DMC

P1106: Pharmacokinetic Characteristics of Antiretrovirals and Tuberculosis Medicines in Low Birth Weight Infants

Bobbie Graham and Stephanie Popson

02-July-2015

If you have questions during the study…

- If you have questions about schedules or forms, e-mail the Protocol Data Managers:
  - Bobbie Graham: graham@fstrf.org
  - Stephanie Popson: popson@fstrf.org
- If you have questions about eData, Smart Update, or other technical issues, e-mail User Support: usersprt@fstrf.org
- If you have questions about patient management or the protocol itself, e-mail the P1106 Protocol Team: impaact.**team**p1106@fstrf.org
- impaact.**prot**p1106@fstrf.org is used by protocol team to convey information to registered sites

Data Collection Forms Schedule

SCHEDULES:

- Days of Life
- Weeks of Life
- Form Week

SCREENING:

Screening may start from any point after birth, up until 14 days of life.

ENTRY:

Entry must wait until at least 7 days of life, but must occur before 14 days of life.

DATA COLLECTION FORMS SCHEDULE 03-23-15

STUDY P1106 - BOOK 1 - Arms 1. 2. 3. and 4

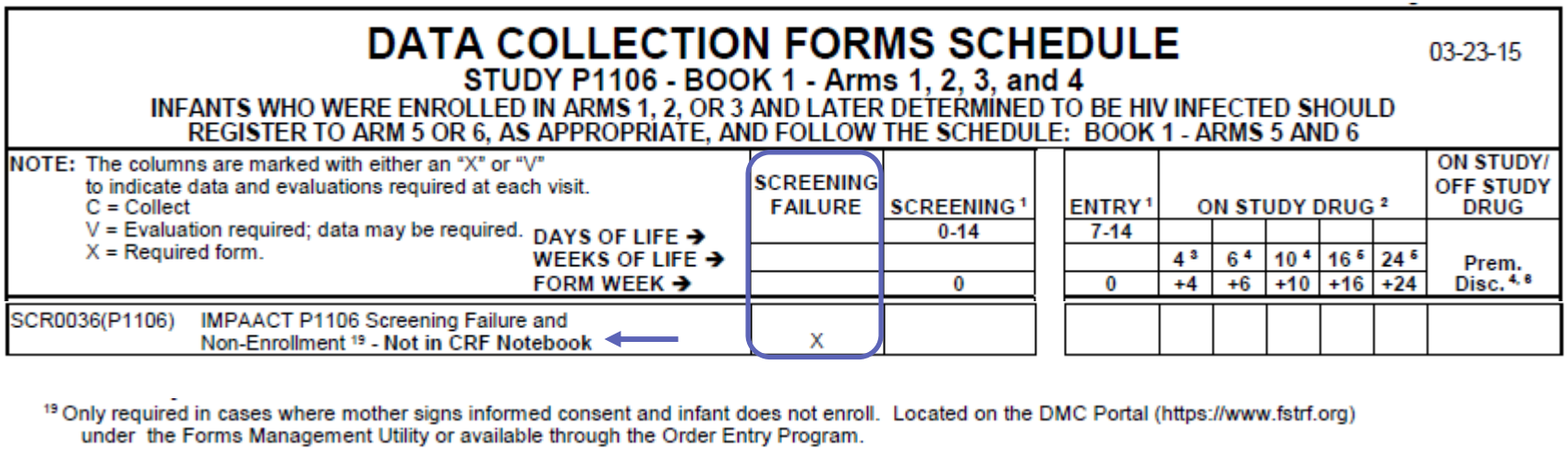
NOTE: The columns are marked with either an "X" or "V" to indicate data and evaluations required at each visit.
C = Collect
V = Evaluation required; data may be required
X = Required form.

