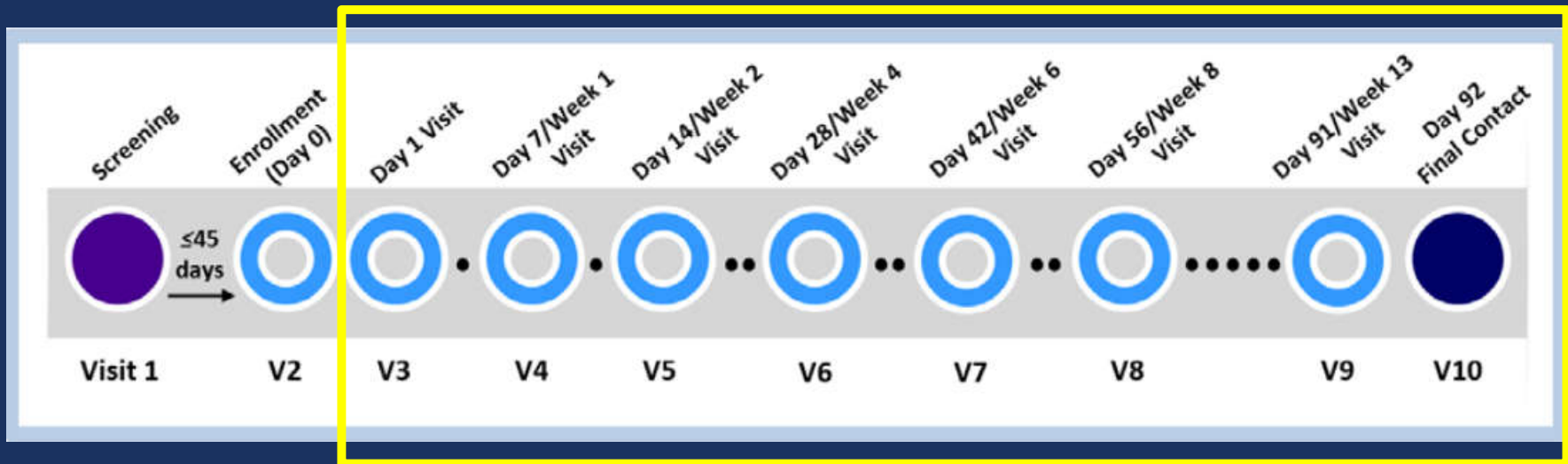


FOLLOW-UP VISIT CONSIDERATIONS

MTN-038 STUDY-SPECIFIC TRAINING | 11 SEPT 2018



PROTOCOL & SSP MANUAL REFERENCES

- Protocol Sections 7.4 (Follow-up) and 9.2-9.4 (Clinical Management)
- SSP Section 5: Study Procedures
- SSP Section 8: Clinical Considerations
- SSP Section 9: AE and Safety Reporting
- SSP Section 10: Laboratory Considerations
- SSP Section 11: Counseling Considerations
- SSP Section 12 Data Management



Scheduled Visits:

- First 2 Weeks of VR use:
 - Day 1, 7, & 14 (V3-5)
- Further follow-up:
 - Day 28, 42, 56, 91/PUEV (V6-9)
- Final Contact:
 - Day 92/V10 (24-72 hrs after PUEV)
- Split visits: permitted but not encouraged, V4-10; not permitted V2 or V3 (Day 1)

Interim visits: phone or clinic visits between scheduled visits

Procedures required will depend on the reason for the visit

- Make-up missed visit
- For administrative reasons
- For product-related reasons
- In response to AEs and/or SAEs.
- For additional STI counseling and testing in response to STI symptoms.
- For any needed HIV counseling and testing in response to participant report of symptoms consistent with acute infection or presumed exposure to HIV.
- For other reasons at participant request

Early Termination:

- Complete procedures per the Day 91/PUEV/Early Termination Visit Checklist
- Collecting the PK/PD blood, pelvic, and rectal specimens will be at management team discretion.

