

# Study Closeout

***There is a lot of work left to be done!***

A brief overview:

- Data cleanup at the sites before database lock at SCHARP
- Communication with IRBs/ECs
- Unblinding of participants
- Planning for dissemination of results (at participant/community level and elsewhere)
- Preparation of manuscripts
- PPD closeout visits
- Destruction of leftover study drug
- Study record retention

...All while maintaining site and community morale

## Data Cleanup

SCHARP starts preparation for closeout about 2 months prior to last study visits. Scott and Tom will identify when last visit will take place at each site.

## Data Cleanup and SCHARP (con't.)

- SCHARP (Tom Perdue) identifies the target date for the final data lock (March 2008) based on study report needs, primary publications or regulatory submissions.
- SCHARP will send out official communications about the timeline for final data clean-up and the final dataset lock.

## Data Cleanup and SCHARP (con't.)

- One to two months prior to the target final study visit, the statisticians determine priority CRFs that contain the key study endpoints.
- These are to be cleaned/queries resolved first!

## Data Cleanup and SCHARP (con't.)

- After priority CRFs are identified, the study team determines the closeout QC report schedule.
- The query frequency rate will increase as closeout draws nearer.
- Query turn-around time must be short.

## Data Cleanup and Database Lock

- Prior to database lock, SAE reconciliation between the FHI and SCHARP databases will take place; you may receive queries from both groups.
- Pregnancies are followed to outcome - so if a participant becomes pregnant in November, the outcome will likely be reported around August. This will NOT hold up the primary HPTN 039 database lock. It is a separate database.

# Data Cleaning and Central Lab

*Prior to final database lock:*

- UW will retest 10% of all HSV-2 positive enrollment samples for HSV-2 ab for QA (done)
- CL and UW will retest all HIV positive seroconvertors baseline samples. CL will test an equal number of HIV negative samples for HIV ab
- CL anticipates completing HIV QA testing by end of August 2007 (dependent upon new seroconvertors)
- Keep shipping to CL quarterly – make sure to ship quickly after last participant visit in October or November

## Data Cleanup and Database Lock

- SCHARP (Tom Perdue) will inform you of the date for the last possible submission of DataFax CRF data.
- **If we want to lock by March 1, all queries must be resolved by February 14<sup>th</sup>.**

## Data Cleanup and Database Lock

- Once all of the CRF data have been submitted to SCHARP, the Investigator of Record at each site must sign the Participant Data Verification Form. This form verifies that all data have been submitted to SCHARP.

# Data Cleanup and Database Lock

- SCHARP will send an official notification to the study team and key DAIDS contractors (e.g., PPD) when the CRF database is finally locked.

# Data Cleanup and Unblinding

- At a time agreed upon by the study team, the randomization code will be broken by the protocol statistician to permit unblinding for (a) preparation of regulatory reports and/or manuscripts and (b) notification to sites of treatment assignments of each participant

# Participant Unblinding

- The study team will discuss and decide on the best time to unblind participants relative to availability/release of the primary study results
- Database does not have to be locked before we can unblind (not an IND trial), but it may be preferable to have preliminary results to share with participants when they are unblinded, so the timing is important (March 08?)
- SCHARP will provide a list with each participant randomization assignment to each site - via secure electronic file (March 08?)
- Once the general timing for unblinding is decided by the study team, sites should
  - should consult their CAB as necessary regarding best methods for informing participants about their study treatment assignment (letters, fact sheets, in person counseling scripts, etc.)
  - consider the level of staffing needed for the effort

# Manuscript Preparation/Publications

- A HPTN 039 publications committee will be formed to facilitate a process whereby manuscript concepts are solicited, prioritized, reviewed and tracked.
- The committee will include the study chairs, have reps from each site, SCHARP, the Central Lab, FHI and NIH.
- For each manuscript concept, lead authors and statisticians will be assigned and writing teams will be formed.
- FHI will facilitate the work of the 039 manuscript committee, submission of manuscripts for review, arrange calls for the committee and writing teams and tracks the progress of manuscript prioritized by the committee on a “manuscript status table”.

