P1026s
Pharmacokinetic Properties of Antiretroviral Drugs During Pregnancy
V 10.0, LoA#1

IMPAAACT Annual Meeting Study Training 31 May 2017
Study Highlight: P1026s
Pharmacokinetic Properties of Antiretroviral Therapy During Pregnancy

As of 16 May 2017, 931 mothers and 442 infants enrolled

Completed pregnancy arms for 17 ARVs, including darunavir, rilpivirine, maraviroc, dolutegravir and elvitegravir

Presented 32 abstracts and published 20 manuscripts
Study Highlight: P1026s

Contributions to Perinatal HHS Guidelines

• P1026s PK data cited for 63% (17) of the 27 ARV drugs in the current published HHS perinatal guidelines
  – P1026s is the only cited source of pregnancy PK data for 15% (4) of these 27 ARV drugs (DTG, EFV, MVC, RPV)
• P1026s responsible for 32% (24) of the 76 PK in pregnancy studies cited in perinatal guidelines

<table>
<thead>
<tr>
<th>Class</th>
<th>P1026s Citations/Total # of PK studies in Pregnancy* Citations</th>
<th>Percent of Data from P1026s</th>
</tr>
</thead>
<tbody>
<tr>
<td>NRTI</td>
<td>3/19</td>
<td>16%</td>
</tr>
<tr>
<td>NNRTI</td>
<td>4/9</td>
<td>44%</td>
</tr>
<tr>
<td>PI</td>
<td>12/40</td>
<td>30%</td>
</tr>
<tr>
<td>INSTI</td>
<td>2/4</td>
<td>50%</td>
</tr>
<tr>
<td>Entry/Fusion</td>
<td>1/1</td>
<td>100%</td>
</tr>
<tr>
<td>PK Enhancers</td>
<td>2/3</td>
<td>67%</td>
</tr>
</tbody>
</table>

*Excludes case reports
P1026s Study Objectives

1. To describe the PK parameters of selected ARV drugs in HIV-infected pregnant women.

2. To describe the PK parameters of selected ARV drugs (EFV, LPV/r) and first line TB drugs when co-administered in HIV-infected pregnant women and of first line TB drugs in HIV-uninfected pregnant women.

3. To describe the PK parameters of second line TB drugs in HIV-infected pregnant women.

4. To describe the PK parameters of ARV drugs in postpartum women before and after starting hormonal contraceptives.

5. To describe the concentrations of ethinyl estradiol, etonogestrel and other progestins in women using hormonal contraceptives and selected ARV drugs.
OPENED:
Original Version - March 17, 2003
Current Version 10.0 – February 2, 2016

DESIGN: Phase IV, prospective pharmacokinetic (PK) study

SAMPLE SIZE:
Minimum enrollment per arm: 12 women
Enrollment target per arm:
• 25 women with evaluable 3rd trimester PK data for pregnancy arms
• 25 women with evaluable postpartum PK data for hormonal contraceptive arms
P1026s Study Populations

ANTEPARTUM

– HIV-infected pregnant women enrolled between 20 and 36 weeks gestation receiving selected ARVs with or without TB drugs

– HIV-uninfected pregnant women enrolled between 20 and 36 weeks gestation receiving TB drugs [control group to evaluate the interaction between ARVs and TB drugs]

– Infants born to mothers enrolled antepartum will be enrolled

POSTPARTUM

– HIV-infected women enrolled 2 to 12 weeks post-delivery receiving ARVs and starting postpartum contraceptives
## IMPAACT P1026s V10: Current Enrollment Status

