



HPTN Study Operations Report

March 2010

HPTN Network Laboratory Update March 2010

HPTN 027 (Uganda only)

Specimens for antibody testing are being tested at the Johns Hopkins Medical Institute.

HPTN 046

A. General Comments

Version 3.0 dated 26 Sept, 2007

Enrollment at all sites has been stopped.

B. Site Specific

1. Harare - No new updates
2. Kampala - No new updates
3. Durban - No new updates
4. Dar es Salaam - No new updates

HPTN 052

A. General Comments

The NL is working on the hepatitis substudy. This is pending due to some IRB revisions needed at some sites to allow for the shipment of samples for hepatitis testing. The NL is working on QAing the viral loads from enrollment samples (<1000 copies/mL) A new QA list including samples for ARV testing and genotyping was sent out to the sites. We are waiting for two sites to ship samples to the NL.

B. Site Specific

1. Pune/NARI – The site has proposed a new site and new timeline has been submitted to DCLOT. The site is preparing the validation documents for the NL to review.
2. Harare - The site is working on the action plan from the NL November visit
3. Chennai - The site is also planning to move part of the laboratory. Pending documentation on the move.
4. Blantyre - The NL is working with the site on some processing issues.
5. Porto Alegre - the site has had a delay in receiving HIV EIA FDA approved kits. The kits were ordered several months ago. This is still pending.
6. Rio sites – No new updates
7. Lilongwe – Inventory has not been received for several months. Reminders have been sent to the lab manager.
8. Chiang Mai – No new updates
9. Johannesburg--WITs – No new updates
10. Soweto – No new updates.
11. Botswana – The lab is using the back-up for chemistry.
12. Kenya – No new updates

HPTN 057

A. General Information

--Cohort 4 has been added to the protocol. Labs have been asked to prepare documentation for Cohort 4.

--A new version of the SSP has been written to include Cohort 4. Lab section has been completed and sent to FHI.

B. Site Specific

1. Blantyre - No outstanding issues.
2. Santa Casa. Porto Alegre.- No outstanding issues.

3. UFMG. Belo Horizonte.- No outstanding issues.
4. HSE Rio.- No outstanding issues
5. HNSC. Porto Alegre - No outstanding issues.

HPTN 058

A. Site Specific

1. Thailand - No new updates
2. China sites.
 - a. **Xinjiang Site.**
Clinic has been moved to a new location while renovations are being made. All relevant validations have been performed.
 - b. **Guangxi.**
An additional clinic will be added in Nanning. All relevant validations have been performed. NL has issued approval for this clinic to perform UDS, pregnancy and HIV rapid testing.
3. An additional site in Vietnam is still being considered. Network Lab has been instructed to not communicate with the site until the site has been approved by the HPTN EC.

HPTN 061 and 064

A. General Information

Team protocol trainings for 061 and 064 have been completed. DCLOT has agreed with the Network Lab proposals for rapid HIV testing which allows sites to follow local state regulations.

B. 061 Site Specific

1. Fenway - No new updates
2. George Washington University - Notes to file submitted for Plasma storage that was not when drawn when 2nd Western Blot was collected.
3. San Francisco - No new updates.
4. Harlem - NL completed mid site assessment visit on February 9th 2010.
5. Atlanta - no new updates
6. New York Blood Center - NL completed mid site assessment visit on February 10th 2010. Protocol Deviation report still pending.
7. UCLA - no new updates

C. 064 Site Specific

1. North Carolina - No new updates.
2. New Jersey - No new updates
3. Washington DC - No new updates.
4. Bronx - No new updates
5. Baltimore - Note to file submitted from site indicating that the CD4 lab indicated in the site SOP was not used. Two PIDs were involved.
6. Harlem - No new updates
7. Atlanta - No new updates.

QC update

The following sites have been submitting their monthly QC reports:

1. UZ-UCSF
2. MUJHU
3. RIHES
4. Guangxi
5. Xinjiang
6. Lilongwe
7. NARI

8. YRG Care
9. Blantyre

NL updates

The NL is working on the incidence testing for both HPTN 043 and the domestic trials.

Travel Updates

- Estelle and LeTanya will be attending the HPTN 043 meeting in Chiang Mai in March.
- Vanessa will be attending the HPTN 063 training in Brazil in March.
- Paul is planning a site visit to Uganda and Tanzania in April.