	SCREENING FAILURE	SCREENING [1]	ENTRY [1]	ON STUDY DRUG [2]					ON STUDY/ OFF STUDY DRUG
DAYS OF LIFE →		0-14	7-14						
WEEKS OF LIFE →				4 [3]	6 [4]	10 [4]	16 [5]	24 [5]	Prem. Disc. [4, 6]
FORM WEEK →		0	0	+4	+6	+10	+16	+24	

SCREENING FAILURE

Notice the Screening Failure visit listed on the schedule.

- Complete for all participants who are consented, but ultimately do not enroll, regardless of the reason for non-enrollment.
- Form is located on the DMC Portal.



DATA COLLECTION FORMS SCHEDULE 03-23-15

STUDY P1106 - BOOK 1 - Arms 1, 2, 3, and 4

INFANTS WHO WERE ENROLLED IN ARMS 1, 2, OR 3 AND LATER DETERMINED TO BE HIV INFECTED SHOULD REGISTER TO ARM 5 OR 6, AS APPROPRIATE, AND FOLLOW THE SCHEDULE: BOOK 1 - ARMS 5 AND 6

NOTE: The columns are marked with either an "X" or "V" to indicate data and evaluations required at each visit. C = Collect V = Evaluation required; data may be required. X = Required form.		SCREENING FAILURE	SCREENING [1]	ENTRY [1]	ON STUDY DRUG [2]					ON STUDY/ OFF STUDY DRUG
	DAYS OF LIFE →		0-14	7-14						
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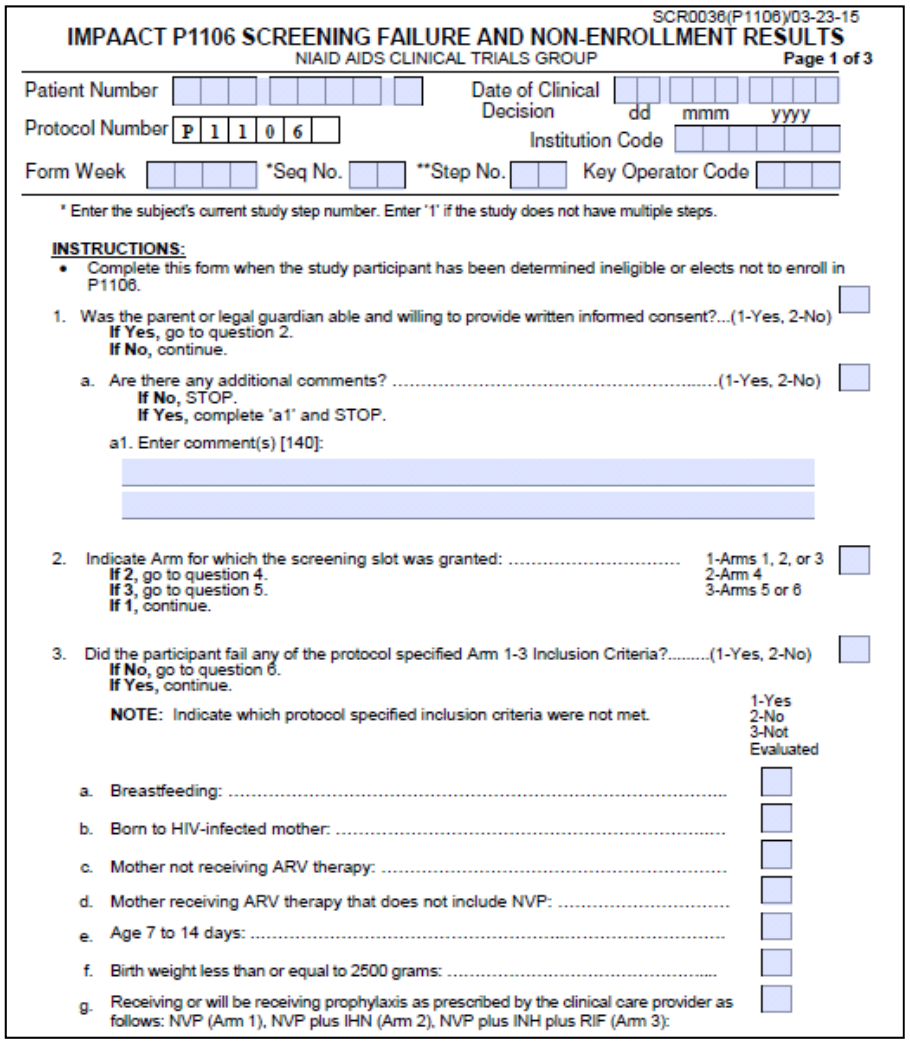
	FORM WEEK →		0	0	+4	+6	+10	+16	+24	
SCR0036(P1106)	IMPAACT P1106 Screening Failure and Non-Enrollment [19] - **Not in CRF Notebook** ←	X								