<table>
<thead>
<tr>
<th>Arm</th>
<th>Number Enrolled</th>
<th>Target Accrual</th>
<th>% Completed</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antepartum/HIV-infected Arms</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DRV/r (800/100)</td>
<td>24</td>
<td>25</td>
<td>96%</td>
</tr>
<tr>
<td>DRV/r (900/100)</td>
<td>2</td>
<td>25</td>
<td>8%</td>
</tr>
<tr>
<td>TAF 25 mg w/o COBI or ritonavir</td>
<td>13</td>
<td>25</td>
<td>52%</td>
</tr>
<tr>
<td>TAF 25 mg with COBI or ritonavir</td>
<td>1</td>
<td>25</td>
<td>4%</td>
</tr>
<tr>
<td>TAF 10 mg with COBI</td>
<td>30</td>
<td>25</td>
<td>100%</td>
</tr>
<tr>
<td>DRV/COBI</td>
<td>11</td>
<td>25</td>
<td>44%</td>
</tr>
<tr>
<td>ATZ/COBI</td>
<td>2</td>
<td>25</td>
<td>8%</td>
</tr>
<tr>
<td><strong>TB Arms</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First line TB drugs with EFV</td>
<td>15</td>
<td>25</td>
<td>60%</td>
</tr>
<tr>
<td>First line TB drugs with LPV/r</td>
<td>1</td>
<td>25</td>
<td>4%</td>
</tr>
<tr>
<td>TB Only</td>
<td>8</td>
<td>25</td>
<td>32%</td>
</tr>
<tr>
<td>Second Line TB drugs (HIV-infected and uninfected)</td>
<td>1</td>
<td>25</td>
<td>4%</td>
</tr>
<tr>
<td><strong>Postpartum Contraception Arms</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EFV + oral contraceptive</td>
<td>27</td>
<td>25</td>
<td>100%</td>
</tr>
<tr>
<td>DRV/COBI or ATZ/COBI + oral contraceptives</td>
<td>0</td>
<td>25</td>
<td>0%</td>
</tr>
<tr>
<td>DRV/COBI or ATZ/COBI + etonogestrel</td>
<td>0</td>
<td>25</td>
<td>0%</td>
</tr>
</tbody>
</table>
P1026s Additional Study Procedures: TB Arms

AUDIOLOGY ASSESSMENT
• For participants treated with any injectable TB medication
• Can be from chart abstraction or otherwise can be performed anytime during follow-up

TSH/fT4
• For participants treated with ethionamide and/or para-aminosalicylic acid
• Follow assay requirements of your testing lab

Refer to the LPC for additional information on the study specific webpage: http://impaactnetwork.org/studies/P1026s.asp
Add arms for new ARV’s:

- Bictegravir/FTC/TDF
- Doravirine
- Others?

New arms for increased dose cobi?
Questions?
Expedited Adverse Event Reporting
Expedited Adverse Event Reporting Requirements

• The SAE Reporting Category, as defined in Version 2.0 of the DAIDS EAE Manual and in addition fetal demise and Grade 4 hepatotoxicities, regardless of relationship must be reported as EAEs

• The study agents for which relationship assessments are required are the drugs (and their boost counterparts) for which PK data is being obtained.

• Applies to both mothers and infants

• The EAE reporting period for this study begins at the time of entry and continues through the end of study follow-up.

• Post study: Deaths within 30 days of study completion, regardless of the cause, must be reported immediately and no later than 3 days of first becoming aware of the death.
Serious Adverse Event (SAE) Definition

An AE that:

- Results in death,
- Is life-threatening,
- Requires inpatient hospitalization or prolongation of existing hospitalization,
- Results in persistent or significant disability/incapacity, or
- Is a congenital anomaly/birth defect
- Is an important medical event that may not be immediately life-threatening or result in death or hospitalization but may jeopardize the patient or may require intervention to prevent one of the other outcomes listed in the definition above
**EAEs in P1026s**

- If a baby is born prematurely and admitted to the NICU and stays longer than usual – this constitutes prolonged hospitalization.

- A pregnant woman who delivers prematurely or is admitted for pre-eclampsia and does not deliver right away. The pre-eclampsia is reportable if it is considered life-threatening, if the baby is born premature, or the hospital stay is prolonged.

- An infant or mom is discharged and then re-admitted for an infection or post-partum preeclampsia or any other reason for a hospital admission outside of labor.

