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HPTN 084: Protocol Version 3.0 Data Updates

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OBJECTIVES

- **How to record data for the new protocol and sub-study**
- **New forms in Rave**

Current Steps/Schedules

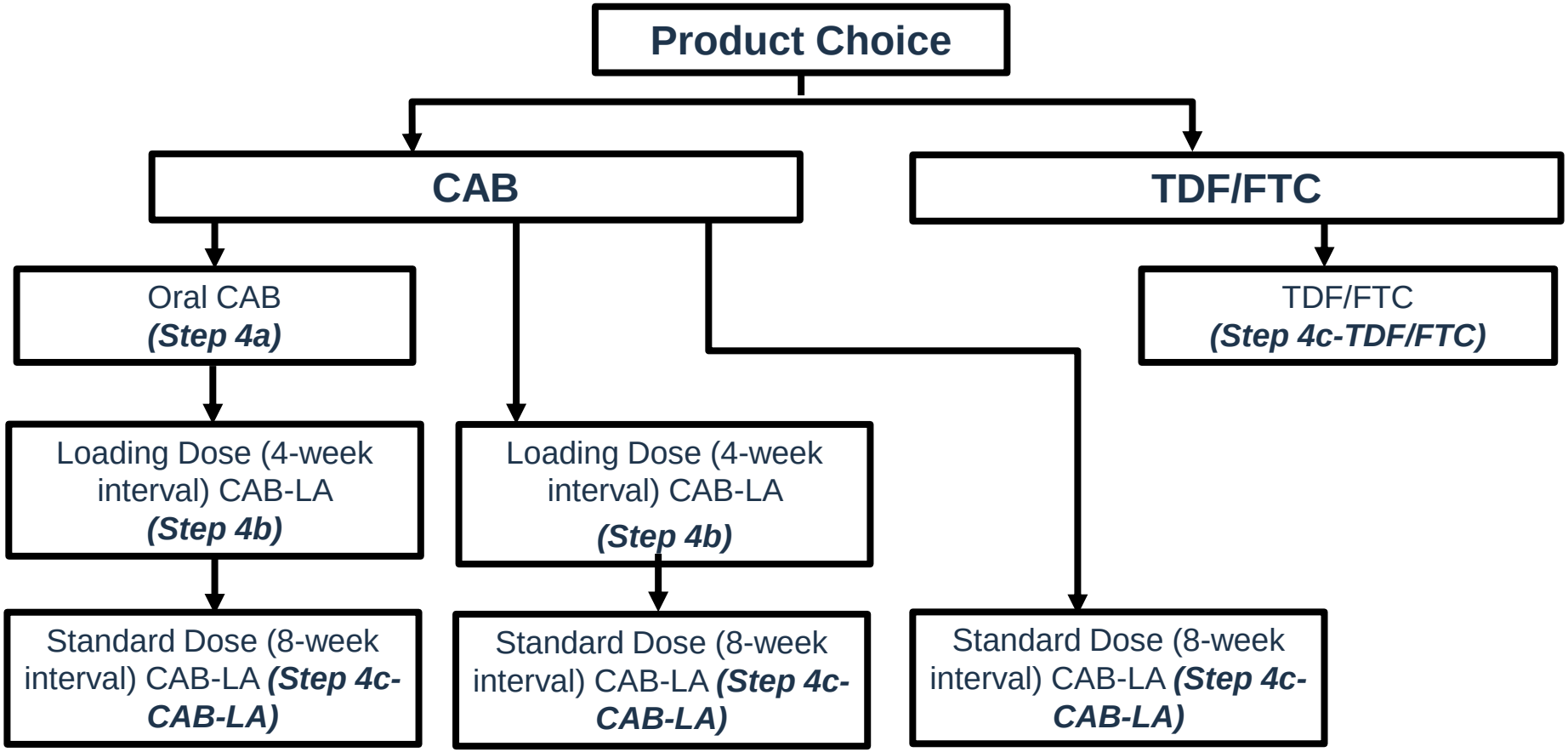
- Once Protocol V3.0 is approved at your site, missed visits for current schedule should not be completed.
- Do not record a product hold when participant moves to OLE schedule.
- Complete Product Choice form instead on the first visit for each participant.

New Steps/Schedules

- New Steps have different visit numbers

Step Name	Treatment Regimen	Visit Numbers
Step 4a	Oral CAB	Visit 55
Step 4b	Loading Dose (4-week interval) CAB-LA	Visit 56
Step 4c	Standard Dose (8-week interval) CAB-LA or TDF/FTC	Visit 57-63 Visit 64-70
Step 4d (Sub-Study)	TDF/FTC or CAB-LA	Visit 76-94
Step 5	TDF/FTC	Visit 71-75

Standard Transition



How to add forms for Steps/Schedules

Step Name	How to Add
Step 4a Step 4b Step 4c Step 4d	Visit folders are automatically generated based on the selection on 'Product Choice' form (first OLE visit); or the response to Change in schedule question on Date of Visit-OLE or Interim Visit-OLE form.
Step 5	Visit folders are automatically generated based on the selection on the response to Change in schedule question on 'Date of Visit-OLE' or 'Interim Visit-OLE' form. This step only applies to participants that discontinue Step 4c- CAB/LA early.

New Forms- OLE

- Product Choice - OLE
- Date of Visit - OLE
- Interim Visit Summary – OLE
- Additional Procedures – OLE
- Contraception –OLE
- Long Term Consent Update
- Product Hold - OLE YN
- Product Hold - OLE
- Pregnancy Test Results-OLE
- Pregnancy Report-OLE
- Pregnancy Outcome Log – OLE
- Ultrasound - OLE

New Forms: Pregnancy Infant Sub-study

- Consent - Pregnancy Infant Sub-study
- Date of Visit - Pregnancy OLE
- Sub-study Infant PTID
- Infant Specimen Collection - Blood (Plasma)
- Specimen Collection - Breast Milk
- Infant Breastmilk Feeding Assessment
- Adverse Event - Infant Y/N
- Adverse Event - Infant

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Product Choice

Page: **Product Choice - OLE**

Is the participant eligible for Open Label Extension?	○ Yes ○ No
If No, Reason (end of form)	...
Will participant move to Open Label Extension (OLE)?	○ Yes ○ No
Date decision was made on whether to move to Open-label extension?	...
If No, Reason (end of form)	...
Other, specify	
If Yes, Date of Informed Consent	...
Select OLE schedule participant will follow	○ CAB (Steps 4a, 4b, 4c) ○ TDF/FTC (Step 4c) ○ Pregnancy and Infant Sub-Study (Step 4d)
If CAB, specify introductory schedule:	...
If CAB regimen selected, Reason	...
Other, specify	
If TDF/FTC regimen selected, Reason	...
Other, specify	

Product Choice Form

- This is the first form to be recorded when participant comes to site after Protocol version 3.0 is approved. After the first visit, this form should **not** be revised.
- If “Will participant move to Open Label Extension (OLE)?” is “No”, termination form should be recorded.
- If “Will participant move to Open Label Extension (OLE)?” is “Yes”, the Visit folder and DOV CRF for the respective step will be automatically added.