[19] Only required in cases where mother signs informed consent and infant does not enroll. Located on the DMC Portal (https://www.fstrf.org) under the Forms Management Utility or available through the Order Entry Program.

SCR0036: IMPAACT P1106 Screening Failure and Non-Enrollment Results

- Only completed if participant was screened, but did not enroll for any reason.
- Collects information as to which Eligibility Checklist criteria were not met.
- In future, may change to use PS2001-IMPAACT Screening System.



SCR0036(P1106)03-23-15

IMPAACT P1106 SCREENING FAILURE AND NON-ENROLLMENT RESULTS

NIAID AIDS CLINICAL TRIALS GROUP

Page 1 of 3

Patient Number | Date of Clinical Decision dd mmm yyyy

Protocol Number P 1 1 0 6 | Institution Code

Form Week | *Seq No. | **Step No. | Key Operator Code

* Enter the subject's current study step number. Enter '1' if the study does not have multiple steps.

INSTRUCTIONS:

- Complete this form when the study participant has been determined ineligible or elects not to enroll in P1106.

1. Was the parent or legal guardian able and willing to provide written informed consent?...(1-Yes, 2-No)
   If Yes, go to question 2.
   If No, continue.

   a. Are there any additional comments? .....(1-Yes, 2-No)
      If No, STOP.
      If Yes, complete 'a1' and STOP.

      a1. Enter comment(s) [140]:

2. Indicate Arm for which the screening slot was granted: .....
   If 2, go to question 4.
   If 3, go to question 5.
   If 1, continue.
   1-Arms 1, 2, or 3
   2-Arm 4
   3-Arms 5 or 6

3. Did the participant fail any of the protocol specified Arm 1-3 Inclusion Criteria?.....(1-Yes, 2-No)
   If No, go to question 6.
   If Yes, continue.

   NOTE: Indicate which protocol specified inclusion criteria were not met.

