

**HPTN 052 Study Monitoring Committee (SMC) Review**  
**Review Date: 1 May 2009**  
**10:00am – 12:00pm ET**

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**Participating SMC Reviewers:**

Jim Hughes, SMC Co-Chair, University of Washington  
Chuck Hicks, Duke University  
Ward Cates, Family Health International  
Craig Hendrix, Network Laboratory, Johns Hopkins University  
Sheryl Zwierski, Division of AIDS (DAIDS), National Institutes of Health  
Deborah Donnell, SCHARP

**HPTN 052 Protocol Chairs/Site Representatives:**

Mike Cohen, University of North Carolina, Chapel Hill, NC, USA  
Suwat Chariyalertsak, Research Institute for Health Sciences (RIHES), Chiang Mai, Thailand  
Sheela Godbole, National AIDS Research Institute, Pune, India  
James Hakim, University of Zimbabwe Clinical Research Center, Harare, Zimbabwe  
Breno Santos, Hospital Nossa Senhora da Conceição, Porto Alegre, Brazil  
N. Kumarasamy, YRG CARE, Chennai, India  
Francesca Conradie, Witwatersrand Clinical Research Site, Johannesburg, SA  
Guy de Bruyn, Chris Hani Baragwanath Hospital, Perinatal HIV Research Unit, Johannesburg, SA  
Joseph Makhema, Botswana–Harvard School of Public Health AIDS, Gaborone, Botswana  
David Celentano, Johns Hopkins Bloomberg School of Public, Baltimore, MD, USA

**Observers:**

David Burns, DAIDS	Nirupama Sista, HPTN CORE, FHI
Vanessa Elharrar, DAIDS	Marybeth McCauley, HPTN CORE, FHI
Estelle Piwowar-Manning, HPTN NL	Jacqueline Talley, HPTN CORE, FHI
San-San Ou, SCHARP	Theresa Gamble, HPTN CORE, FHI
Ying Chen, SCHARP	Phaedrea Watkins, HPTN CORE, FHI
Lei Wang, SCHARP	Charlyne Rich, HPTN CORE, FHI

**Meeting Format:**

10:00am – 10:30am: Review of closed report (SMC and SCHARP attendance only)  
10:30am – 11:15am: Review of open report (SMC, SCHARP, NL, and FHI)  
11:15am – 11:45am: Q and A session with protocol chair and site representatives  
11:45am – 12:00pm: Summary of SMC comments and recommendations (SMC, SCHARP, NL, and FHI)

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**Executive Summary:**

The HPTN Study Monitoring Committee (SMC) conducted its sixth review of HPTN 052 via teleconference on 1 May 2009. Data and performance indicators available from study visits conducted on or before 31 March 2009 were considered during the review. The SMC also conducted a confidential review of data in a closed session prior to the full SMC review.

The SMC congratulated the HPTN 052 team for doing an excellent job on what is a very challenging study, and in particular for addressing the enrollment concerns expressed on previous SMC reviews. It was noted during the call that – per the recommendation of the SMC from their May 2008 review – adjustments were made in order to reflect a more realistic rate of enrollment, and more realistic site-specific recruitment target numbers. Given these adjustments, and that two of the three new sites have or will begin enrollment soon (but later than originally anticipated), accrual is progressing such that enrollment is expected to be completed between December 2009 and June 2010.

In addition to enrollment as noted above, the SMC's review focused on retention of partners, adherence to study drug, possible prior exposure to ART for a small percentage of index cases, and operational concerns regarding HIV testing at the Rio de Janeiro site in Brazil, and the site in Pune, India.

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### Summary and Recommendations:

- The SMC recognized that much has been accomplished in the study to date, particularly with regard to improvements in enrollment. It was noted that the accrual numbers have been adjusted to reflect more realistic recruitment goals per site, and a more realistic timeframe in which to complete recruitment. It also was recognized that the site in Gaborone, Botswana has begun enrollment, and that the site in Soweto, South Africa will begin enrollment very soon. The site in Kenya will begin enrollment sometime later in the year, more likely toward the end of the summer/early fall.
- The SMC noted three items in the closed report that were deemed important to share with the Protocol Team, and in particular with the sites mentioned below. It was noted that sharing these items from the closed report would not otherwise impact study integrity:
  - 1) Tables 4a and 4b in the closed report (Expectation and Completion of HIV Testing per Quarterly Visit) indicate that at the some sites, Rio de Janeiro in particular, there is a surprisingly low rate of HIV testing among the partners who reported for study visits. The Table(s) will be shared with the team so that the sites have the relevant information to address the issue. It was recognized that it is possible that the HIV test result DataFax forms have not yet been sent to SCHARP from the visits in question. These tables will be added to future SMC open reports.
  - 2) Table 6 (ART Adherence by Pill Count, by Site for the Index Case), indicates that some sites show a relatively small percentage of participants that have  $\geq 95\%$  adherence to study drug (particularly sites in Porto Alegre, Brazil; Lilongwe, Malawi; and Chennai, India). The SMC recommended that all sites review their site-specific data, and for sites where adherence is low, review their adherence counseling or practices accordingly to ensure that participants understand the importance of taking their study drugs, and that high adherence rates are maintained. A modified version of this table (showing adherence percentage only) will be added to future SMC open reports.
  - 3) The SMC recommended that the HPTN Network Laboratory follow-up with the site in Pune, India regarding their HIV testing methodology, given that the closed report identified discrepant results in five out of five (100%) cases between a standard EIA test and a confirmatory western blot test that were performed for partners.
- The SMC recommended that the Protocol Team pay close attention to retention of couples, and in particular partners, since it was noted that there is a steady decrease in partner retention as the study has progressed. In addition, the SMC recommended that in future SMC reports SCHARP distinguish participants who were lost to follow-up and no longer in the risk set (e.g., terminated due to end of relationship) from those who are still in the risk set (i.e., terminated from the study but still has a sexual relationship with a index participant), because the latter category is more relevant to the analysis of the HIV transmission endpoint.
- The SMC recommended that the HPTN Network Laboratory (NL) perform quality control (QC) antiretroviral therapy (ART) drug screening on stored samples available at the NL in order to confirm ART use in index cases with undetectable viral load reported at enrollment. It was noted that in 40 index cases (4%) to date (see Table 10 of the open report), there was an undetectable viral load reported at enrollment. In addition, the SMC noted that there could be a site-specific

trend regarding this issue, *e.g.* 30% of index cases at the Johannesburg site had undetectable viral load at enrollment. The HPTN NL will report back to each site the results from this QC testing.

- The SMC recommended that the HPTN 052 Protocol Manager at SCHARP (Leslie Cottle) follow-up with the site in Johannesburg, South Africa, regarding their high QC rate (22.6 per 100 records, while the overall study has 5.5 per 100 records).
- The HPTN Network Laboratory had no additional concerns to discuss from what was already included in the open report.
- Lei Wang, one of the HPTN 052 protocol statisticians at SCHARP, read a brief statement submitted to the SMC from the Chair of the HPTN 052 Protocol Safety Review Team stating that, to date, there are no safety concerns in the study.
- It was noted that the next DSMB review of HPTN 052 is scheduled for May 19, 2009 at which time only accrual and retention issues will be considered. The next full DSMB review is scheduled for November, 2009.