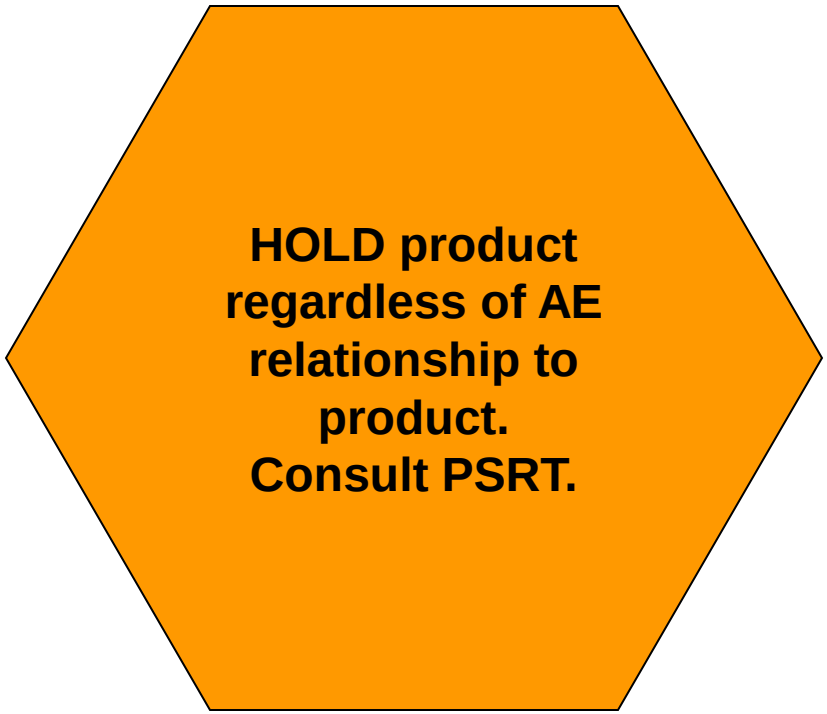
General AEs by Grade



Grade 3 Adverse Events



Grade 4 Adverse Events



Participant Non-compliance or other safety concerns

- HOLD product if a participant is unable or unwilling to comply with required study procedures, or otherwise might be put at undue risk to her safety and well-being by continuing product use, according to the judgment of the IoR/ designee.
- CONSULT the PSRT on all product holds instituted for this reason for further guidance on resuming product use, continuing the temporary hold, or progressing to permanent discontinuation.

Sexually Transmitted Infections and Reproductive Tract Infections

CONTINUE product, unless other product hold guidelines apply.

Consult the PSRT if a temporary hold is deemed necessary and instituted by the IoR/designee.

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

CO-ENROLLMENT

- If co-enrollment in another study is identified, obtain as much information as possible about the other study from the participant and the other study team.
- CONSULT the PSRT regarding ongoing product use and potential safety concerns.

Protocol Reference: Section 9.3

What are your questions related to clinical management?