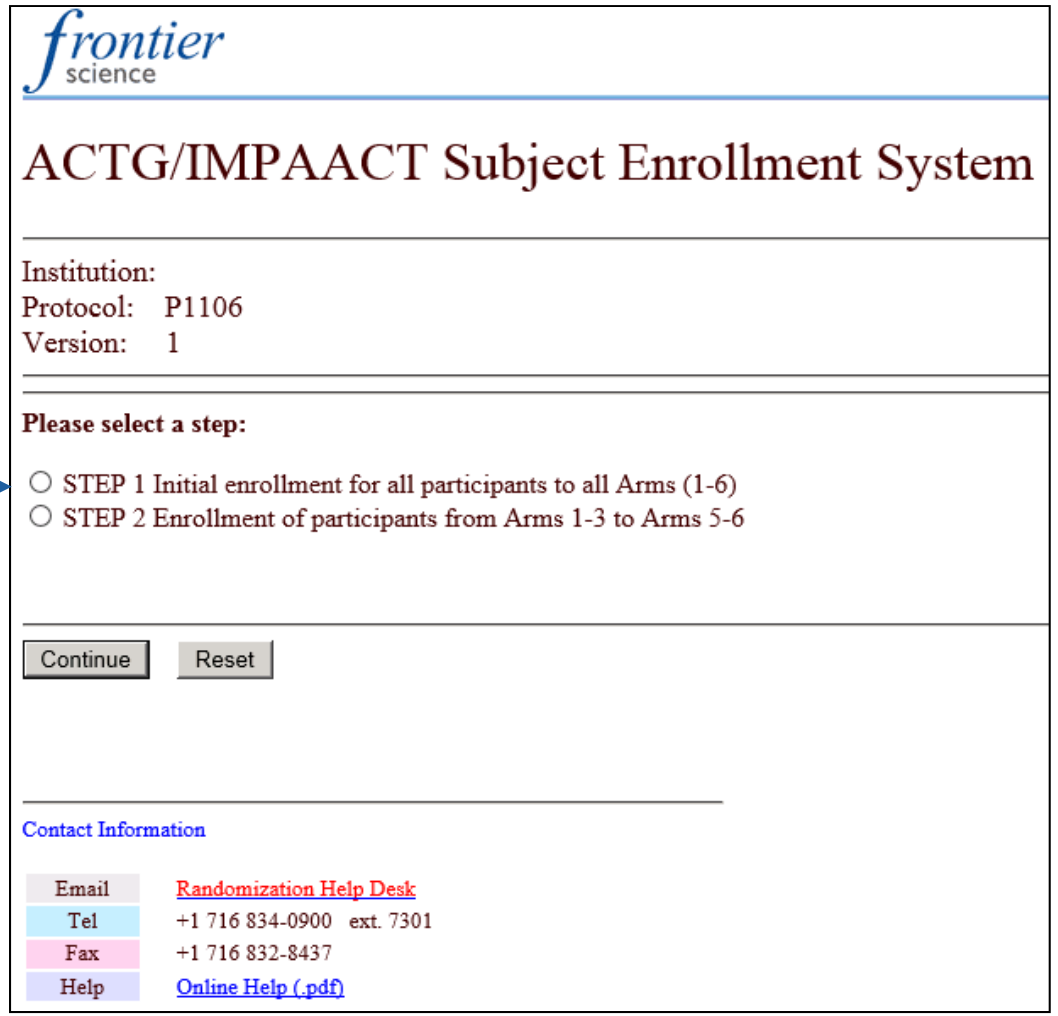
   1-Yes
   2-No
   3-Not Evaluated

   a. Breastfeeding: .....
   b. Born to HIV-infected mother: .....
   c. Mother not receiving ARV therapy: .....
   d. Mother receiving ARV therapy that does not include NVP: .....
   e. Age 7 to 14 days: .....
   f. Birth weight less than or equal to 2500 grams: .....
   g. Receiving or will be receiving prophylaxis as prescribed by the clinical care provider as follows: NVP (Arm 1), NVP plus IHN (Arm 2), NVP plus INH plus RIF (Arm 3):

ELIGIBILITY CHECKLIST

Notice that "STEP" appears in both enrollment options.

<u>EVERY</u> participant starts by enrolling under STEP=1. This applies to ALL Arms (1-6).



What does this statement mean?

DATA COLLECTION FORMS SCHEDULE

03-23-15

STUDY P1106 - BOOK 1 - Arms 1, 2, 3, and 4

INFANTS WHO WERE ENROLLED IN ARMS 1, 2, OR 3 AND LATER DETERMINED TO BE HIV INFECTED SHOULD REGISTER TO ARM 5 OR 6, AS APPROPRIATE, AND FOLLOW THE SCHEDULE: BOOK 1 - ARMS 5 AND 6

NOTE: The columns are marked with either an "X" or "V" to indicate data and evaluations required at each visit.
C = Collect
V = Evaluation required; data may be required.
X = Required form.