Date of Visit – OLE, Interim Visit – OLE

- Form design is similar
- New questions added based on data collection requirements
  - Includes pill dispensing questions. When on OLE no need to record Open Label Truvada Log or Pill Dispensation Step 2 and 3.

Date of Visit – OLE, Interim visit – OLE

- “Is the participant moving to a new step or visit schedule?”
- Response for this question should be “Yes” only if the participant is moving to a new schedule.
- If Yes is marked, the new schedule is then selected.

Interim visit – OLE

- Please DO NOT use the original Interim visit option once the participant moves to OLE.
- A new Interim visit – OLE is available in Add Event drop down once the participant moves to OLE.

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Product Hold/Discontinuation – OLE

Which study product is being held?	○ Oral CAB ○ CAB-LA injection ○ TDF/FTC
Date of last oral study product or CAB injection	...
Date when this study product hold or discontinuation was initiated:	...
At what visit was this product hold/discontinuation initiated?	...
Interim visit code	
Why is the study product being held or discontinued?	...
If Other marked, specify:	
If product hold was associated with an Adverse event, select the applicable AE(s): Adverse Event #1	
Adverse Event #2	
Adverse Event #3	
If product hold was associated with an Injection Site Reaction, select the applicable Injection Site Reaction:	
If product hold was associated with new or updated Concomitant Medications, select the applicable medication(s).	
Complete this section only if participant has either resumed or permanently discontinued study drug.	...
Has the participant resumed study product?	
Date participant resumed study product:	...
Date participant **permanently** discontinued study product:	...

Product Hold/Discontinuation – OLE

- Form design is not changed
- Last question changed to record separate dates for study product resumed or permanently discontinued
- Response for “Has the participant resumed study product?” should only be recorded when the decision is made to either resume or discontinue product.

Product Hold/Discontinuation – OLE

- Each time a change in schedule is marked on Date of Visit-OLE / Interim Visit-OLE form, a Product hold (OLE) log line will need to be recorded with that same date. This will be recorded as permanent hold.
- If a participant terminates early at a particular step, please DO NOT record a hold/discontinuation for that specific step. This is same as the original study.

Ongoing Logs (Existing forms)

- For the forms below, continue entering new data the same as since the beginning of the study.
  - Adverse Events
  - Concomitant Medications
  - Protocol Deviation
  - Social Impact
  - Injection Site Reaction
  - Open Label Truvada *(only for non-OLE visits)*

Ongoing Logs (Existing forms)

- Product Hold – Y/N
  - If the participant did not have any product hold in the duration of the study prior to moving to OLE version, the form will need to be submitted as No.

Ongoing Logs (New forms)

- The forms below have been added in this folder
  - Product Hold – OLE Y/N
  - Product Hold/Discontinuation – OLE
- Please DO NOT USE the original Product hold form to document any hold during the OLE schedule.

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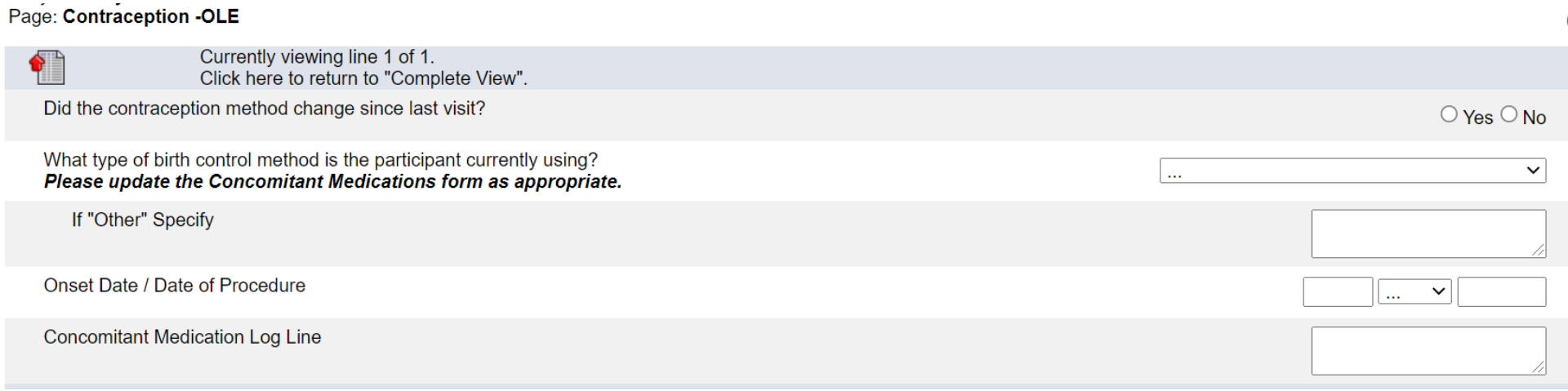
Contraception - OLE

- Contraception data collection simplified
- CRF resides within OLE visits
- Contraception CRF in Ongoing logs should no longer be completed


Page: **Contraception -OLE**

Currently viewing line 1 of 1.
Click here to return to "Complete View".

Did the contraception method change since last visit? ○ Yes ○ No

What type of birth control method is the participant currently using?
Please update the Concomitant Medications form as appropriate. ...

If "Other" Specify

Onset Date / Date of Procedure ... ...

Concomitant Medication Log Line

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Pregnancy Test- OLE

- If positive pregnancy test, second confirmatory test is required.
- Items 6. and 7. are sub-study questions.

Page: **Pregnancy Test Results - OLE**

1. Was a pregnancy test done?	...
If no, end of form.	
2. Date of pregnancy test	...
3. Specimen type *(Mark only one)*:	○ Urine ○ Plasma ○ Serum
4. Test result *If Negative, end of form.*	○ Positive ○ Negative
5. If Test result is positive, was the pregnancy confirmed on a second independent sample on same day? *If No, go to Question 6.*	○ Yes ○ No
5a. If Yes, Specimen type *(Mark only one)*:	○ Urine ○ Plasma ○ Serum
5b. If Yes, Test result	○ Positive ○ Negative
6. Is the participant eligible for Pregnancy and Infant Sub-Study?	○ Yes ○ No
7. Did the participant consent to participate in Pregnancy and Infant Sub-Study?	○ Yes ○ No
8. Select if additional pregnancy test results form is required.	☐

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Pregnancy Report- OLE

- To be used for all pregnancies that occur on OLE.

