DATE: October 29, 2004

RE: LETTER OF AMENDMENT #3 for PACTG P1057, “A Phase I/II Randomized Trial of the Safety and Immunogenicity of Cold Adapted Influenza Vaccine (Flumist™) in HIV-Infected Children and Adolescents”, Version 1.0, dated August 13, 2004

TO: Pediatric ACTG PIs & Study Coordinators at Sites Participating in PACTG P1057

FROM: The PACTG P1057 Protocol Team

THE FOLLOWING INFORMATION IMPACTS THE P1057 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 modify Appendix I of the P1057 protocol. The modification will allow sites the option of conducting home visits for completion of the day 3 and day 14 post-vaccination visits for subjects enrolled in Arm A.

1. Section 3.0, page 15, under Clinical Evaluations, the last sentence of the third bullet should read “Subjects on Arm A (Flumist™) will be seen in clinic or at home on those days.”

2. Section 8.5, page 32, Stopping Rules, the second sentence of the fourth paragraph should read “The same information will be collected via personal contact for Arm A-Flumist™ during clinic visits on Days 3, 14 and 28 (or home visits on Days 3 and 14), and by phone on Days 7, 21, and 42.”

3. In the columns for 3 and 14 days post-vaccination, Footnote 11 will be added to the top of the column.

4. **Footnote 11** will be added to the end of the list of footnotes in Appendix I:

   “Sites have the option of completing the day 3 and day 14 post-vaccination visits at the subject’s home. Height and weight will not be required for these visits if they are completed in the subject’s home; do not use a scale available in the subject’s home since there is no way to guarantee accuracy. If a subject or their caretaker reports an acute diarrheal illness since vaccination, the subject will be required to complete the visit at the clinic so that accurate height and weight measurements can be obtained. The subject/caretaker should be contacted by telephone prior to any planned home visits to determine if a clinic visit is necessary.”
“All other evaluations (vital signs, symptoms, chest auscultation, and nasal swab collection) will be completed if the day 3 and/or day 14 post-vaccination visit are done in the subject’s home.”

In addition, this Letter of Amendment will change the date that vaccinations must be completed. Rather than requiring all vaccinations to be administered by November 19, 2004, the team has agreed that vaccinations may be administered through December 3, 2004.

1. Schema – Regimen: Should be changed to read “All subjects will receive influenza immunization starting as soon as possible in September 2004 and as late as December 3, 2004.”

2. Section 3.0 – Study Design: Third sentence of first bullet should be modified to read “Sites will continue to vaccinate subjects through December 3, 2004.” The last sentence should be modified to read “The date of November 19th was chosen in anticipation of allowing 2 weeks for an immune response to be present by the time influenza infection is present in the community; however, the lack of flu vaccine availability until later than anticipated forced the study team to change the last date for vaccinations to December 3, 2004 to allow adequate time for accrual.”

3. Section 4.7 – Enrollment Procedures: Second paragraph (after first bullet) should be modified to read “The vaccination period is anticipated to begin with availability of the designated vaccines at PACTG sites in September 2004 and continue until December 3, 2004.”

4. Section 5.1 – Vaccine Regimens, Administration, and Duration: Second paragraph should be changed to “Influenza Virus Vaccine Live, Intranasal (FluMist™) or Influenza Virus Vaccine, Intramuscular (IAIV) will be administered as a single dose in September 2004 through December 3, 2004.”

5. Section 8.4 – Sample Size and Accrual: Second sentence of first paragraph should be changed to “All subjects (150 in each arm) need to be enrolled between the time the study opens to accrual at PACTG sites and the last date of vaccination (December 3, 2004) because of the changing nature of the influenza vaccines from year to year.”

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 P1057. Please contact the protocol team at actg.teamp1057@fstrf.org if you have any questions.