Implementations Issues and Problems Summary March 2010

052

Enrollment is expected to be completed by the end of April 2010.

Refer to the Network Laboratory report for any issues and problems related to the clinical site laboratories.

058

Study drug cannot be shipped to the new site in Nanning until the site is officially approved within China for study drug dispensation. The study drug supply for this first shipment has an August 2010 expiry date.

061

To improve the number of index referrals, the study team has decided to expand "index" status to all participants who test HIV negative at enrollment. The LoA to allow this change should be sent to the medical officer for review in the first week of March. Analysis of the focus group data is taking place at this time, with the first transcript from each site already coded and reviewed. The qualitative team is finalizing the questionnaire for the qualitative interviews, expected to begin in March.

062

Accrual will be dependent on one site and its ability to identify acutely infected individuals within the lifespan of CHAVI 001.

063

The Zambian MOH did not approve the protocol because of the ban on sample exportation. The decision has been appealed and the site is in close communication with the MOH however, the study-specific training has been postponed until the MOH provides some indication that the study will be able to be approved.

The Brazilian central IRB (CONEP) took longer than expected to approve the study. The original submission was on 04 May 2009. The approval is dated for 16 December 2009, although the site was not notified of the approval until 03 February 2010. The site is now waiting to receive approval/sign-off from their MOH so that state department clearance can be issued. It is not clear how long this process will take. The site has confirmed that MOH approval is a formality once CONEP and local IRB approval are received which have both been done. However, we must have this approval in order to receive state department clearance.

064

Accrual and retention are both being monitored very closely at all sites to ensure study targets are met.

Report for HPTN Study Operations Group

HPTN 027

A PHASE I STUDY TO EVALUATE THE SAFETY AND IMMUNOGENICITY OF ALVAC-HIV vCP1521 IN INFANTS BORN TO HIV-1 INFECTED WOMEN IN UGANDA

Based on available data through: 8 March 2010

Participating Study Site:

Makerere University-Johns Hopkins University Research Collaboration/Mulago Hospital
Kampala, Uganda

Study Implementation Status:

24-month study follow-up is complete. Site has de-registered.

CRF Database was locked from any further submissions on 29 October.

Study samples are en route from the site to JHU for analysis. Some of the lab data assay data has been received from the Richmond Lab.

Accrual Status:

60 of 60 have been enrolled. Accrual is complete.

Status of Intervention Delivery:

N/A

Retention Status:

N/A

Report for HPTN Study Operations Group

HPTN 046

A phase III trial to determine the efficacy and safety of an extended regimen of nevirapine in infants born to HIV-infected women to prevent vertical transmission during breastfeeding

Based on available data through: 5 March 2010

Participating Study Sites:

CAPRISA Umlazi; Durban, South Africa
Muhimbili Hospital; Dar es Salaam, Tanzania
Mulago Hospital; Kampala, Uganda
Chitungwiza Clinics; Chitungwiza, Zimbabwe

Study Implementation Status:

Enrollment closed on 21 January. Randomizations will continue until all eligible enrolled infants reach 6 weeks of age. Randomization should continue until early March. As of 2 March, there were 6 infants remaining to be randomized.

Accrual Status:

The study enrolled 1674 mother-infant pairs [1699 infants in all].

Status of Intervention Delivery:

Retention Status:

There have been no retention issues identified at this time.

Implementation Issues and Problems:

No issues at this time.

Report for HPTN Study Operations Group

HPTN 052

A Randomized Trial to Evaluate the Effectiveness of Antiretroviral Therapy plus HIV Primary Care versus HIV Primary Care Alone to Prevent the Sexual Transmission of HIV-1 In Serodiscordant Couples *Based on available data through: 5 March 2010*

Participating Study Sites:

Gaborone, Botswana
Porto Alegre and Rio de Janeiro, Brazil
Chennai, India
Pune, India
Blantyre, Malawi
Lilongwe, Malawi
Johannesburg, South Africa
Soweto, South Africa
Chiang Mai, Thailand
Harare, Zimbabwe
Kisumu, Kenya

Study Implementation Status:

All sites listed above are operating under Version 3.0 of the protocol.

Accrual Status:

Below is site-reported screening and enrollment data; refer also to the SCHARP enrollment summary.