- A life threatening PP hemorrhage requiring significant medical intervention.
# Mapping Relationship Categories FOR EAE Reporting

<table>
<thead>
<tr>
<th>Relationship Category</th>
<th>Maps To</th>
<th>Relationship Category for EAE Reporting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definitely related</td>
<td></td>
<td>Related</td>
</tr>
<tr>
<td>Probably related</td>
<td></td>
<td>Related</td>
</tr>
<tr>
<td>Possibly related</td>
<td></td>
<td>Related</td>
</tr>
<tr>
<td>Probably not related</td>
<td></td>
<td>Not Related</td>
</tr>
<tr>
<td>Not related</td>
<td></td>
<td>Not Related</td>
</tr>
</tbody>
</table>
Questions?
Screening
Enrollment
Retention
Impaact p1026

Emily Barr CPNP, CNM, MSN
Field Representative p1026
IMPAACT Study Coordinator
University of Colorado
Children's Hospital Colorado
Screening

- All new patients referred to our program are screened for studies immediately
- Monthly screening meeting with all providers
- Review
  - Barriers (language, job, children, disclosure, delivery site)
  - Medication (will this be changed during pregnancy? Are they adherent?)
  - Concomitant medications, twins, or medical conditions that might preclude them
- We do not exclude people based on substance use or other challenges as we have found that these women often benefit a great deal being on studies and should have the same opportunities as other women.
Review Open Arms

- Check to see how many spots are available
- If less than 5 you could let the team know you plan to consent and when you plan to enroll
- Spots are not guaranteed just because you have consented
- The limit is 25 per arm but it's common to over enroll by a couple to ensure we get all of the data, but do not count on this.
- If it's close, check before you consent.
Planning for Consent and Enrollment

- Plan when to consent and enroll
- It's better to enroll early to allow for 2nd TM enrollment
- You have more time to receive the PK data prior to delivery
- You have more time to collect data and it's easier to do forms when you start in the 2nd TM
Consenting

- Simplify the main reasons for this study
- Discuss how this research helps women and children around the world
- Talk about how being on the study can be of benefit to them
- Review risks, extra labs and visits for mom and newborn
- Emphasize that it's voluntary
What do you do at your site to remove barriers to participation in studies?

- Interpreters
- Child care
- Transportation
- Meals
- Social support (time with social worker or mental health provider)
- Combine with clinical care
- Share pertinent labs with other providers so blood draws aren't duplicated
Plan out and schedule dates ahead of time

Reminder (text, call or email) to take all doses two weeks ahead

Reminders to change to morning dosing three days before the visit can be done a week ahead and again 4 days ahead

Reminder to bring medication in original bottle 4 days prior and the day before

Reminder to not miss doses the three days prior and the day before

Reminder “Do not take your medicine the morning of the appointment- but bring it with you!”
Vaginal Secretion Collection

* How are sites doing with this?
* Variety of ways to collect
  * Nurse can collect
  * Self collect using the aspirator
  * Gloved finger – self collect
  * Insert cup for 20 minutes and remove and nurse can collect.
  * Time of collection would be at the time of removal
Newborn Washout PK

* 2-10, 18-28 and 36-72 hours after birth
  * These should all be done prior to D/C
  * Dried Blood Spots done by nurses in the newborn nursery
  * Samples can be combined with clinical labs and also when on multiple studies
* 5-9 days of life
  * This is scheduled to occur during first visit after discharge from the hospital
* 16-24 weeks
  * Critical off study visit to collect final HIV Infection status and any follow up of toxicities or congenital anomalies.
Retention and Support

* 1026 provides extra time with clients
  * Provide social support
  * Mental health assessment
  * Counseling
  * Access to housing and food
* Doula support
* Discuss other studies available
Pack and play provided for newborn while in hospital
Baby items as needed
See clinical care providers when in for PK visits
Important Data

- Capturing all PK visits
  - 2nd, 3 TM, and PP visits
  - L and D
  - Cord Blood
- Wash out PK visits
- Follow up for any major complications EAEs
- Follow up any infant congenital anomalies
- Follow up for infant infection status
Antiretroviral Pregnancy Data Collection

- http://www.apregistry.com/
- This Registry is the only project established to evaluate first trimester, and later prenatal exposures to antiretroviral medications.
- Registry data supplement other sources of data and assist clinicians and patients in weighing potential risks and benefits of treatment.
- Data can be collected on paper forms or directly into the computer data system.
- If you have any questions the staff are very helpful.
- Monitors may look to see that these are being done, but will not be monitoring the data.
Thank You!

