

## Clarification Memo # 1 to:

### HPTN 077: A Phase IIa Study to Evaluate the Safety, Tolerability and Pharmacokinetics of the Investigational Injectable HIV Integrase Inhibitor, GSK1265744, in HIV-uninfected Men and Women, Version 2.0, dated November 18, 2014

Final Version: 04 December 2014

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#### Summary of Revisions and Rationale

Section 3.1, Inclusion Criteria, correctly indicates that total bilirubin and direct bilirubin should be completed at Screening. Direct bilirubin was inadvertently omitted in the following corresponding sections of the protocol that discuss screening or general procedures: Section 5.1, Section 9.1 and the Schedule of Procedures and Evaluations. This Clarification Memo corrects this omission. Additionally, in Section 6.4.2, only total bilirubin should be reported, and this has been clarified.

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#### Implementation

The modifications included in this memorandum have been approved by the Division of AIDS (DAIDS) Medical Officer and are to be implemented immediately upon each site's respective study activation of Version 2.0 of the protocol. Investigational Review Board (IRB)/Ethics Committee (EC)/other regulatory entity approval of HPTN 077 Protocol Clarification Memo #1 to HPTN 077 V. 2.0 is not required by DAIDS; however, sites may submit it to the responsible IRBs/ECs/other regulatory entities for their information or, if required by the IRBs/ECs/other regulatory entities, for their approval prior to implementation.

None of the clarifications being made impact the sample informed consent forms, and the benefit-to-risk ratio for participants is not affected in any way.

The modifications included in this Clarification Memo will be incorporated into the next full protocol amendment. Text appearing below in highlighted **bold** will be added.

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#### **Revision 1** Section 5.1: Screening

##### Laboratory Evaluations

- HIV testing (see SSP Manual), including testing for acute HIV infection within 14 days prior to enrollment
- Hepatitis testing: HBsAg, HBsAb, HBcAb, HCAb
- CBC with differential
- Chemistry testing (see Appendix I)
- Liver function testing (AST, ALT, total **and direct** bilirubin, and alkaline phosphatase)
- Syphilis testing
- GC/CT testing (urine for men and either urine or vaginal swab for women)
- Plasma storage
- Urine pregnancy testing (for women of reproductive potential)

**Revision 2** Section 6.4.2: Reporting Requirements for this Study

The Serious Adverse Event (SAE) Reporting Category, as defined in Version 2.0 of the DAIDS EAE manual, will be used for this study (the definition of an SAE is also included in the manual).

In addition to SAEs, sites will report in an expedited manner the following results (must be both in order to require expedited reporting): ALT $\geq$ 3xULN AND **total** bilirubin $\geq$ 2xULN.

These reporting requirements are required for each study participant from enrollment (week 0) until their follow-up in the study ends. After this time, sites must report serious, unexpected, clinical suspected adverse drug reactions if the study site becomes aware of the event on a passive basis, i.e., from publicly available information.

The study agents for the purposes of EAE reporting are GSK1265744 30 mg oral tablet or placebo and 744LA injectable suspension (200mg/mL) or placebo (also outlined in Section 4.1.).

**Revision 3** Section 9.1: Local Laboratory Specimens

The following types of tests will be performed at the local laboratory:

- HIV testing (see SSP Manual)
- HBV and HCV testing to include hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (HBsAb), hepatitis B core antibody (HBcAb) and hepatitis C antibody (HCV) tests
- CBC with differential and platelets
- Chemistry testing (BUN/urea, Na, K, Cl, CO<sub>2</sub>, CPK, creatinine, total protein, glucose, calcium, phosphorous, amylase, lipase, magnesium)
- LFTs (AST, ALT, total **and direct** bilirubin, alkaline phosphatase)
- Fasting lipid profile (total cholesterol, HDL, triglycerides, LDL – calculated or measured (participants should be fasting for at least 8 [preferably 12] hours prior to sample collection)
- Syphilis serologic testing (men and women)
- Urine for GC/CT testing for men and women. (may be replaced with a vaginal swab in women if desired)
- Urinalysis (protein and glucose)
- Urine test for pregnancy\*
- Rectal swabs for GC/CT for men and women (for non-US sites, batch and ship to the HPTN LC; for US sites, testing will be performed locally)
- Plasma storage
- Plasma storage for Pharmacology testing
- Sample storage for Pharmacogenomic testing (sites may choose to opt out of this testing if is not acceptable to local regulatory bodies or for other reasons approved by the protocol team)
- Following a positive or reactive HIV test result: HIV viral load, CD4 cell count, HIV resistance testing at a local laboratory (real-time resistance testing for clinical management is optional, at the site's discretion), plasma storage.

Revision 4 Appendix I: Schedule of Procedures and Evaluations. Only the section called “Local Laboratory Evaluations & Procedures” from the Schedule of Procedures and Evaluations is shown below for ease of reference.

	Screening	Oral Phase			1-WEEK	Injection And Tail Phase Follow-up								
		Day 0 Enr	Week 2 Safety	Week 4 Post Oral Drug		Week 5 First Injection	Week 6, 9, 13 Safety	Week 17 Second Injection	Week 18, 23 Safety	Week 29 Third Injection	Week 30, 35 Safety	Week 41 Primary Endpoint	Week 53, 65, 77 Tail Phase	Week 81 Final Visit
<b>LOCAL LABORATORY EVALUATIONS &amp; PROCEDURES</b>														
HIV testing <sup>7</sup>	X	X	X	X		X	X	X	X	X	X	X	X	X
HBV and HCV testing <sup>8</sup>	X													
CBC with differential	X	X	X	X		X	X	X	X	X	X	X		
Chemistry testing <sup>9</sup>	X	X	X	X		X	X	X	X	X	X	X		
LFTs (AST, ALT, total bilirubin, [at screening only, direct bilirubin in addition to total], alkaline phosphatase)	X	X	X	X		X	X	X	X	X	X	X	X	X
Fasting lipid profile <sup>10</sup>		X										X		
Syphilis serologic testing men and women <sup>5</sup>	X									X			X	
Urine/ vaginal swab GC/CT testing men and women <sup>5</sup>	X									X			X	
Rectal swab GC/CT testing <sup>5</sup>		X								X			X	
Urinalysis <sup>11</sup>		X										X		