HPTN 052 Cumulative Screening and Enrollment Data															
Week Ending: 5 March 2010															
	Lilon gwe	RIHE S	NARI	Blant yre	Brazil - FIOCR UZ	Brazil - HGNI	Brazil - HNSC	YRG CARE	Zimb abwe	WITS SA	Bots wana	Sowe to	Kenya	Indivi duals	Cou ples
Date First Screened	04- Apr- 05	13- Jun- 05	22- Jun- 05	16- Aug- 05	13- Sep-05	03- Oct- 05	04- Jan- 06	08- Nov- 05	07- Dec- 05	07- Apr- 08	11- Mar- 09	21- May- 09	21- Oct- 09		
Date First Enrolled	12- Apr- 05	24- Jun- 05	01- Jul-05	25- Aug- 05	14- Sep-05	13- Oct- 05	30- Jan- 06	10- Nov- 05	09- Jan-06	20- May- 08	16- Apr- 09	11- Jun- 09	03- Nov- 09		
# Screened*	1494	546	696	1860	376	342	266	1106	2232	182	458	391	370	10357	n/a
# Enrolled - Individuals	498	212	336	442	206	144	174	500	430	86	128	82	76	3328	n/a
# Enrolled - Couples	251	107	168	224	103	72	87	250	221	43	64	41	44	n/a	1682
Eligible	506	206	376	442	208	144	174	600	482	82	160	92	80	3574	n/a
Ineligible	952	336	304	1370	164	186	94	498	1694	94	290	262	232	6492	3246
Eligibility Unknown	36	4	16	48	4	12	2	8	56	6	8	37	58	291	n/a
Individuals # Screened/Individuals # Enrolled	3.0	2.6	2.1	4.2	1.8	2.4	1.5	2.2	5.2	2.1	3.6	4.8	4.9	3.1	3.0

- *One participant may have multiple screening attempts.
- ** Fenway and HSE have been phased out of participation in HPTN 052 and will no longer screen and enroll participants.

- ***Total enrollment numbers in above chart account for couples enrolled at both Fenway and HSE, though not shown. As such, the total number of couples is always going to be 7 more than what each individual site enrolled adds up to – this is explained in the table below.

Termination/Transfer Status of Couples at Fenway and HSE:

	HSE	Fenway
# Couples enrolled during run-in period	5	2
# Terminated couples	2	2
# Transferred couples to IPEC	3	N/A
Date of last terminated/transferred couple	26 July 2007	9 May 2007

Retention Status:

Refer to the SCHARP retention summary.

Implementation Issues and Problems:

Enrollment is expected to be completed by the end of April 2010.

Refer to the Network Laboratory report for any issues and problems related to the clinical site laboratories.

Report for HPTN Study Operations Group

HPTN 057

A Phase I Open Label Trial of the Safety and Pharmacokinetics of Tenofovir Disoproxil Fumarate in HIV-1 Infected Pregnant Women and their Infants

Based on available data through: 5 March 2010

Participating Study Sites:

Malawi - Queen Elizabeth Central Hospital, Malawi College of Medicine-JHU Research Project, Blantyre (QECH)

Brazil - Federal University of Minas Gerais, Belo Horizonte (UFMG)

- Irmandade Santa Casa de Misericordia de Porto Alegre, Porto Alegre (Santa Casa)

- Hospital dos Servidores do Estado – Serviço de Doenças Infecciosas, Rio de Janeiro (HSD)

- Hospital Nossa Senhora da Conceicao Serviço de Infectologia, Porto Alegre (Conceicao)

Study Implementation Status: Enrollment into Cohorts 1, 2 and 3 was completed on Sept 16, 2008. A total of 81 evaluable mother/infant pairs were enrolled. Follow-up of participants in Cohorts 1, 2, and 3 is complete.

Accrual at all sites is temporarily closed pending protocol registration and site activation of protocol amendment Version 2.0, which will add a fourth cohort looking at a maternal dose during labor and daily infant dosing for 1 week.

The protocol amendment is final. Cohort 4 is anticipated to begin enrollment in early Q1 2010.

Study Drug is available for shipment to sites pending protocol registration

Accrual Status:

Below is the site reported enrollment summary for Cohorts 1, 2 and 3; refer also to the SHARP enrollment summary.