Emily Barr
720-777-6752
Emily.Barr@childrenscolorado.org
1026s Data Management
Visit Preparation

- Binder preparation
- Flowsheets in advance
- Cryovial labeling
- Labor and Delivery Binder (30 Weeks)
  - Tool for window calculation
- Perinatal On Call and communication with research nursing at delivery
ARV Reporting (ARVs in pregnancy arm)

ARV History: 1 year prior to EDC and all ARVs during current pregnancy up until day of study enrollment reported on PE5822: Maternal HIV-Related Treatment History

ARVs after enrollment:
- Starting on the day of enrollment, all ARVs (including doses) and changes are recorded on TXW0278: Maternal Antiretroviral Regimen Record-II

Example flowsheet: Date of enrollment March 1, 2017/EDC June 1, 2017

<table>
<thead>
<tr>
<th>Medication</th>
<th>Start</th>
<th>Stop</th>
<th>Source/comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triumeq</td>
<td>4/25/15</td>
<td>10/9/16</td>
<td>Start: Rx by ID provider 4/25/17</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Stop: With change to Odefsey</td>
</tr>
<tr>
<td>Odefsey</td>
<td>10/10/16</td>
<td>2/28/17</td>
<td>Start: New script for Odefsey written 10/4/16, per patient picked up and started</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>10/10/16 Odefsey, 250 mg tablet qd (study med)</td>
</tr>
<tr>
<td></td>
<td>3/1/17</td>
<td></td>
<td>Start: Start as study medication on day of enrollment</td>
</tr>
<tr>
<td></td>
<td>Ongoing</td>
<td></td>
<td>Stop: Ongoing</td>
</tr>
</tbody>
</table>
Concomitant Medication Reporting (ARVs in Pregnancy Arm)

- **ALL** prescription medications taken during the current pregnancy (pregnancy start=date of LMP), Labor and Delivery, and postpartum, through date of off study

- Include blood products, vaccines, anesthesia medications, etc

- Prenatal vitamins are the only over the counter medication required to be reported on CRFs

- Keeping track of non-CRF reportable medications during pregnancy may be helpful if patient is coenrolled on another study that requires over the counter medications in pregnancy to be recorded (such as PHACS SMARTT)
Sign and Symptom Reporting

- Basic rule: All grade 2 and higher symptoms from date of LMP until off study date reportable on CRFs
  - Saves time tracking grade 1 symptoms
  - Grade 3 and 4 symptoms require Event Evaluation CRF

- EXCEPTIONS:
  - Only ≥Grade 3 nausea, constipation, headache, fatigue, reflux/heartburn
  - Do not need to report symptoms related to diagnosis already reported on CRFs (i.e. patient with Grade 2 Bronchiolitis, with related Grade 2 cough and Grade 2 fever—no need to report cough and fever if Bronchiolitis is already reported)
  - Additional reporting for DRV/r and LPV/r
  - Specific requirements for proteinuria and hypertension

- Site examples of systems for tracking and reporting signs and symptoms, or for remembering reporting exceptions?
Diagnosis Reporting

- At entry: Lifetime history of major obstetrical diagnoses, and any HIV-related diagnoses that are ongoing at entry are reported on PE5831: Maternal Diagnosis History—II

- After entry: All new Appendix 100 Diagnoses since last visit reported on PE6853 Diagnoses-IV CRF (and use best judgment for diagnoses not specifically listed in appendix)