	SCREENING FAILURE	SCREENING [1]	ENTRY [1]	ON STUDY DRUG [2]					ON STUDY/ OFF STUDY DRUG
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FORM WEEK →		0	0	+4	+6	+10	+16	+24	

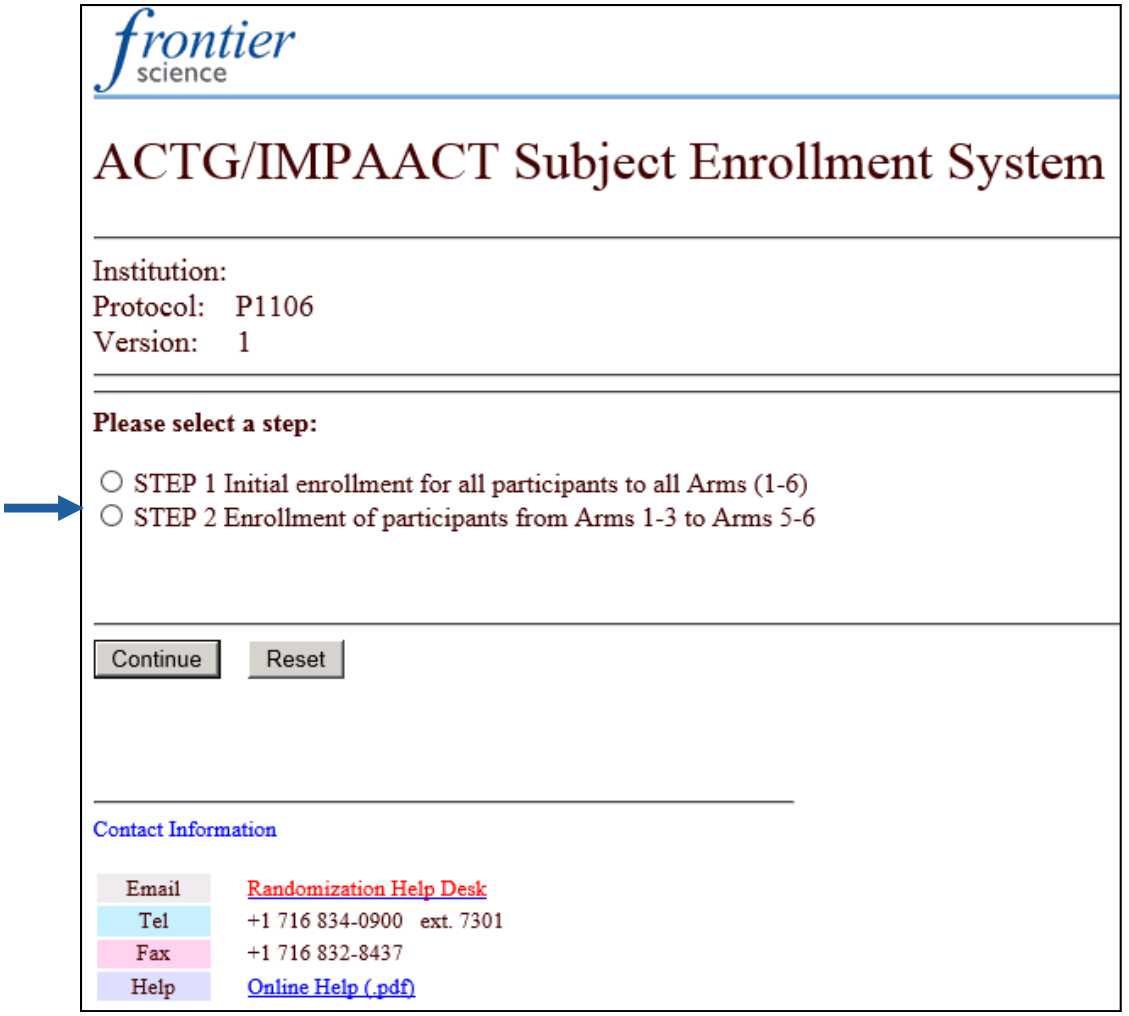
It is possible that small subset of HIV-Exposed participants from Arms 1-3 may eventually test as HIV+. This subset of infants are encouraged to enroll into Arms 5-6.