# Manuscript Preparation/Publications

- The HPTN Publication Policy to be followed
  - Specifies content and review requirements, authorship guidelines, etc.
  - Posted on HPTN website
- Lead author ensures adherence to timelines and submission for reviews
- HPTN Manuscript Review Committee (MRC) reviews draft manuscripts and meeting abstracts prior to submission to journals/meetings

# Communication with IRBs/ECs

- Must notify IRB/EC when all participant follow-up visits have been completed and provide this notification documentation to FHI.
- Determine your IRB/EC's requirements for
  - approval of materials or scripts used to inform participants of their treatment arm and the study results
  - continued annual renewal (e.g., when do they consider the study closed, their oversight responsibility completed and no longer require annual renewal)
  - post-trial reporting requirements (i.e., what must be included in a final report (SAEs, trial results, etc.)

# Additional Considerations for Study Closeout

- Close-out procedures must follow DAIDS and HPTN policies (both currently undergoing revision) – will be shared/reviewed with the study team and sites when finalized
- FHI to provide sites with a specific closeout checklist
- PPD will make a final close-out monitoring visit to each sometime after the final follow-up visit and before database closure.
- Leftover study product- will be destroyed according to your SOPs; however, if you have an Ancillary participant, DO NOT destroy replacement bottles. You will not have to destroy Ranbaxy product in conjunction with 039.

## Considerations for Study Closeout (con't.)

- Participants visits toward the end will need to be monitored closely to ensure that they are completed on time - the sooner the visits take place, the sooner data lock (Participants have 30 days after scheduled closeout date to complete the visit.)
- Participants might seroconvert at their last visit, potentially extending the Ancillary Study to July 08.
- Preliminary trial results (unlocked, unofficial) should be available late December with official results March 08.

## Dissemination of Data to Study Participants (con't.)

- Materials will be developed by the study team and others (UW, FHI, DAIDS) summarizing the study results for use/adaptation by site teams to develop scripts and other messages for the participants and for their communities
- Sites will need to plan for translation of these materials into local languages (and timeline for IRB approvals)
- Site should consider appropriate community forums to discuss the overall results of the trial and to answer questions
- Are there any other additional findings not related to the primary question that might be interesting to your community (secondary endpoints, adherence, implications of the study to the community, etc.)

# Post-trial access to acyclovir to participants

- We would like to offer acyclovir free of charge for one year to participants that were on placebo
- Logistics are difficult
  - Site staff availability for one year of dispensation (when can the clock start?)
  - Dispense 3 months' worth at a time?
  - Can the product be purchased in each country, therefore no shipping charges or time delays?
  - Manufacturing schedule.
  - This is NOT part of 039. What type of minimal health monitoring needs to continue and how will this be provided?
  - Possibly offer to all participants and not just those on placebo?

# Communication with the Media

## Press Release for Initial Public Release of Results

- To be drafted in collaboration with NIH then circulated to site PIs

## Media Communication Plan

- To be discussed in detail tomorrow
- Internal Site PI communication plan when results are unblinded (talk to staff)

# Disposition of Study Specimens

- No study specimens can be destroyed or used for any other purpose until all study-specific testing and QA is completed (as confirmed by the CL and SCHARP) and approval is obtained for destruction.
- Sites will need to work with SCHARP to determine which participants consented for long-term storage of their specimens; specimens from those who did not consent will need to be destroyed according to DAIDS/HPTN procedures.

# Study Record Retention

- **No study records are permitted to be destroyed without prior authorization from DAIDS.** For studies like HPTN 039 that are not under an IND, investigators must retain study records for a minimum of two years after study close-out. For all studies, retention of study records must also be in accordance with local Investigational Review Board/Ethics Committee (IRB/EC) policies and procedures.
- Sites will need to plan for long-term storage of records (security, space, etc.)

# THANKS!

I cannot stress to you enough what a privilege it has been for me professionally and **PERSONALLY** to have spent the past 4 years of my life with each and every one of you. You are a special group and I shall remember you all throughout my life.