Page: **Pregnancy Report-OLE**

Date pregnancy reported	...
At what visit was the pregnancy reported?	...
If 'Interim Visit' is chosen, provide interim visit code.	
First day of last menstrual period	...
Estimated date of delivery	...
What information was used to estimate the date of delivery?	...
If other, specify:	

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Ultrasound - OLE

- Form design updated to accommodate data for more than one fetus.

Page: **Ultrasound - OLE**

1. Was an ultrasound exam performed? If yes, go to exam date.	○ Yes ○ No
1a. Reason ultrasound not performed.	
2 Exam Date	...
3. Number of fetuses observed on ultrasound	
Currently viewing line 1 of 1. Click here to return to "Complete View".	
4. Estimated gestational age (at time of ultrasound) - Weeks	
5. Estimated gestational age (at time of ultrasound) - Days	
6. **If estimated gestational age is less than 14 weeks, complete crown-rump length and skip biparietal diameter and femur length (Mark "Or Not done/not collected") . If estimated gestational age is greater than or equal to 14 0/7 weeks, skip crown-rump length (Mark "Or Not done/not collected") and complete biparietal diameter and femur length.** Crown-rump length	cm
Crown-rump length Unit	
Or Not done/not collected	☐
7. Biparietal diameter	cm

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Pregnancy Outcome Log - OLE

- Question 3- *Infant PTID* for Pregnancy and Infant Sub-study.

Page: **Pregnancy Outcome Log - OLE**

1. Did this pregnancy have an obtainable outcome? ○ Yes ○ No

1a. If an outcome was not obtainable, please specify why:

END OF FORM.

2. How many pregnancy outcomes resulted from this reported pregnancy?

Currently viewing line 1 of 1.
Click here to return to "Complete View".

3. Infant PTID

4. Pregnancy outcome date

5. Place of delivery/outcome

5a. If other, specify:

6. Pregnancy outcome

6a. If Stillbirth, Intrauterine fetal demise (≥ 20 weeks) or Other, specify:

6b. If outcome was full-term or premature live birth, select delivery methods.

Delivery method

7. Provide a brief narrative of the circumstances.

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Pregnancy and Infant Sub-study

- The following CRFs and data entry are for sub-study.

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Date of Visit - Pregnancy OLE

- Form design similar to DOV- OLE

Page: **Date of Visit - Pregnancy OLE**

Please assign a sequential number to this sub-study pregnancy. *Only the pregnancies during the sub-study should be counted.*	...
Did the participant complete this visit?	○ Yes ○ No
Visit Date	...
Weight	kg
Weight Unit	
OR Not Done	☐
BMI calculated	kg/m2
Systolic blood pressure	mmHg
Diastolic blood pressure	mmHg
Pulse	beats/min
How many bottles of study drug (TDF/FTC or oral CAB) were dispensed at this visit?	...
Did the participant complete the CASI questionnaire for this visit?	○ Yes ○ No
Did the participant have any additional procedures at this visit?	○ Yes ○ No
If yes, complete the Additional Procedures form, indicating which additional forms were needed for this visit.	
Did the product get held/discontinued at this visit?	○ Product Hold ○ Product Discontinued

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Consent - Pregnancy Infant Sub-study

- CAB LA or TDF/FTC can be selected.

Page: **Consent - Pregnancy Infant Sub-study**

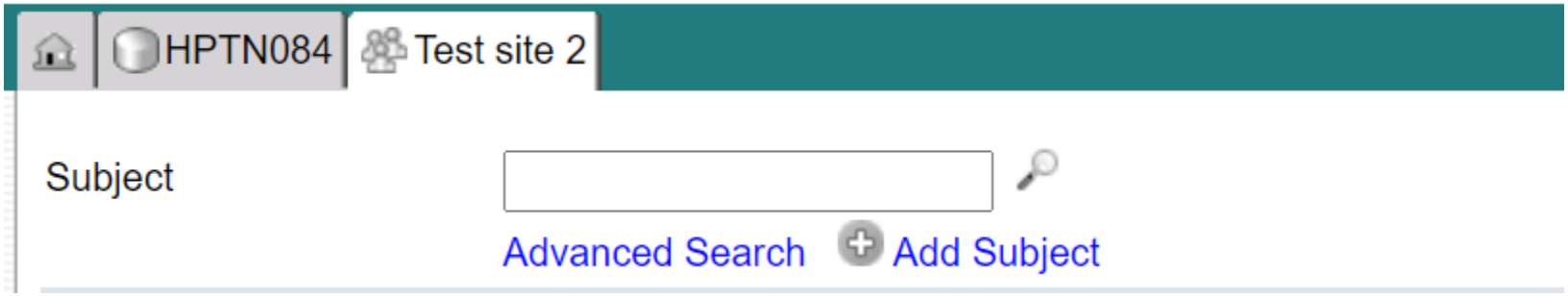
For which OLE regimen did the participant consent during pregnancy?	○ CAB LA ○ TDF/FTC ○ None
Did the participant consent to having her sample collected during pregnancy?	○ Yes ○ No
If yes, did the participant consent to having her sample stored for future testing during pregnancy?	○ Yes ○ No
Did the participant consent to having her infant's sample collected after pregnancy?	○ Yes ○ No
If yes, did the participant consent to having her infant's sample stored for future testing during pregnancy?	○ Yes ○ No

Infant PTID and Pregnancy Outcome-OLE

- When ‘Pregnancy outcome’ is live birth, the site will create a *new PTID* similar to original study, which will be used as infant PTID.
- Pregnancy outcome:
  - Full term live birth (>=37 weeks)
  - Premature live birth (<37 weeks)

