HPTN 084: Tips and Lessons Learned from 084 Sites

Questions regarding the safety assessments and clinical management of participants in HPTN 084 should be directed to the HPTN 084 Clinical Management Committee (084CMC@hptn.org).

General non-clinical questions should be directed to (084mgmt@hptn.org). Staff members from the HPTN LOC, HPTN Statistical and Data Management Center (SDMC), and HPTN Laboratory Center (LC) will receive the email. Emails with questions will be responded to by the most appropriate HPTN representative.

1. Missed Visits or Injections

- It has taken close to an hour for injectable product preparation; be sure to plan for any pharmacy-related delays for Injection Visits.
- Refer to your site's Pharmacy Establishment Plan (PEP) which outlines how the site Pharmacist of Record (PoR) will dispense study products- whether to a clinician, or directly to a participant. Both are acceptable so long as the clinician and participant remain BLINDED (unless unblinding has occurred for safety or pregnancy).
- If the syringe and needle need to be replaced, the study product must be prepared again by the site pharmacist.
    - If the site staff pulls back slightly on the plunger and sees blood present, the prepared syringe must be discarded. The content of the prepared injectable study product in the syringe MUST NOT be transferred from one syringe to another syringe by the site pharmacist as the content of the prepared syringe is now contaminated with participant's blood. Replacing injectable product is for the safety of site study personnel including site pharmacist and clinic staff. A new prescription must be sent to the site pharmacist with an explanation written on the prescription.
- Week 4 missed or late: Contact the CMC for guidance before you do anything!!! Participants who miss Week 4 must complete Week 4 procedures before moving to Week 5, regardless of the visit window. Week 4 is a mandatory visit, irrespective of the interval between Week 2 and Week 4 visit. The CMC will provide guidance on whether a transition to Step 2 may take place and if so, under what circumstances.

2. Adherence

- Pill counts are only conducted at Weeks 2 and 4 (Oral Safety Visits). These pill counts are done to insure adequate participant study product exposure before moving to injectable product. Pill counts are not formally conducted at visits in Step 2 or Step 3. Do collect pills at each visit so there are no spare bottles or study product at the participant's home.

3. Pregnancy

- At the first positive pregnancy test contact the CMC at 084cmc@hptn.org

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4. CPK, Liver Function, other laboratory testing/ results

- Contact 084mgmt@hptn.org for questions about lab redraws.
- Sites can proceed with the Week 5 injection while awaiting the LDL result. Contact SDMC for guidance on eCRF completion. Try to have the participant come back within 72 hours for LDL testing (after the Week 5 visit).
- In a scenario where there is a clinical indication for syphilis at the screening visit and syphilis testing is done at screening visit, it must be repeated at enrollment. STI positivity does not exclude enrollment. In fact, it demonstrates that the participant is high risk and a good candidate.
- The protocol inclusion and exclusion criteria were created with the goal of ensuring the safety of the participants. Therefore, laboratory values that are gradable but not exclusionary need to be considered in the context of the overall health of the participant.
- If a woman is on her menses at the enrollment visit and TV swab cannot be obtained, it should be collected as close to the enrollment visit as possible.
- A participant had a grade 2 platelets result of 81,000 at screening and the platelets were clumped/ reported as an inaccurate reflection of true platelet count.

  This is a legitimate result from the instrument, but the lab should not have released this as a result. A new draw had to be performed (Complete Blood Count or CBC). Some instruments have a tendency to have this happen (clumping) more frequently than others. As a reminder the sites should make sure they are following appropriate mixing of the tubes when collecting as this could attribute to platelet clumping.

5. Other

- One site mentioned that good Community engagement is critical for recruitment.
- One site is conducting mock visits to make sure it has thought through everything before participants come in.
- Carefully pre-screening study candidates and then having a group discussion amongst site staff (perhaps a weekly meeting) about each potential participant is helpful to avoid enrolling participants who may not be retainable. If a participant meets all inclusion/ exclusion criteria but you feel that she will not be retainable, you may invoke the “Investigator’s decision” clause in the Exclusion criteria. Be careful, though, as some difficult to retain participants may also be our highest risk. Contact the CMC if you have any doubts.
- Printing out the schedule of visits at Enrollment and again at Week 5 and giving it to participants so they can plan for those visits will hopefully reduce missed visits.
- One site has suggested that women who wish to be screened for the study, first be HIV-tested (after providing consent of course). That way, women who are HIV-infected will not need to undergo all of the additional screening procedures. You could also perform pre-screening,

which may include HIV rapid testing outside of the parameters of the study and would not require the long study consent. Of course, you will STILL need to perform all HIV testing procedures required at Screening when that visit does occur, making sure to obtain consent first.

- A PTID is generated when a participant signs the consent. In the event she doesn't return after the first visit, she is counted as a screen out.
- After participants complete the CASI and return tablets, staff must be careful not to hit buttons to go back into the participant's CASI session where it would be possible to change participant responses accidently. The SDMC has been alerted to this issue. In the meantime, site staff should take care not to accidently go back into the CASI session.
- Medidata Rave can be challenging to learn but with some practice, it is easy to use.
- Not all participants are computer literate, so it helps to assess that at the Screening visit, so that additional time can be allocated to computer education at the Enrollment visit.
- Check NA in Medidata for the Contraceptive Sub-study until it is up and running (question regarding whether the participant consented to participate).
- Check the prohibited meds list as some antacids may contain prohibited medication. Always contact the CMC if you have any doubts.
- In general, we want to avoid enrolling participants with underlying medical conditions and concomitant medications that can cause difficulty in deciding whether an adverse event should be attributed to the pre-existing condition or study product. The protocol eligibility criteria state the following: *"No medical condition that, in the opinion of the study investigator, would interfere with the conduct of the study".* This leaves the determination regarding enrolment of participants with comorbid conditions to the discretion of the site investigator. Sites should not feel compelled to enroll a participant that they are unsure would be suitable.
- Split visit at enrollment: A participant came for enrolment on the 15 October and completed the procedures prior to enrolment including blood draw and CASI. It was found that she was not fasting and so was informed that she would have to come in again to have the fasting blood test. She misunderstood this to mean she should leave and so left without being randomized.

  In instances of split Enrollment visits, both HIV rapid tests and pregnancy tests are required to be conducted the day of randomization (so those would likely be repeated). In this particular case, all labs should be repeated when the participant returns, and the HIV RNA test blood draw/ result must match the strict "14 day" guidelines noted in the protocol.