HOW do you do this?

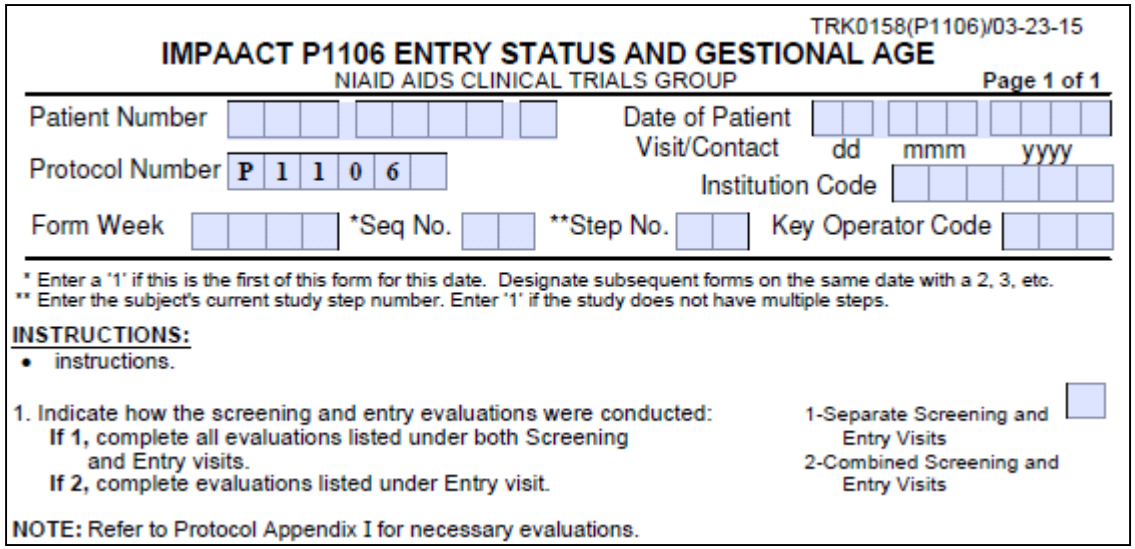
ELIGIBILITY CHECKLIST

That subset of participants are then consented and enrolled onto either Arm 5 or 6.

NOTE: Although the word STEP is not used within the protocol, the study is managed as a STEP protocol.



TRK0158: IMPAACT P1106 ENTRY STATUS and Gestational Age



TRK0158(P1106)/03-23-15

IMPAACT P1106 ENTRY STATUS AND GESTIONAL AGE

NIAID AIDS CLINICAL TRIALS GROUP

Page 1 of 1

Patient Number

Date of Patient Visit/Contact dd mmm yyyy

Protocol Number P 1 1 0 6

Institution Code

Form Week *Seq No. **Step No. Key Operator Code

* Enter a '1' if this is the first of this form for this date. Designate subsequent forms on the same date with a 2, 3, etc.
** Enter the subject's current study step number. Enter '1' if the study does not have multiple steps.

INSTRUCTIONS:

- instructions.

1. Indicate how the screening and entry evaluations were conducted:
   If 1, complete all evaluations listed under both Screening and Entry visits.
   If 2, complete evaluations listed under Entry visit.