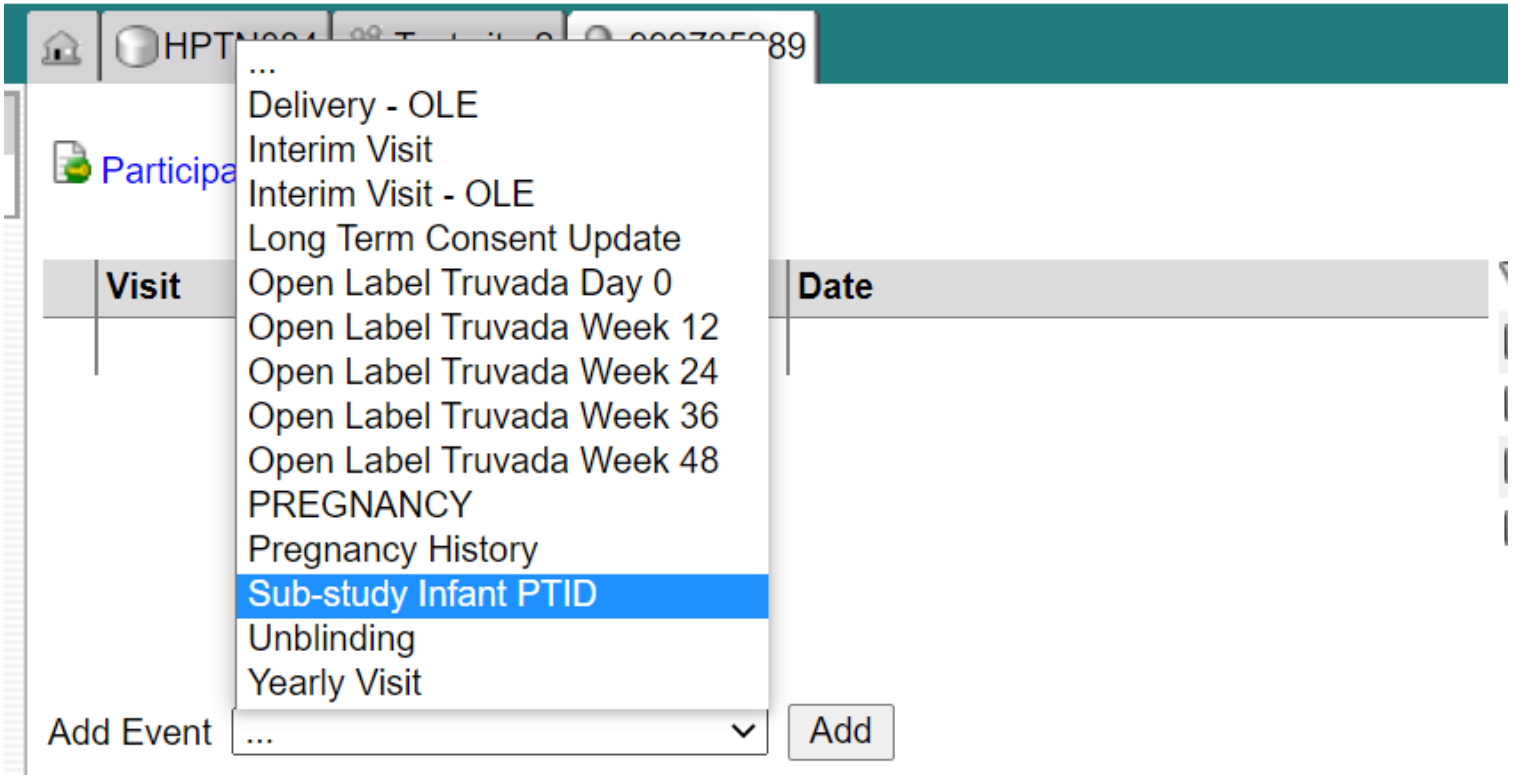
Create Infant PTID

- Once Pregnancy Outcome Log – OLE (outcome of live birth) is saved, generate new PTID using ‘Add Subject’ on home page.
  - *This new PTID is Infant PTID.*
  - Infant PTID will be entered for all respective infant data.



Sub-study Infant PTID

- Use ‘Add Event’ on home page to populate Sub-study Infant PTID form.



Sub-study Infant PTID

- Record mother's PTID to link mother and infant PTIDs.
- *This is the ONLY data to be collected for the Infant's PTID. All remaining data will be collected under the mother's PTID.*

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Infant Specimen Collection - Cord Blood

- Infant PTID is entered.

Page: **Infant Specimen Collection - Cord Blood**

Currently viewing line 1 of 1.
Click here to return to "Complete View".

Infant PTID	
Was specimen collected?	○ Yes ○ No
If "No", record reason why sample was not collected (max. 200 characters).	
Specimen collection date	...
Specimen collection time	:
Was the minimum required volume obtained?	○ Yes ○ No
If "No", record reason why minimum required volume was not obtained (max. 200 characters).	
Was sample stored?	○ Stored ○ Not stored
If "Not stored", record reason why sample was not stored (max. 200 characters).	

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Infant Specimen Collection - Blood (Plasma)

- Infant PTID is entered.

Page: **Infant Specimen Collection - Blood (Plasma)**

Currently viewing line 1 of 1.
Click here to return to "Complete View".

Infant PTID	
Was specimen collected?	○ Yes ○ No
If "No", record reason why sample was not collected (max. 200 characters).	
Specimen collection date	...
Specimen collection time	:
Was the minimum required volume obtained?	○ Yes ○ No
If "No", record reason why minimum required volume was not obtained (max. 200 characters).	
Was sample stored?	○ Stored ○ Not stored
If "Not stored", record reason why sample was not stored (max. 200 characters).	

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Infant Breastmilk Feeding Assessment

- Infant PTID is entered.

Page: **Infant Breastmilk Feeding Assessment**

Currently viewing line 1 of 1.
Click here to return to "Complete View".

Infant PTID	
Was a feeding assessment completed?	Yes No
Date of assessment	...
Has the infant ever been fed breastmilk?	Yes No
Is the infant currently fed breastmilk?	Yes No
Date infant last received breast milk	...

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Infant Assessment

- Similar Pregnancy Outcome- OLE CRF.
- Infant PTID is entered.

Page: **Infant Assessment**

1. How many live pregnancy outcomes had resulted from this pregnancy?
   Complete one log line for each live outcome.

Currently viewing line 1 of 1.
Click here to return to "Complete View".

2. Infant PTID

3. Is the infant alive? ○ Yes ○ No

4. Was an infant assessment done? ○ Yes ○ No
   If No, end of form.

5. Date of assessment ...

6. Length cm

7. Weight kg

8. Head circumference cm

9. Abdominal circumference

10. Were any previously unreported fetal/infant congenital anomalies identified? ...
    If "Yes", mark all that apply.
    If "No" or "Not assessed", end of form.

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Adverse Event - Infant

- CRF is added to Ongoing logs folder for all live births.
- Design similar to main study.
- Infant PTID is entered.

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CASI Survey in Datstat (Ilume)

- Changes in the login screen of survey.
  - PTID and pregnancy status also required.
  - You will be prompted if the CASI ID and PTID combination don't match based on the information in Rave.
  - Pregnancy question has been added in case the site needs to complete 2 surveys at the same visit, one before pregnancy confirmed and one after the pregnancy is confirmed.
  - All OLE visits can be selected from the dropdown. If a survey for a scheduled visit is missed and is completed later, select the visit when you are doing the visit and not when it was expected.