Site	# Evaluable Mother/Infant Pairs Enrolled (# c-section deliveries)		
	Cohort 1	Cohort 2	Cohort 3
Queen Elizabeth Central Hospital, Blantyre Malawi	24 (3)	16	15 (2)
Santa Casa, Porto Alegre Brazil	3 (2)	4	4 (2)
University of Minas Gerais, Belo Horizonte Brazil	3 (2)	1	2 (1)
Conceicao, Porto Alegre Brazil	-	-	4 (1)
Hospital do Servidores, Rio de Janeiro Brazil	-	-	5 (5)
Total	30	21	30

Status of Intervention Delivery:

TDF dispensing is complete. There were no reported significant problems with the dispensing of tenofovir to the mothers or infants.

Retention Status:

Two mother/infant pairs for Cohorts 1 – 3 have been lost to follow-up.

Implementation Issues and Problems:

**Report for HPTN Study Operations Group
HPTN 058**

**A Phase III randomized controlled trial to evaluate the efficacy of
drug treatment in prevention of HIV infection and death among
opiate dependent injectors**

Based on data available through 5 March 2010

Participating Study Sites:

- Xinjiang Uighur Autonomous Region, Centers for Disease Control and Prevention, Xinjiang, China
- Heng County, Guangxi Zhuang Autonomous Region, Centers for Disease Control and Prevention, Guangxi, China
- Guangxi Zhuang Autonomous Region, Centers for Disease Control and Prevention, Nanning, Guangxi, China
- Research Institute for Health Sciences, Chiang Mai, Thailand

Study Implementation Status:

Enrollment in Chiang Mai was capped at 202 participants. Xinjiang has enrolled 228 participants. Heng County, Guangxi has enrolled 211 participants. The clinic in Urumqi remains relocated to their proposed satellite site due to orders from the Chinese authorities. DAIDS issued an approval for this temporary relocation. It is hoped that the ban on foreign communication in Xinjiang will soon be lifted.

The Nanning site (also in Guangxi Province) has been approved by NIH and the local authorities and the site is working towards site activation which will not occur until study drug is on site.

Adding a site in Vietnam still remains a possibility. The team held a Site Selection Committee on 3 February 2010. The team discussed approving the site for development predicated on the site being able to meet certain deadlines for obtaining all approvals. This request was submitted to the EC for discussion on the 3 March call.

Marek Chawarski is in the process of revising the Counseling Manual. The team has continued regular conference calls with the counselors to address any questions they have about this component of the study.

A Data Safety Management Board (DSMB) review occurred on 26 February 2010 in Nanning. Several members of the protocol team attended. Trainings and assessments were held at both China sites and a US-China Joint Working Group Meeting was held 1 March 2010 in Beijing.

Discussions are under way to formulate a plan to allow Suboxone compassionate use for participants who have completed 058 follow-up.

Accrual Status:

	Chiang Mai	Guangxi	Xinjiang
Date First Screened	11-Apr-07	19-Dec-08	19-Dec-08
Date First Enrolled	30-May-07	24-Dec-08	21-Dec-08
# Individuals Screened	281	439	420
# Individuals Enrolled	202	211	228

Status of Intervention Delivery:

Study drug has been generally well tolerated.

Retention Status:

All Sites	
Week 26	87%
Week 52	83%
Week 78	75%
Week 104	80%
Week 130	74%

Implementation Issues and Problems:

Study drug cannot be shipped to the new site in Nanning until the site is officially approved within China for study drug dispensation. The study drug supply for this first shipment has an August 2010 expiry date.

Report for HPTN Study Operations Group

HPTN 061

Feasibility study of a community-level, multi-component intervention for Black men who have sex with men in preparation for a community-level randomized trial to test the efficacy of the intervention in reducing HIV incidence among Black men who have sex with men

Based on data available through: 01 March 2010

Participating Study Sites:

- Ponce de Leon Center CRS (site 5802) and Hope Clinic CRS (site 31440) in Atlanta and Decatur, Georgia, respectively
- San Francisco Vaccine and Prevention CRS in San Francisco, California (site 30305)
- New York Blood Center (NYBC)/Union Square CRS (site 31605) and Harlem Prevention Center CRS (site 30276) in New York City, New York
- University of California at Los Angeles (UCLA) Vine Street CRS (site 31607) in Los Angeles, California
- The Fenway Institute CRS (site 31602) in Boston, Massachusetts
- George Washington University CRS (site 31608) in Washington, D.C.