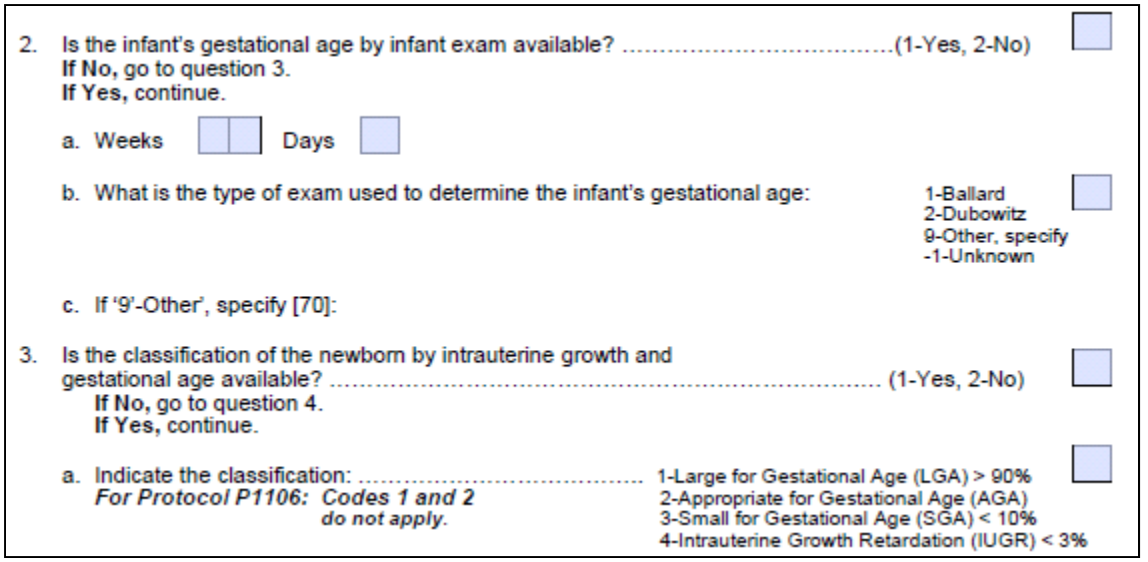
1-Separate Screening and Entry Visits
2-Combined Screening and Entry Visits

NOTE: Refer to Protocol Appendix I for necessary evaluations.

- Documents whether Screening and Entry visits were separate or combined
- Affects the Delinquency expectations

TRK0158: IMPAACT P1106 Entry Status and GESTATIONAL AGE

Information needed by statisticians to describe participant population.



2. Is the infant's gestational age by infant exam available? .....(1-Yes, 2-No)
If No, go to question 3.
If Yes, continue.

   a. Weeks ☐☐ Days ☐

   b. What is the type of exam used to determine the infant's gestational age:
   1-Ballard
   2-Dubowitz
   9-Other, specify
   -1-Unknown

   c. If '9'-Other', specify [70]:

3. Is the classification of the newborn by intrauterine growth and gestational age available? ..... (1-Yes, 2-No)
If No, go to question 4.
If Yes, continue.

   a. Indicate the classification: .....
   For Protocol P1106: Codes 1 and 2 do not apply.
   1-Large for Gestational Age (LGA) > 90%
   2-Appropriate for Gestational Age (AGA)
   3-Small for Gestational Age (SGA) < 10%
   4-Intrauterine Growth Retardation (IUGR) < 3%

TXW0277: P1106 Antiretroviral Regimen Record

TXW0277(P1106)/03-23-15

IMPAACT P1106 ANTIRETROVIRAL REGIMEN RECORD
NIAID AIDS CLINICAL TRIALS GROUP

Patient Number | Date of Patient Visit/Contact dd mmm yyyy
Protocol Number P 1 1 0 6 | Institution Code
Form Week | *Seq No. | **Step No. | Key Operator Code

For Arms 1-3: ***Record all antiretrovirals ever taken since birth on this form, including ARVs for PMTCT.***