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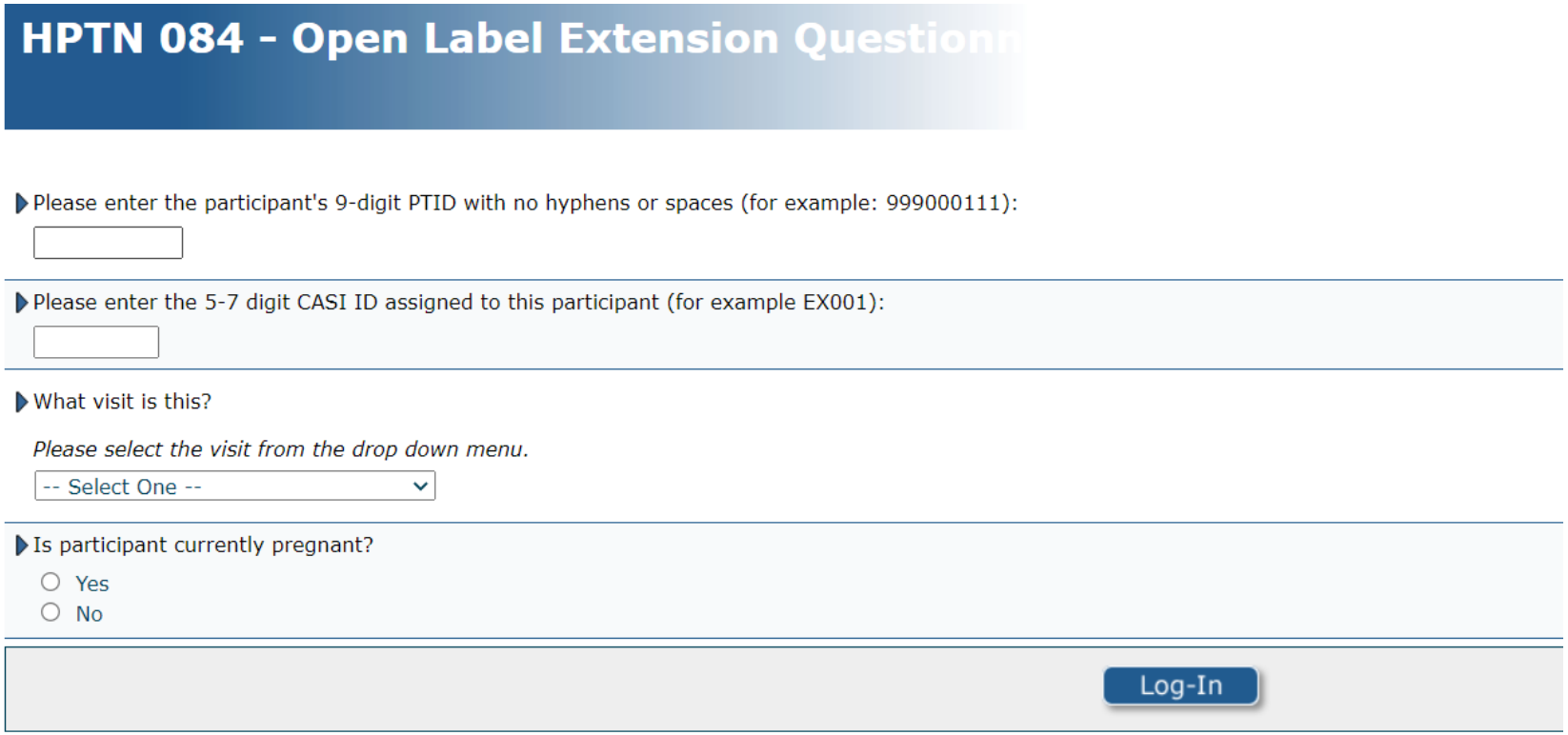
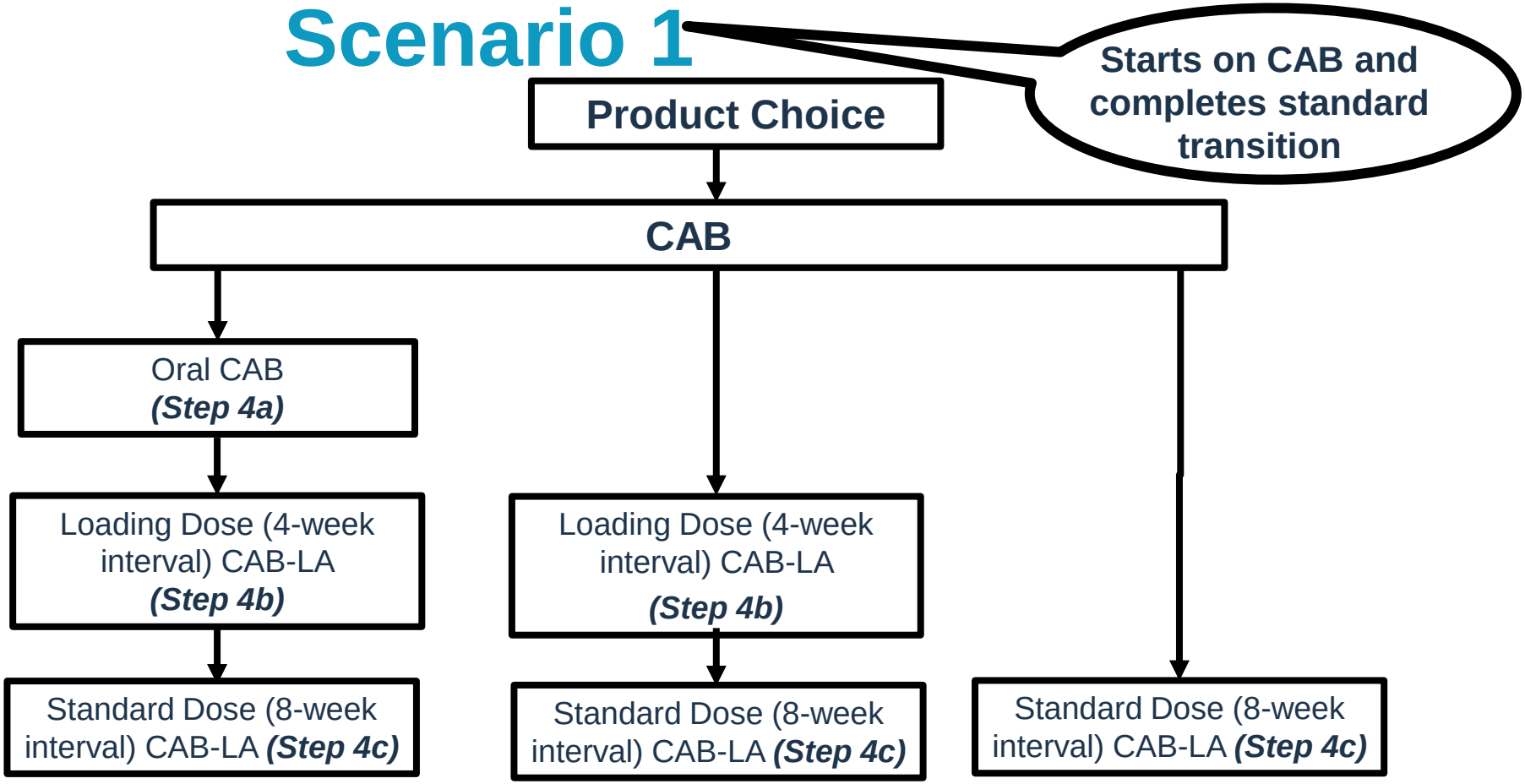
CASI Survey in Datstat (Ilume)

- Below is the Snapshot from the login screen of the new survey.