SCHEDULED AND INTERIM VISITS

VISITS 3-5 (DAY 1, 7, AND 14) PROCEDURES

Administrative	Co-enrollment check, update locator, schedule next visit, provide reimbursement, <i>offer condoms*</i>
Behavioral	None
Counseling	<i>HIV Pre-Post Test and STI Risk Reduction*</i> Contraceptive Protocol Adherence
Clinical	Review/collect/update medical/menstrual/meds history Assess AEs <i>Targeted Physical Exam*</i> Pelvic Exam – Check for VR Evaluate/provide findings; <i>RX/refer for RTI/UTI/STI*</i>
Laboratory	Blood – TFV levels, <i>CBC w/ platelets/diff., serum creatinine, Syphilis, HIV *</i> Pelvic – CVF for TFV levels and biomarkers, <i>cervical biopsies ‡, NAAT for Trich and GC/CT, wet mount w/ pH*</i> Rectal fluid for TFV (Days 1 & 14 only) <i>Urine – Pregnancy/ dipstick/ Culture analysis*</i>

**If indicated*
‡ per biopsy schedule

VISITS 6-8 (DAY 28 , 42 AND 56)

Administrative	Co-enrollment check, update locator, schedule next visit, provide reimbursement, <i>offer condoms*</i>
Behavioral	Ring Adherence CRF (Visit 6 & 8 only) Follow-up CASI questionnaire
Counseling	<i>HIV Pre-Post Test and STI Risk Reduction*</i> Contraceptive Protocol Adherence
Clinical	Review/update medical/menstrual/meds history Assess AEs <i>Targeted Physical Exam*</i> Pelvic Exam- check for VR Evaluate findings; <i>RX/refer for RTI/UTI/STI*</i>

**If indicated*

VISITS 6-8 (DAY 28 , 42 AND 56), CON'T

Laboratory Specimen Collection	Day 28/Visit 6	Day 42/Visit 7	Day 56/Visit 8
Urine for pregnancy test	X	<i>If indicated</i>	X
Blood for TVF	X		X
CVF for TVF	X		X
CVF for anti-HSV-2 activity	X		X
CVF for biomarkers	X	X	X
Vaginal swabs for microbiota	X		X
Vaginal Gram Stain	X		X
CVL for PK, PD and biomarkers	X		X
Cervical Biopsies (‡ per sampling assignment)	X ‡		X ‡
<i>HIV-1/2, urine dipstick/culture, AST/ALT, CDC w/ diff & plat., creatinine, syphilis, NAAT for CG/ GT & trich, wet mount w/ pH</i>	<i>If indicated</i>	<i>If indicated</i>	<i>If indicated</i>