Study Implementation Status:

All sites for the HPTN 061 protocol are enrolling and following participants.

Site	Date of Activation	Date of First Enrollment
The Fenway Institute	06 July 2009	17 July 2009
George Washington University	20 July 2009	28 July 2009
San Francisco Vaccine and Prevention CRS	11 August 2009	13 August 2009
New York Blood Center	24 August 2009	01 October 2009
Hope Clinic CRS	04 September 2009	16 September 2009
UCLA	25 September 2009	29 September 2009
Ponce de Leon CRS	09 October 2009	N/A
Harlem Prevention Center	05 January 2010	08 January 2010

Accrual Status (participants enrolled at each site) as of 01 March 2010:

Fenway	GWU	Emory :Ponce +Hope	San Fran	UCLA	NYBC	Harlem	TOTAL
105	86	90	120	121	59	31	612

Status of Intervention Delivery:

To improve the number of index referrals, the study team has decided to expand "index" status to all participants who test HIV negative at enrollment. The LoA to allow this change

should be sent to the medical officer for review in the first week of March. Analysis of the focus group data is taking place at this time, with the first transcript from each site already coded and reviewed. The qualitative team is finalizing the questionnaire for the qualitative interviews, expected to begin in March.

Retention Status:

The early-activating sites are beginning to conduct six month visits. So far retention has been good with only a few participants not returning for their visits, but the site teams are confident that they will be able to locate those people and get them to come back.

Implementation Issues and Problems:

See above in "Status of Intervention Delivery"

Report for HPTN Study Operations Group

HPTN 062

Feasibility and Acceptability Study of an Individual-Level Behavioral Intervention for Individuals with Acute and Early HIV-Infection

Based on data available through: 02 March 2010

Participating Study Sites:

University of North Carolina Project, Kamuzu Central Hospital, Lilongwe, Malawi

Study Implementation Status:

Version 2.0 of the protocol, dated 10 September 2009, was approved by DAIDS and distributed to the sites on 16 September 2009. All IRB approvals have been received.

As of early February, the Blantyre site is no longer a participant in this study; this decision was made by the Prevention Management Group in January and is based on the cost of including Blantyre now that CHAVI 001 has ended there. A Letter of Amendment will be developed to address this change and a few other items in the protocol.

Lilongwe site was activated on 24 February 2010.

Accrual Status (completed at all sites):

No enrollment yet.

Status of Intervention Delivery:

No enrollment yet.

Retention Status:

N/A

Implementation Issues and Problems:

Accrual will be dependent on one site and its ability to identify acutely infected individuals within the lifespan of CHAVI 001.

Report for HPTN Study Operations Group

HPTN 063

Preparing for International Prevention Trials Involving HIV-Infected Individuals in Care Settings

Based on data available through: 01 March 2010

Participating Study Sites:

- Matero Clinic CRS; Lusaka, Zambia
- Chiang Mai University AIDS Prevention CRS; Chiang Mai, Thailand
- Instituto de Pesquisa Clinica Evandro Chagas (IPEC) CRS; Rio de Janeiro, Brazil

Study Implementation Status:

Version 1.0 of the protocol was granted final approval on 15 September 2008 and distributed to sites on the same day. The English version of the CRFs and ACASI scripts are final. The ACASI and CRFs have been translated into all 4 local languages (Portuguese, Thai, Bemba, and Nyanja). The Thai and Portuguese translations are complete. The Zambia sites and protocol team are currently finalizing the Bemba and Nyanja translations. The audio recordings are expected to be final in February and March.

The qualitative assessments for HPTN 063 were final as of 26 March 2009 and have been translated by the sites.

The Brazil site has received local and central IRB (CONEP) approvals and is currently awaiting state department clearance. Study specific training is currently taking place and will run from 1-5 March 2010.

The Zambia site received local and UAB IRB approvals but received a non-approval letter from the Ministry of Health (MOH) on 13 January 2010, due to a current ban on sample exportation. They have appealed the decision and are awaiting feedback.

