DATE: April 25, 2006

RE: LETTER OF AMENDMENT #5 for PACTG P1059, “A Phase I, Open-Label Study to Evaluate the Safety and Tolerability of Recombinant HIV-1 Vaccines in HIV-1 Infected Young Adults with Control of HIV-1 Replication and on Stable Highly Active Antiretroviral Therapy (HAART)”, Version 1.0, dated January 31, 2005 – ECG at Early Discontinuation Visit

TO: Pediatric ACTG PIs & Study Coordinators at Sites Participating in PACTG P1059

FROM: The PACTG P1059 Protocol Team

THE FOLLOWING INFORMATION IMPACTS THE P1059 STUDY AND MUST BE FORWARDED TO YOUR INSTITUTIONAL REVIEW BOARD (IRB)/ETHICS COMMITTEE (EC) AS SOON AS POSSIBLE FOR THEIR INFORMATION AND REVIEW. THIS MUST BE APPROVED BY YOUR IRB/EC BEFORE IMPLEMENTATION.

THE FOLLOWING INFORMATION MAY ALSO IMPACT THE SAMPLE INFORMED CONSENT. YOUR IRB/EC WILL BE RESPONSIBLE FOR DETERMINING THE PROCESS OF INFORMING SUBJECTS OF THE CONTENTS OF THIS LETTER OF AMENDMENT.

PLEASE FILE THIS LETTER AND ANY IRB/EC CORRESPONDENCE IN YOUR REGULATORY FILE AND OTHER PERTINENT FILES. YOU ARE NOT REQUIRED TO SUBMIT THESE DOCUMENTS TO THE PROTOCOL REGISTRATION OFFICE UNLESS THE CHANGES RESULT IN A CHANGE TO THE INFORMED CONSENT FOR YOUR SITE.

This Letter of Amendment is being issued to change entry criteria, criteria for immunization, and toxicity management of hyperbilirubinemia in subjects being treated with atazanavir.

Inclusion criterion 4.14 will be changed to read as follows:

4.14 The following lab values:
Creatine Phosphokinase ≤ 1.5 x ULN. (If 1-1.5 x ULN, CPK must be fractionated and MB must be within normal limits.)
Troponin I ≤ 1.0 x ULN
Hemoglobin >10 g/dL
Absolute Neutrophil Count >1000 mm3
Platelets >100,000 mm3
ALT, AST ≤ 1.5 x ULN
* total bilirubin ≤ 1.5 x ULN; for potential subjects receiving atazanavir, see below.
Creatinine <1.5 mg/dL

* Subjects on atazanavir may be enrolled with any value of total bilirubin less than Grade 4 if direct bilirubin and concurrent transaminase values are ≤ 1.5 x ULN and subjects are asymptomatic. Subjects with a Grade 4 total bilirubin can be re-screened and enrolled if a subsequent level is less than Grade 4 and all other hepatic measures remain unchanged in grade from initial protocol screening values.
Section 4.6, Criteria for Immunization, will have the following information added to the second from last bullet point:

- Any Grade 3 or non-life threatening Grade 4 laboratory values diagnosed since the immediate prior immunization (or since screening if subject is receiving first immunization) unresolved within 7 days of the current immunization. Subjects being treated with atazanavir must have total bilirubin values <Grade 4 with concurrent transaminase values ≤1.5 x ULN and be asymptomatic.

Section 6.15 will have the following statement added:

6.15 If a Grade 3 or non-life threatening Grade 4 toxicity is unrelated to immunization and resolves to no greater than 1 grade above value at screening within 7 days of the next scheduled immunization, the next dose of study vaccine may be administered. If there is no recurrence of toxicity after the next dose, subsequent immunizations will continue. If the toxicity recurs, immunizations will be discontinued. For subjects being treated with atazanavir, total bilirubin values must be <Grade 4 with concurrent transaminase values ≤1.5 x ULN and be asymptomatic.

The above information will be incorporated into the next version of the protocol at a later time if it is amended.

Thank you for your interest in PACTG P1059. Please contact the protocol team at actg.teamp1059@fstrf.org if you have any questions.