

Protocol Clarification Memorandum #2 for:

HPTN 046: A PHASE III TRIAL TO DETERMINE THE EFFICACY AND SAFETY OF AN EXTENDED REGIMEN OF NEVERAPINE IN INFANTS BORN TO HIV-INFECTED WOMEN TO PREVENT VERTICAL HIV TRANSMISSION DURING BREAST-FEEDING, VERSION 3.0, DATED 26 SEPTMEBER 2007

DAIDS Document ID 10142

Clarification Memo Date: 20 February 2009

Summary of Revisions and Rationale

It is clarified that the laboratory parameters on which infant enrollment criteria are based (ALT, hemoglobin, absolute neutrophil count and platelet count) can be re-assessed prior to final eligibility determination/enrollment if initial testing reveals exclusionary abnormalities in an infant otherwise likely to be eligible for study participation. The “birth specimen” is considered the final blood sample obtained on or before Day 7 of life that is used to confirm eligibility for enrollment. While this was the original intent and represents no change in study procedures, it was not explicitly stated in the current version of the protocol.

Implementation

The procedures clarified in this memorandum have been approved by the NIAID Medical Officer. IRB approval of this Clarification Memorandum is not required by the sponsor prior to implementation; however sites may submit it to the responsible IRBs/ECs for their information or, if required by the IRBs/ECs, for their approval prior to implementation.

The modifications included in this Clarification Memorandum will be incorporated into the next full protocol amendment.

Section 4.2 Infant Enrollment Criteria

The following text (in bold) will be added after the last bullet:

Infants who meet any of the following criteria will be excluded from enrollment into the study:

- ALT from birth specimen is Grade 2 or higher.
- Hemoglobin, absolute neutrophil count or platelet count from birth specimen is Grade 3 or higher

- Skin rash grade 2B (urticaria) or skin rash grade 3 or above
- Confirmed or suspected clinical hepatitis, defined as clinical signs and symptoms of clinical hepatic dysfunction including but not necessarily limited to enlarged liver (>4 cm below right costal margin), hepatic tenderness and/or ascites.
- Serious illness or condition that would prohibit compliance with study procedures as judged by site clinician

Note: Abnormal laboratory results as specified above (ALT, hemoglobin, absolute neutrophil count and platelet count) may be re-assessed as necessary on or before Day 7, and if the infant meets all the eligibility criteria, s/he can be enrolled. The “birth specimen” is considered the final specimen obtained on or before Day 7 of life that is used to confirm eligibility for enrollment.