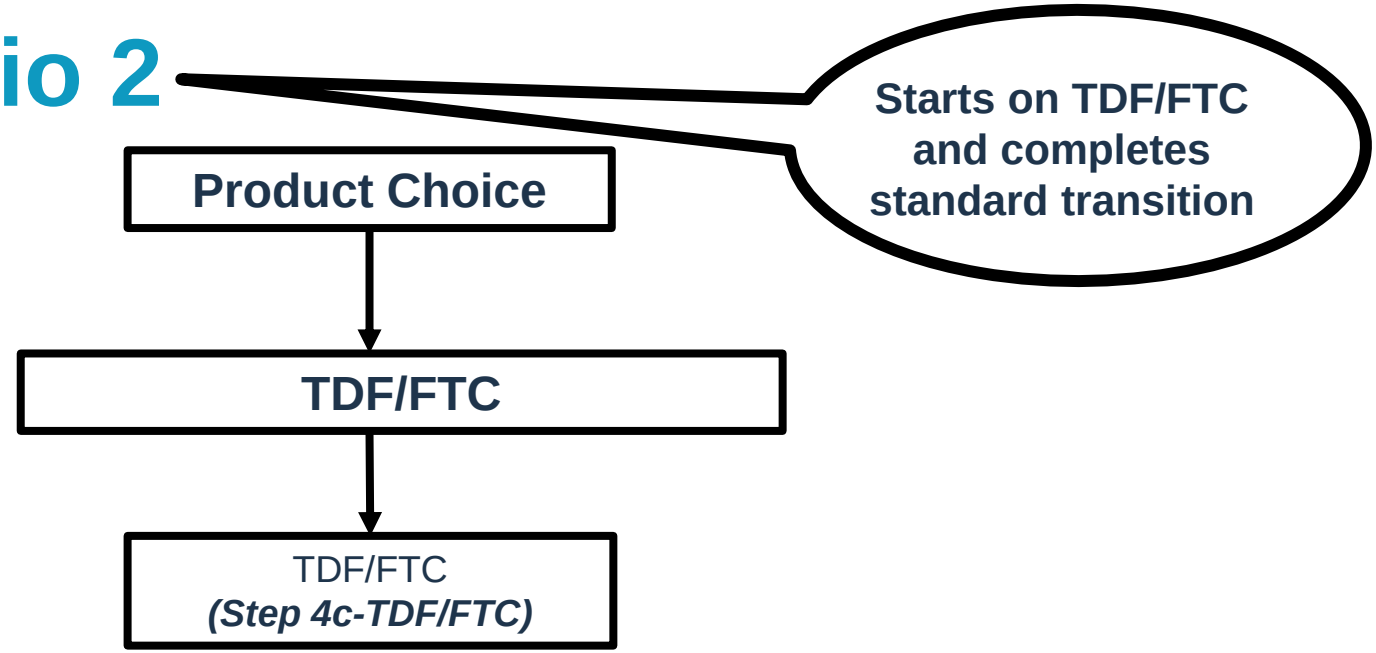
Scenario 1


Starts on CAB and completes standard transition
Product Choice
CAB
Oral CAB
(Step 4a)
Loading Dose (4-week interval) CAB-LA
(Step 4b)
Standard Dose (8-week interval) CAB-LA (Step 4c)
Loading Dose (4-week interval) CAB-LA
(Step 4b)
Standard Dose (8-week interval) CAB-LA (Step 4c)
Standard Dose (8-week interval) CAB-LA (Step 4c)

Scenario 1

- Participant starts on CAB (either Step 4a, 4b or 4c), finishes last visit of Step 4c (Visit 63)
- On Product Choice form select CAB, then select step 4a, 4b or 4c as appropriate. This would populate the Date of Visit form for corresponding visit. Once the current visit is recorded the next visit will auto populate.
- Record the Termination form once participant completes 4c Week 48 (V63).

Scenario 2


Starts on TDF/FTC and completes standard transition
Product Choice
TDF/FTC
TDF/FTC
(Step 4c-TDF/FTC)

Scenario 2

- Participant starts on TDF/FTC (Step 4c) and completes all visits until Week 48, V 70.
- On Product Choice form select TDF/FTC which will populate Step 4c,Day 0 (V 64).
- Record the Termination form once participant completes Week 48 (V 70) or at an earlier visit if participant discontinues product.