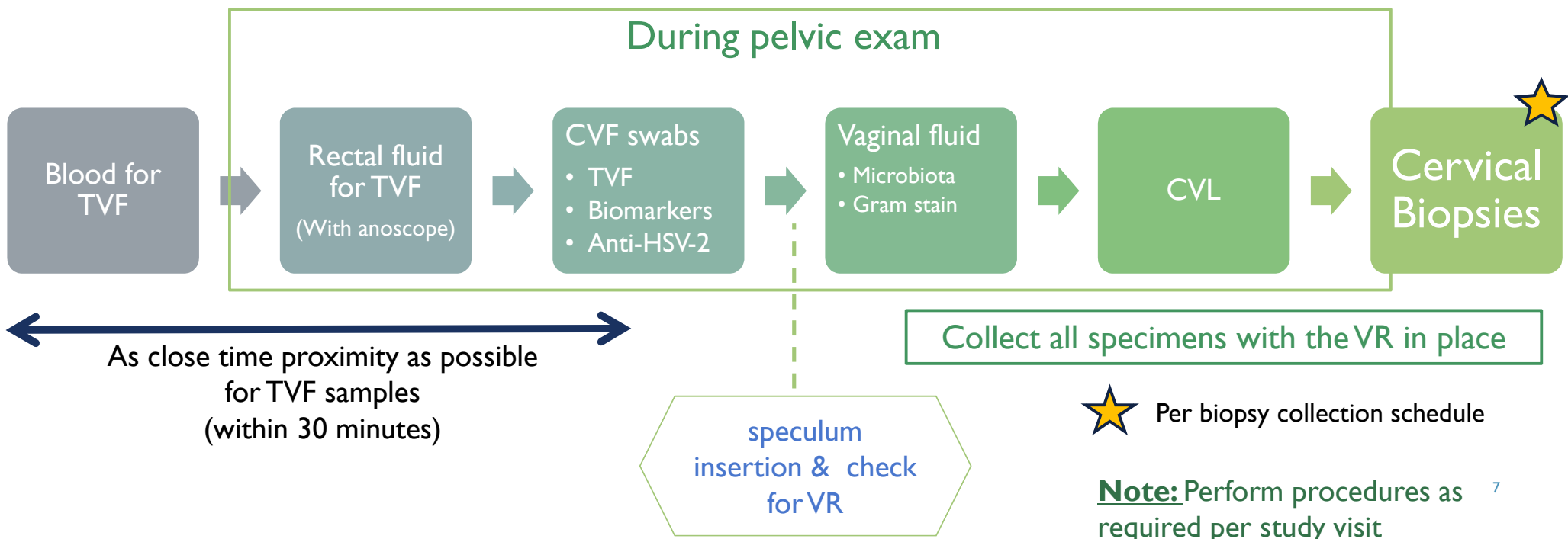
MTN-038 SITE-SPECIFIC TRAINING | 11 SEPT 2018- FOLLOW VISIT CONSIDERATIONS

Slide 6

LL3 added swabs for microbiota. Also added 'day 28 only' for biopsies
Lisa Levy, 9/5/2017