REPORTABLE OR NOT REPORTABLE ON CRFs?
- PPROM in a previous pregnancy
- Placenta previa in current pregnancy
- Bronchiolitis diagnosed during current pregnancy but resolved prior to patient entry
- Bronchiolitis diagnosed at patient enrollment visit
- PCP that was diagnosed and resolved prior to current pregnancy
- LGSIL pap smear that is ongoing at study entry
- Iron deficiency anemia diagnosed since patient’s last 1026s visit
Event Evaluation CRF

- Required for to be completed for:
  - Grade 3 and 4 signs, symptoms, and diagnoses, and lab values
  - Neurological symptoms or diagnoses of any grade in infants
  - Any event of any grade that requires EAE reporting
  - Any event of any grade leading to a change in study treatment
  - Note: Grade 3 and 4 diagnoses during the current pregnancy that have resolved prior to entry visit do not require an event evaluation

- Event evaluation form is similar but not identical to information required EAE reporting

- Differences
  - Need more specific assessment than ‘related’ or ‘not related’ to study and concomitant medications
  - Not able to report two related diagnoses on one form: need one event evaluation per event
Queries

- Even if you have already submitted an EAE report and/or an Event Evaluation CRF for a given event, you are still likely to get a query requesting additional information
  - Respond with as much detail as possible
  - May wish to include information from EAE report narrative summary in your query response
  - Verify start dates of medications as requested (and see if possible to narrow down accurate start dates of ARVs), especially when the event in question is a congenital anomaly
P1026s Data Management Training

IMPAACT Annual Network Meeting
Elise Tjaden, PDM
May 31, 2017
Combining Entry and First PK Visit

- Combining entry visit and first PK visit (2nd or 3rd trimester visit depending on mother’s gestation at entry):
  - Report week 0 for combined visit
  - Complete all required entry visit CRFs designated by an ‘X’
  - In addition, complete:
    - F3008
    - PKW0337
    - QL5013
    - TXW0278
  - Do NOT complete:
    - PE6853
    - QL7001 (DRV/RTV participants only)
Off Study Forms

- Discontinuation or Premature Discontinuation
- Off Study forms are the same for Moms (all Tx arms) and Infants
- Required:
  - F1601: Off Study
  - PE4005: Permanent Discontinuation of Study Drug(s)
- If Necessary:
  - PE1414: Death Report

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DATA COLLECTION FORMS SCHEDULE

<table>
<thead>
<tr>
<th>WEKS</th>
<th>Through Day 3 of Life</th>
<th>6-9 Days of Life</th>
<th>16-24 Weeks of Life</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ON STUDY</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ADM0046(P1026S) Visit Status Report</strong></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>PE9005(P1026S) Hospitalization Record - III</strong></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td><strong>TRK0103(P1026S) Specimen Consent/Decline for Non-Protocol Defined Testing</strong></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td><strong>DSG0109(P1026S) Audiology Assessment</strong></td>
<td>X</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| **F0101(P1026S) Sensitive Data** | | X | X*
| **F0120(P1026S) Protocol Initiation** | | X | |
| **F1601(P1026S) Off Study - Revised** | E | | |
| **F3008(P1026S) Master Specimen Tracking - Revised** | N | X* | X*
| **FPE0302(P1026S) Detailed Pediatric Vital Signs** | | X | X
| **FPEU13(P1026S) Non-Antiretroviral Concomitant Medications/Therapies - II** | | X | X
| **PE1414(P1026S) Death Report - IV** | L | L | |
| **PE4005(P1026S) Permanent Discontinuance of Study Drug(s) - II** | E | | |
| **PE8021(P1026S) Newborn Demographics** | M | X | X
| **PE8831(P1026S) Infant Follow-Up - II** | | X | X
| **PE886(P1026S) Newborn Exam - III** | | X | X
| **PE9813(P1026S) Hematologies - IV** | | X | X
| **PE9815(P1026S) Chemistry - V** | | X | X
| **PE9893(P1026S) Signs and Symptoms - IV** | | X | X
| **PE9893(P1026S) Diagnoses - IV** | | X | X
| **PE9995(P1026S) Event Evaluation - VI** | | V | V
| **PKW0366(P1026S) IMPACT P1026S Infant Washout PK Specimen Tracking** | | | |
| **TXW0073(P1026S) Infant Antiretroviral Regimen Record - II** | | | |