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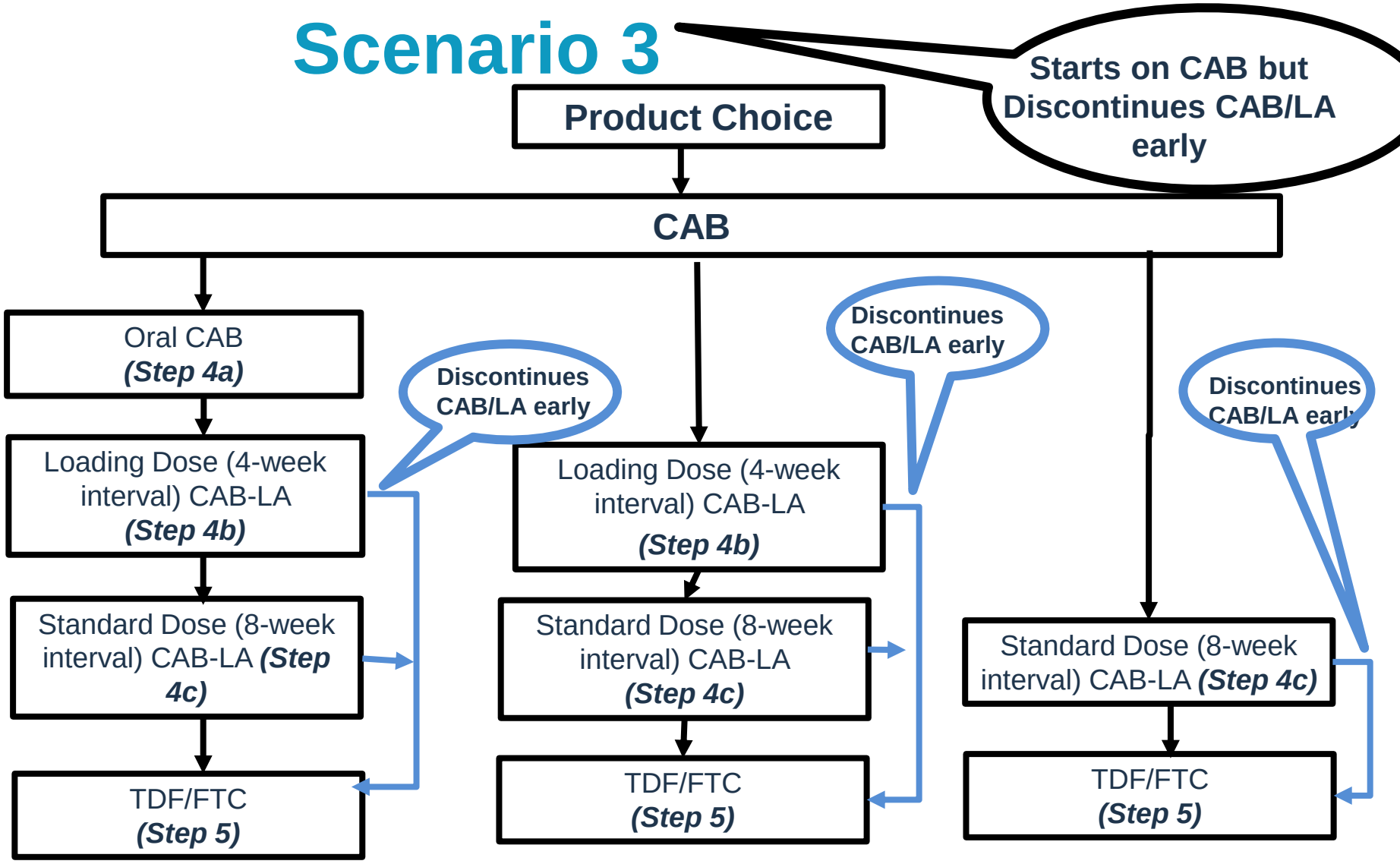
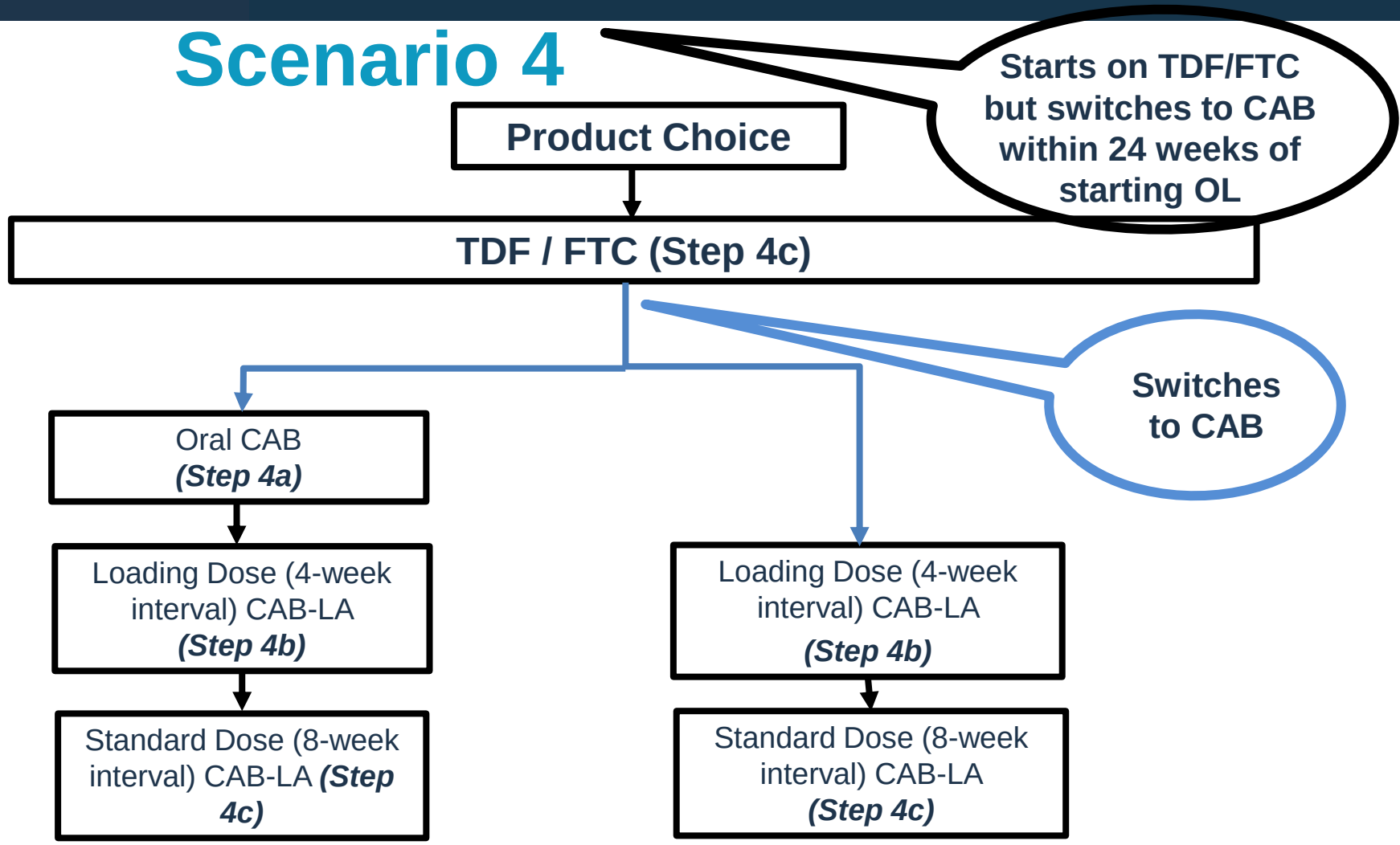
Scenario 3



Scenario 3

- Participant starts on CAB (either Step 4a, 4b or 4c) but decides to discontinue CAB/LA early. They will be transitioned to TDF/FTC Step 5 (Visits 71 – 75).
- On Product Choice form select CAB, then select 4a, 4b or 4c as appropriate. At the visit when participant wants to change mark Yes for the schedule change question on Date of Visit/Interim Visit form, then select TDF/FTC. This would stop the current schedule's visit and populate visit 71.
- Record the Termination form once participant completes visit 75 or if terminated sooner.