TM4 ok
Tara McClure, 9/5/2017

VISITS 3-8: SPECIMEN COLLECTION PROCEDURES

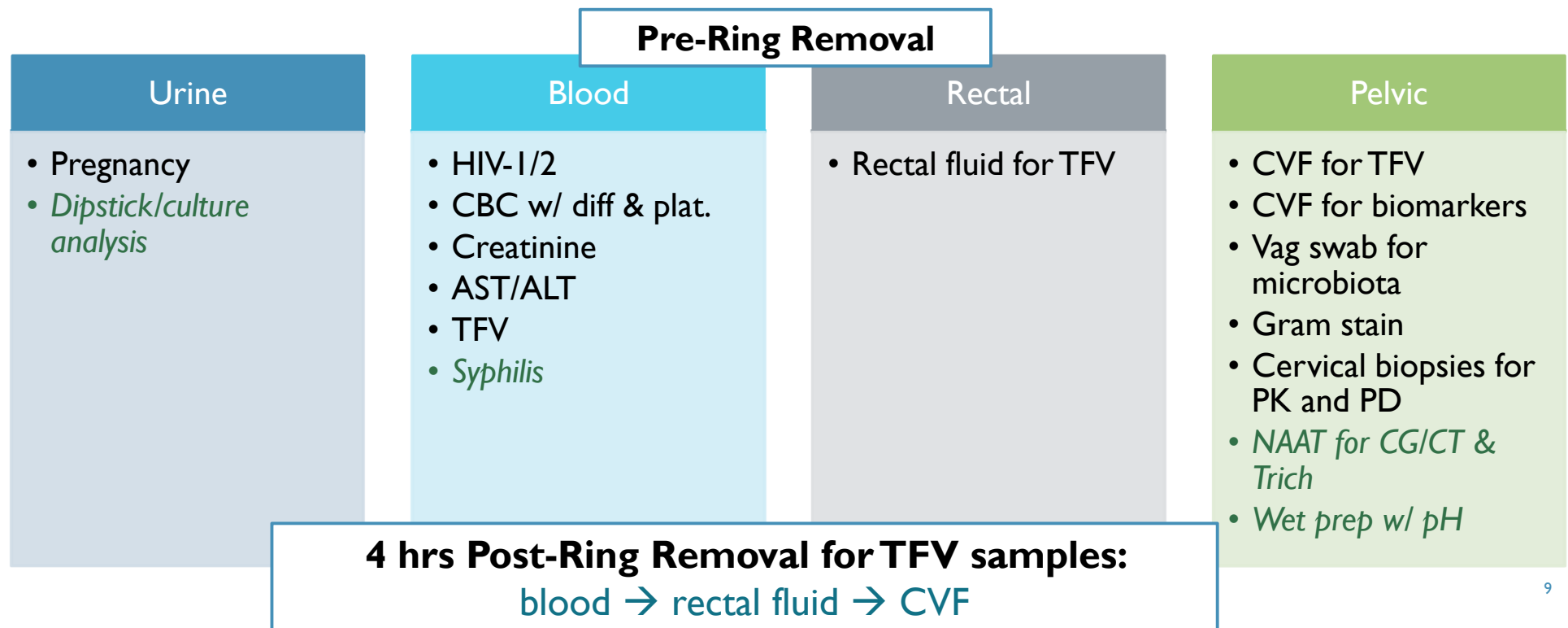


VISIT 9/ PUEV (DAY 91)/ EARLY TERMINATION

Administrative	Co-enrollment check, update locator, schedule next visit, provide reimbursement, <i>offer condoms*</i>
Behavioral	Ring Adherence CRF Exit CASI questionnaire <i>IDI (if selected/agreed at enrollment)*</i>
Counseling	HIV Pre-Post Test and STI Risk Reduction Contraceptive Protocol Adherence <i>*If indicated</i>
Clinical	Review/update medical/menstrual/meds history Assess AEs <i>Targeted Physical Exam</i> Pelvic Exam – check for VR Evaluate findings; <i>RX/refer for RTI/UTI/STI*</i> VR removal

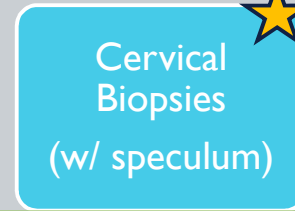
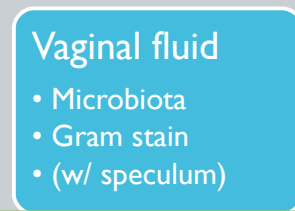
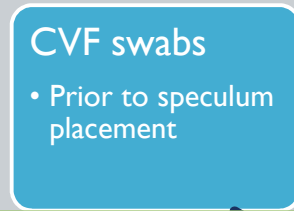
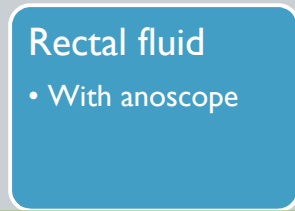
Serves as Early Study Termination Visit:
Complete all procedures and Study ⁸
Discontinuation CRF

VISIT 9/ PUEV (DAY 91) / EARLY TERMINATION, CON'T



VISIT 9/PUEV: SPECIMEN COLLECTION AND VR PROCEDURES

Pre-VR Removal



As close time proximity as possible (within 30 minutes)

Per biopsy collection schedule



Post-VR Removal

*Collect TFV samples within 30 minutes

Hour 4

- Blood
- Rectal fluid
- CFV

VISIT 10/ FINAL CONTACT (IN-CLINIC)

Administrative	Update locator, provide results from last visit, schedule next visit if needed, provide reimbursement, offer condoms
Behavioral	None
Counseling	<i>HIV Pre-Post Test and STI Risk Reduction*</i>
Clinical	Review/update medical/menstrual/meds history Assess AEs <i>Targeted Physical Exam*</i> Evaluate findings; <i>RX/refer for RTI/UTI/STI*</i>
Laboratory	Blood – TFV levels, <i>CBC w/ platelets/Diff, creatinine*</i> Rectal - fluid for TFV levels Pelvic – CVF for TFV levels, <i>wet mount w/ pH*</i> <i>Urine – Pregnancy, dipstick/ Culture analysis*</i>

Schedule 24-72 hours
after Day 91/PUEV

STUDY PROCEDURE EXCEPTIONS OF NOTE

- **Condoms offered** per site SOP/practice. Meant to provide exemption for when condoms use is not applicable such as if a participant has sex exclusively with women or is abstinent per the protocol inclusion criteria requirements.
- **Pregnancy test and contraceptive counseling** not required for participants who have undergone supracervical hysterectomy or bilateral oophorectomy verified by medical records
- If **HIV test results** will not be available during the visit, post-test counseling may occur upon provision of test results over the phone or in person as part of a split visit or at an interim visit, if indicated per local standard of care.

MISSED VISITS

- Visits not completed within the allowable visit window are considered “missed”
- Missed Visit CRF must be completed. If the visit is made-up *outside of the visit window*, log a PD with this reason selected.
- Follow your site-specific retention SOP for procedures to be done and proper documentation of efforts to contact participant

If **Visits 3-10 (Days 1, 7, 14, 28, 56, and/or Day 91/PUEV)** are missed:

- Make up the missed visit and required study procedures (as soon as possible) at an interim visit, and
- Retain the participant for her remaining scheduled study follow-up visits.
 - Note: If Day 91 is missed, the visit should be made-up as soon as possible and the Final Contact Visit should be schedule based on the actual PUEV (interim visit).



QUESTIONS? COMMENTS?