All footnotes are located on page 2.
Subject Enrollment System (SES)

- Verify that you have selected the appropriate version of the eligibility checklist
  - If completing on paper first, make sure the checklist date in the SES matches the paper copy you have filled out
- Answer Yes to ALL treatment questions applicable for each participant
- Review checklist answers before you click ‘Enroll’
F0120: Protocol Initiation

- Header date is the date the participant enrolled to P1026s
- Date of first known dose:
  - Mothers: first dose following enrollment
  - Infants: date of mother’s first dose following enrollment
• Report the correct Version number the participant consented to at Entry

• Infants: If mom re-consents to a newer Protocol Version prior to infant birth, report the most recent Version in question 4a1 and make a comment in question 6 that indicates the mother had originally consented to Version X but re-consented to Version Y on [date]
PKW0337: Intensive Pharmacokinetics

- >1 Study Drug
  - Report current, last, and prior to last doses of each study drug of interest
  - Plan 24-hour PK collection around QD study drug if mother is on both a QD and BID regimen of interest
- Report combination drugs (e.g. Genvoya) as a single drug
• **Study Entry:** for ongoing ARVs
  – Dose Status = 1 (Initial dose)
  – Date Modification Started = date of first known study drug dose taken on study

• **Study Exit:** All ARVs taken during the study **must** be reported as discontinued
  – Dose Status = 6 (Permanently discontinued)
  – Total Daily Dose = 0.0 mg
  – Date Modification Started = date of last known dose on study

• **Delivery Visit:** ARVs given only on the day of delivery
  – Two entries; Report both the start and stop dates as the same date (delivery date)
Mothers: Report the last known date the participant took study drug
  – If LFU, use the date of the participant’s last clinic evaluation
  – This date should be the same as the discontinuation date reported on the TXW0278

Infants: Report the last known date of exposure to study drug
  – If mother stops treatment prior to delivery, use mother’s treatment discontinuation date
  – If infant does not breastfeed, use infant date of birth (last exposed in utero)
  – If infant is breastfeeding, use date of last exposure to breastmilk
How to Report Combination Drugs

Do This:

- All combination drugs should be reported as prescribed
  - Do NOT list out the breakdown of each combination drug on separate lines
- TXW0278 and PKW0337
How to Prevent Duplicate Reporting

- Make sure you are using the most recent version of the CRF

<table>
<thead>
<tr>
<th>Form Name</th>
<th>Old</th>
<th>New (1-Mar-2016)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnoses</td>
<td>PE6852</td>
<td>PE6853</td>
</tr>
<tr>
<td>Signs and Symptoms</td>
<td>PE6832</td>
<td>PE6833</td>
</tr>
<tr>
<td>Chemistries</td>
<td>PE6817</td>
<td>PE6818</td>
</tr>
<tr>
<td>Hematologies</td>
<td>PE6812</td>
<td>PE6813</td>
</tr>
<tr>
<td>Event Evaluation</td>
<td>PE6865</td>
<td>PE6866</td>
</tr>
</tbody>
</table>

- Begin using the new CRFs as soon as they become available
- Report the continuation of ongoing events on the updated CRF (even if initially reported on the old version)
Tips for Submitting Resolve Proposals

- After submitting Resolve proposals, do NOT modify data on the CRF in question until the proposal is resolved by the DM. If data is modified prior to DM resolution, we will not be able to approve the proposal.
- Provide useful comments that help us determine why the data is correct even though the logical check was triggered.

**Do this:**

<table>
<thead>
<tr>
<th>Institution Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Data are correct. Verified data in source document. date of onset: 01 Sep 2016. As per query request received it was requested to change onset date to 01 Sep 2016. Please exempt or advise on LC.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Institution Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct bilirubin value verified and is correct. 0 was the value reported by the lab.</td>
</tr>
</tbody>
</table>

**Not this:**

<table>
<thead>
<tr>
<th>Institution Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hi, Data verified correct, Please resolve, thank you.</td>
</tr>
</tbody>
</table>
Need Help?

