Clarification Memorandum #1 for:

IMPAACT P1026s

Pharmacokinetic Properties of Antiretroviral and Related Drugs During Pregnancy and Postpartum, Version 9.0, dated 22 September 2014

(DAIDS Document ID 10040)
IND # 64,535 held by NIAID

Clarification Memorandum Date: 24 November 2014

Information/Instructions to Study Sites

This Clarification Memorandum has been approved by the NIAID Medical Officers. Institutional Review Board/Ethics Committee (IRB/EC) 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.

This Clarification Memorandum should be maintained in each site’s essential documents file for IMPAACT P1026s. It is the responsibility of the Investigator of Record to ensure that all study staff are made aware of and follow this Clarification Memorandum.

Summary of Clarifications and Rationale

Minor clarifications of the required timing and frequency of evaluations for infants are incorporated and minor inconsistencies are corrected.

Implementation

The modifications included in this Clarification Memorandum will be incorporated into the next protocol amendment as specified below. Additions to the text are indicated in bold; deletions are indicated by strike-through.

1. Protocol Cover-Page and Protocol Team Roster

   Protocol cover page - Brookie Best, PharmD, MAS is added as a Protocol Vice-Chair, as is indicated, in the IMPAACT Protocol Team Roster and Nahida Chakhtoura, MD, MsGH replaces Lynne Mofenson, MD as the NICHD Medical Officer.

   Protocol Team Roster - Nahida Chakhtoura, MD, MsGH replaces Lynne Mofenson, MD as the NICHD Medical Officer.
2. Sections 4.21 and 4.22

Antiretroviral drug is clarified to mean antiretroviral or other study drug in exclusion criterion 4.21, as specified below.

4.21 Women on medicines known to interfere with absorption, metabolism, or clearance of the antiretroviral drug being evaluated (See Section 7.0). (rifampicin permitted for women being evaluated for TB and ARV drug interactions).

4.22 Women; If pregnant, carrying multiple fetuses

3. Appendix II, Schedule of Evaluations for Infants

- The “24 weeks of life” visit is clarified as follows: 24 weeks means 24 +/- 8 weeks. The column header is clarified, as follows:

  24 weeks of life
  +/- 8 weeks

- The ‘5 – 9 days of life’ visit is for pk sampling and thus applies to infants undergoing washout PK sampling, the column header is clarified, as follows: [Note: Site specific consent forms may be modified to address this clarification]

  5 – 9 days of life
  (infants undergoing washout PK only)

4. Appendix III, Maternal Intensive PK Sampling Schedule for ARV Medicines, Tuberculosis Treatment and Hormonal Contraceptives

Due to a typo, the pharmacokinetic sampling instructions for the two efavirenz with contraceptive arms were interchanged and have been corrected, as follows:

<table>
<thead>
<tr>
<th>ARVS WITH CONTRACEPTIVES</th>
<th>24 hour sampling 2-12 weeks postpartum for ARVs and 24 hour sampling 6-7 weeks after contraceptive initiation for both ARVs and contraceptives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atazanavir/ritonavir/tenofovir with ethinyl estradiol containing contraceptives</td>
<td>24 hour sampling 2-12 weeks postpartum for ARVs and 24 hour sampling 6-7 weeks after contraceptive initiation for both ARVs and contraceptives</td>
</tr>
<tr>
<td>Efavirenz with ethinyl estradiol containing contraceptives</td>
<td>24 hour sampling 2-12 weeks postpartum for ARVs and 24 hour sampling 6-7 weeks after contraceptive initiation for both ARVs and contraceptives</td>
</tr>
<tr>
<td>Atazanavir/ritonavir/tenofovir with etonogestrel implant</td>
<td>24 hour sampling 2-12 weeks postpartum for ARVs and 24 hour sampling 6-7 weeks after contraceptive initiation for ARVs and a single sample for etonogestrel implant PK.</td>
</tr>
<tr>
<td>Efavirenz with etonogestrel implant</td>
<td>24 hour sampling 2-12 weeks postpartum for ARVs and 24 hour sampling 6-7 weeks after contraceptive initiation for ARVs and a single sample for etonogestrel implant PK.</td>
</tr>
</tbody>
</table>

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