The Chiang Mai site has received local and JHU IRB approvals for the protocol and informed consent forms. They submitted the final Thai language ACASI scripts for approval on 10 February 2010. Study specific training took place 25-29 January 2010. It is estimated that the site will be ready for activation in mid to late March.

Site activation activities are continuing at each site. The site training schedule is as follows: Thailand (25-29 January, 2010 - **Completed**), Zambia (8-12 March, 2010 - **Postponed**), and Brazil (1-5 March, 2010 - **In progress**).

Accrual Status:

Pending, no sites have been activated.

Retention Status:

Pending, no sites have been activated.

Implementation Issues and Problems:

The Zambian MOH did not approve the protocol because of the ban on sample exportation. The decision has been appealed and the site is in close communication with the MOH; however, the study-specific training has been postponed until the MOH provides some indication that the study will be able to be approved.

The Brazilian central IRB (CONEP) took longer than expected to approve the study. The original submission was on 04 May 2009. The approval is dated for 16 December 2009, although the site was not notified of the approval until 03 February 2010. The site is now waiting to receive approval/sign-off from their MOH so that state department clearance can be issued. It is not clear how long this process will take. The site has confirmed that MOH approval is a formality once CONEP and local IRB approval are received which have both been done. However, we must have this approval in order to receive state department clearance.

Report for HPTN Study Operations Group
HPTN 064
Women's Seroprevalence Study (ISIS)
Based on data available through: 05 March 10

Participating Study Sites:

- Emory University, Atlanta, Georgia (Ponce de Leon Center CRS and Hope Clinic CRS)
- Johns Hopkins Adult AIDS CRS, Baltimore, Maryland
- University of North Carolina-Chapel Hill, North Carolina (UNC AIDS CRS and Wake County Health and Human Services CRS)
- Columbia University, New York, New York (Bronx-Lebanon Hospital Center CRS and Harlem Prevention Center CRS)
- New Jersey Medical School Adult Clinical Trials Center, Newark, New Jersey
- George Washington University School of Public Health and Health Services, Washington D.C.

Study Implementation Status:

All HPTN 064 study sites have been activated and screening and enrollment is well underway.

The Bronx-Lebanon Hospital Center (BLHC) and the UNC AIDS CRS (both Durham and Wake counties) have both successfully enrolled a total of 210 women. GWU plans to enroll the additional 10 women during for a total of 210 women. All other sites, with the exception of Decatur and Harlem, have met their half-way points for recruitment.

The team had its first Study Monitoring Committee (SMC) Review on February 22, 2010. A draft of the recommendations and comments from the committee is in progress. Once the committee approves the draft, the final recommendations will be sent out to the team. The team will plan for another SMC review in approximately six months.

Accrual Status:

Please see SCHARP Enrollment Report.

Status of Intervention Delivery:

N/A

Retention Status:

Please see SCHARP Retention Report.

Implementation Issues and Problems:

Accrual and retention are both being monitored very closely at all sites to ensure study targets are met.

Appendix: HPTN Protocols and INDs

Protocol #		IND	IND Sponsor	Study Status
HPTN 027	A Phase I Study to Evaluate the Safety and Immunogenicity of ALVAC-HIV vCP1521 in Infants Born to HIV-1 Infected Women in Uganda	BB-IND 12023	DAIDS	Closed to Accrual
HPTN 046	Phase III Trial to Determine the Efficacy and Safety of an Extended Regimen of Nevirapine in Infants Born to HIV Infected Women to Prevent Vertical HIV Transmission During Breastfeeding	72,592	DAIDS	Closed to Accrual
HPTN 052	A Randomized Trial to Evaluate the Effectiveness of Antiretroviral Therapy Plus HIV Primary Care versus HIV Primary Care Alone to Prevent the Sexual Transmission of HIV-1 in Serodiscordant Couples	68,535	DAIDS	Enrolling
HPTN 057	A Phase I Open Label Trial of the Safety and Pharmacokinetics of Tenofovir Disoproxil Fumarate in HIV-1 Infected Pregnant Women and their Infants	72,531	DAIDS	Closed to Accrual
HPTN 058	A Phase III randomized controlled trial to evaluate the efficacy of drug treatment in prevention of HIV infection and death among opiate dependent injectors	73,797	DAIDS	Enrolling