- Questions about eData, technical issues, access/permissions to portal programs, etc.?
  - Contact User Support 24/7
    - Telephone: (716)834-0900 ext. 7302
    - Email: user.support@fstrf.org
- Questions related to enrollment issues?
  - Contact Randomization
    - Telephone: (716)834-0900 ext. 7301
    - Email: rando.support@fstrf.org
- Questions regarding CRFs, delinquency, Resolve/logical checks, etc.?
  - Contact the Protocol Data Manager
    - Telephone: (716)834-0900 ext. 7272 (Elise), ext. 7404 (Ben), ext. 7339 (Tia)
    - Email: tjaden@fstrf.org, johnston@fstrf.org, reding@fstrf.org
- Questions about patient management, co-enrollment, or the protocol?
  - Contact the P1026s Protocol Team
    - Email: impaact.teamp1026s@fstrf.org
P1026s Laboratory Processing Charts

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Laboratory Technologist
Laboratory Processing Charts

5 SoE and 5 LPCs in Version 10.0

- On ARV without TB Tx
- *Additional Monitoring Requirements for HIV-Infected Pregnant Women on DRV/RTV, LPV/RTV and NFV*

- On ARV with TB Tx
- *Additional Monitoring Requirements for HIV-Infected Pregnant Women on DRV/RTV, LPV/RTV and NFV*

- HIV Neg with TB Tx

- On ARV and Hormonal Contraceptives

- For Infants
**Local Laboratory Tests**

<table>
<thead>
<tr>
<th>Lab evaluations at Site</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hematology:</strong></td>
</tr>
<tr>
<td>Hgb</td>
</tr>
<tr>
<td><em>CBC for Additional Monitoring Requirement</em></td>
</tr>
<tr>
<td><strong>Chemistry:</strong></td>
</tr>
<tr>
<td>Albumin, BUN, creatinine, bilirubin, AST, ALT</td>
</tr>
<tr>
<td><em>Add electrolytes, glucose, total amylase (+/- lipase) for Additional Monitoring Requirement</em></td>
</tr>
<tr>
<td><strong>Immunology:</strong></td>
</tr>
<tr>
<td>CD4 cell count</td>
</tr>
<tr>
<td><strong>Virology:</strong></td>
</tr>
<tr>
<td>HIV RNA</td>
</tr>
</tbody>
</table>

*Progesterone will be assayed at the site lab*
Specimens in Version 10.0

PK specimens (plasma):

• Intensive PK of ARV drugs
• Intensive PK of ARV+TB Medicines
• Intensive PK of TB Medicines
• Intensive PK of ARV+ Hormonal Contraceptives
• PK for Etonogestrel Implant
• Cord Blood
• Maternity Delivery Sample
PK specimens (plasma):
- Intensive PK of ARV+TB Medicines
- Intensive PK of TB Medicines

For **TB drug arms** – please schedule as early in window as possible to capture women while still on TB treatment to allow for collection of additional PK sample(s) for the TB drugs.
- Determine expected end date of TB treatment and schedule accordingly.
Other Specimens in Version 10.0

- Vaginal Swab (HIV RNA viral load)
- Vaginal Secretions (ARV levels)
- Dried Blood Spot (genetics)
# Vaginal Swab: Processing and Shipping

<table>
<thead>
<tr>
<th>Vaginal Swab</th>
<th>Copan swabs</th>
<th>Send to local IMPAACT processing.</th>
<th>F3008 RNAHIV DNAHIVQT</th>
<th>Label a vial with LDMS labels and freeze within 4 hours at -70°C or colder.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Copan swabs</strong></td>
<td>A vaginal swab will be collected. After collection, the swab will be inserted into a cryovial, the end broken off, and the vial capped. The vial will be labeled with the subject’s Patient Identification Number (PID), Study Identification Number (SID), date and time of collection, and specimen type.</td>
<td><strong>F3008 RNAHIV DNAHIVQT</strong></td>
<td><strong>LDMS spec. code:</strong> VAG/NON/SWB</td>
<td><strong>All Sites (except Thailand):</strong> Ship specimens bached every 6 months. NIAID Labs ship to BRI and NICHD Labs ship to Fisher repository (see shipping instructions at end of LPC). <strong>Thai Sites:</strong> Ship all specimens bached every 6 months to Tim Cresssey, PhD PHPT Laboratory (see shipping instructions at end of LPC).</td>
</tr>
</tbody>
</table>