Scenario 4

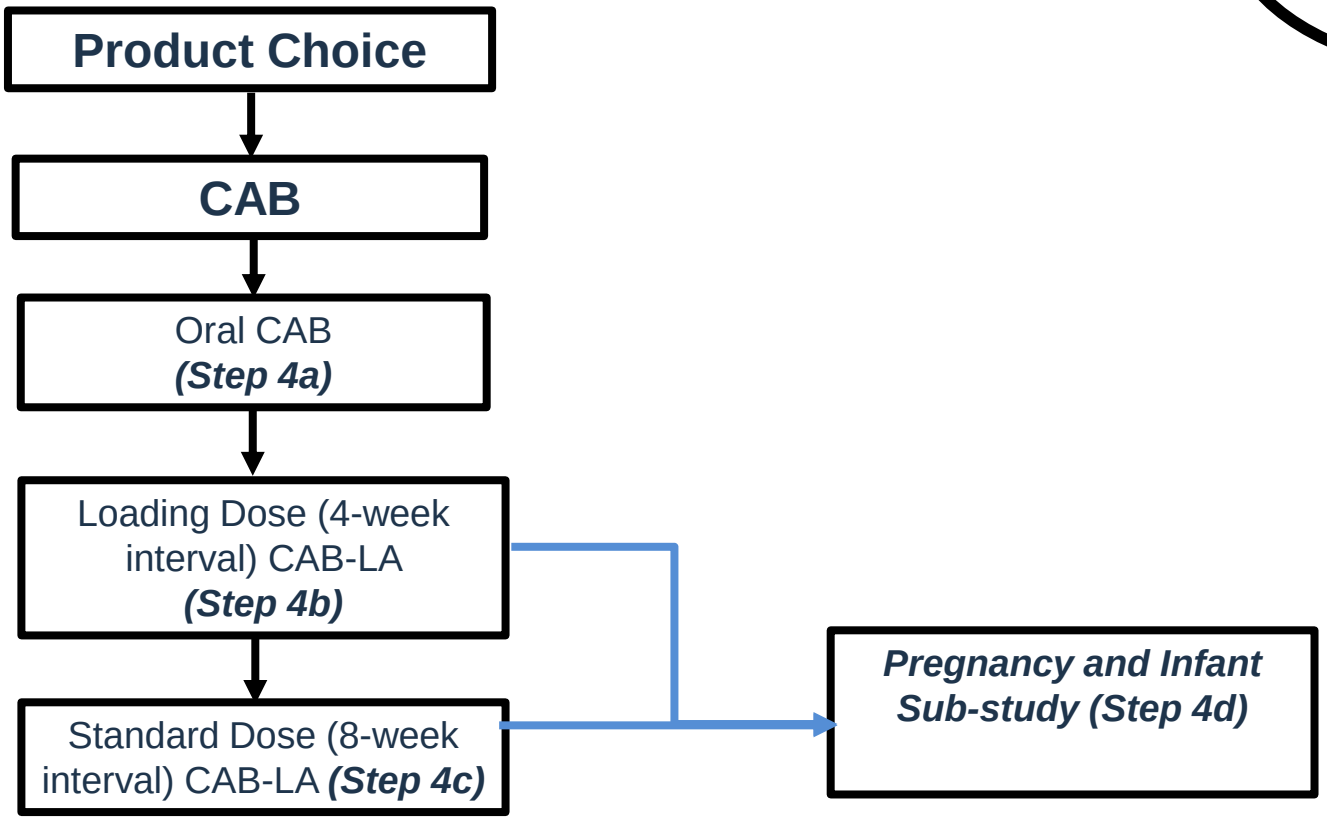

Starts on TDF/FTC but switches to CAB within 24 weeks of starting OL
Product Choice
TDF / FTC (Step 4c)
Switches to CAB
Oral CAB (Step 4a)
Loading Dose (4-week interval) CAB-LA (Step 4b)
Standard Dose (8-week interval) CAB-LA (Step 4c)
Loading Dose (4-week interval) CAB-LA (Step 4b)
Standard Dose (8-week interval) CAB-LA (Step 4c)

Scenario 4

- Participant starts on TDF/FTC (Step 4c), changes to CAB (Step 4a or 4b / Visit 55 or 56).
- On Product Choice form select TDF/FTC which will populate visit 71. At the visit when participant wants to change, mark Yes for the schedule change question on Date of Visit/Interim Visit form, then select “oral CAB” or “loading dose CAB-LA”. This will stop the current schedule’s visit and populate Visit 55 or 56.
- From here the participant would follow standard transition to 4c.
- Record the termination form once participant completes visit 63, or at an earlier visit if participant decides to terminate.

Scenario 5

Starts on CAB, becomes pregnant (Step 4b or 4c), joins Sub-study



Scenario 5

- Participant starts on CAB then becomes pregnant and decides to join the Pregnancy and Infant Sub-study (Visits 76-94).
- On Product Choice form select CAB, then select 4a,4b,4c as appropriate.
- At the visit when participant becomes pregnant on the Pregnancy Test-OLE CRF indicate participant will consent to Sub-study and on the DOV- OLE indicate change of schedules, Step 4d.
- On DOV Pregnancy-OLE, participant will select product.
- Complete Pregnancy Report –OLE and other required pregnancy and infant forms per schedule.
- Record the Termination form once participant completes all visits and outcomes/infant assessments are completed.
- *Participants who start on TDF/FTC in OLE study and have received at least one CAB injection in the past are also eligible for Pregnancy Infant sub – study and the above information would apply to them as well.*

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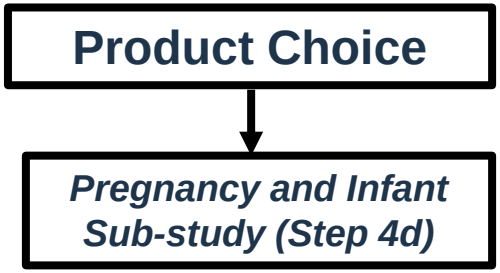
Scenario 6

Participant on Protocol V2 Pregnancy Schedule, is eligible for and decides to join Sub-study



Scenario 6

- Participant on Protocol V2 Pregnancy Schedule, is eligible for and decides to join Sub-study.
- On Product Choice form select Step 4d Pregnancy and Infant sub-study.

Scenario 7

- Participants who have seroconverted during Version 2 of the protocol would continue using Step 2 visit codes as before and terminate once all visits have been completed.
- Participants on Open Label Truvada Schedule or Annual schedule since previous version and are not eligible for OLE would also continue to use the visits per Version 2 and terminate once all visits have been completed.

TRAINING ATTENDEES

- Please send an email to Stephanie Orme (sbeigelo@scharp.org) with the name and designation of all individuals who attended this training today.

Questions?