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**Standard Cryovial**

[Image of Cryovials]
# Vaginal Secretions: Processing and Shipping

## Vaginal Secretions

Vaginal aspirators can be ordered from:

**Angela Kashuba, Pharm. D.**

3318 Kerr Hall, CB# 7569
University of North Carolina at Chapel Hill
Chapel Hill, NC 27599-7360
Phone: 919-966-9998
Fax: 919-962-0644
Email: akashuba@unc.edu

### Soft plastic aspirator

**Time points:** Pre-dose, 1, 2, and 4 hours post dosing.

Send to local IMPAACT processing.

Specimens will be collected using a soft plastic aspirator (Roymeter, Recipe Pharmaceuticals, Munich, Germany) available through the UNC School of Pharmacy. Vaginal fluid can be collected by the subject or by the clinician without use of a vaginal speculum. Aspirates will be placed into a 2mL pre-weighed cryovial and stored at -70°C or colder.

### PKW0337 PKRAN

Transfer to laboratory within 1 hour of collection at room temperature, or keep all time points on wet ice or refrigerated (2-8°C) and transfer on wet ice to processing lab within 1 hour of last collection.

Label a vial with LDMS labels and freeze at -70°C or colder.

**LDMS spec code:**

VSC/NON/SEC

LDMS time/unit: 0/Pre-dose, Or 1, 2, 4/Hour

Enter the post-weight minus the pre-weight volume into the LDMS (Unit: grams)

### Pre-weighed Cryovial

+ Vaginal Secretions

= Post-weighed Cryovial

***Record Pre-weighing and Post weighing in CRF PKW0037***
<table>
<thead>
<tr>
<th>Genotyping (Pharmacogenetics)</th>
<th>EDTA</th>
<th>F3008 PKGENO</th>
<th>EDTA - Dried Blood Spot (250 microliters of whole blood required to apply 50 microliters to each of the 5-spots on Whatman 903 card).</th>
</tr>
</thead>
<tbody>
<tr>
<td>For subjects consenting to pharmacogenetic sampling</td>
<td>Obtain at first PK evaluation Use blood collected during the PK sampling visit. <strong>Note:</strong> A separate 1.0 ml EDTA blood can be drawn for DBS preparation at any of the PK time-points but <strong>without exceeding</strong> the total blood draw volume indicated for that PK time-point. Any remaining blood should be processed for PK plasma storage. Send to local IMPAACT processing.</td>
<td>Take two Whatman 903 Protein Saver Cards. In one card, take 50 μL of whole blood and apply to the first spot. Skip the second spot and apply in the third spot. Skip the fourth spot and apply in the fifth spot. In the second card, take 50 μL of whole blood and apply to the first spot. Skip the second spot and apply in the third spot. In the second card, take 50 μL of whole blood and apply to the first spot. Skip the second spot and apply in the third spot. Label each spot with a different Laboratory Data Management System (LDMS) Global ID. Ensure the DBS cards are completely dry before packing. Place both cards in a gas impermeable bag with a desiccant pack and humidity indicator card. The sealed bag containing the DBS should be stored in a -20°C freezer until it is shipped. The DBS should not be stored at room temperature. During storage the desiccant should be replaced if humidity exceeds 30%.</td>
<td></td>
</tr>
</tbody>
</table>

**Dried Blood Spot**

Obtain at first PK evaluation (any time point)
Questions?

Please send any questions to:

kittipong16@gmail.com
impaact.teamp1026s@fstrf.org