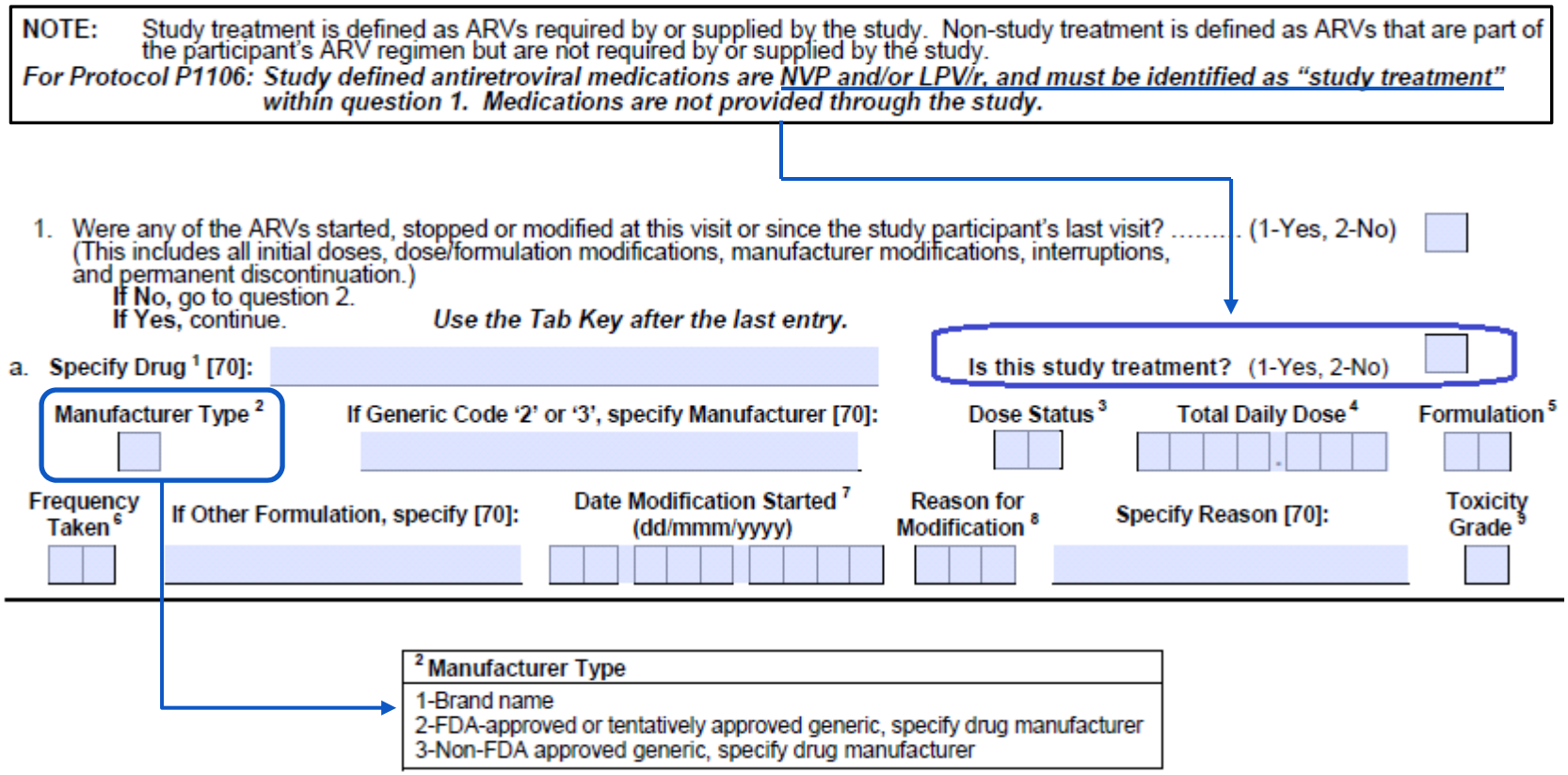
Note different instructions for Arms 1-3 vs Arms 5-6.

For Arms 5-6: ***For infants originally enrolled in Arms 5 or 6, record all prior antiretrovirals taken since birth on the Antiretroviral Concomitant Medications (PE0420) form. After entry, record all antiretrovirals taken while on study on this form.***

For infants who were initially enrolled in Arms 1-3 and later determined to be HIV infected and then enrolled onto Arms 5-6, continue to record all antiretrovirals on this form, however indicate the step change.

TXW0277, Continued

Indicate whether ARV is “study treatment” and indicate “manufacturer type”.



Expected vs Unexpected Events

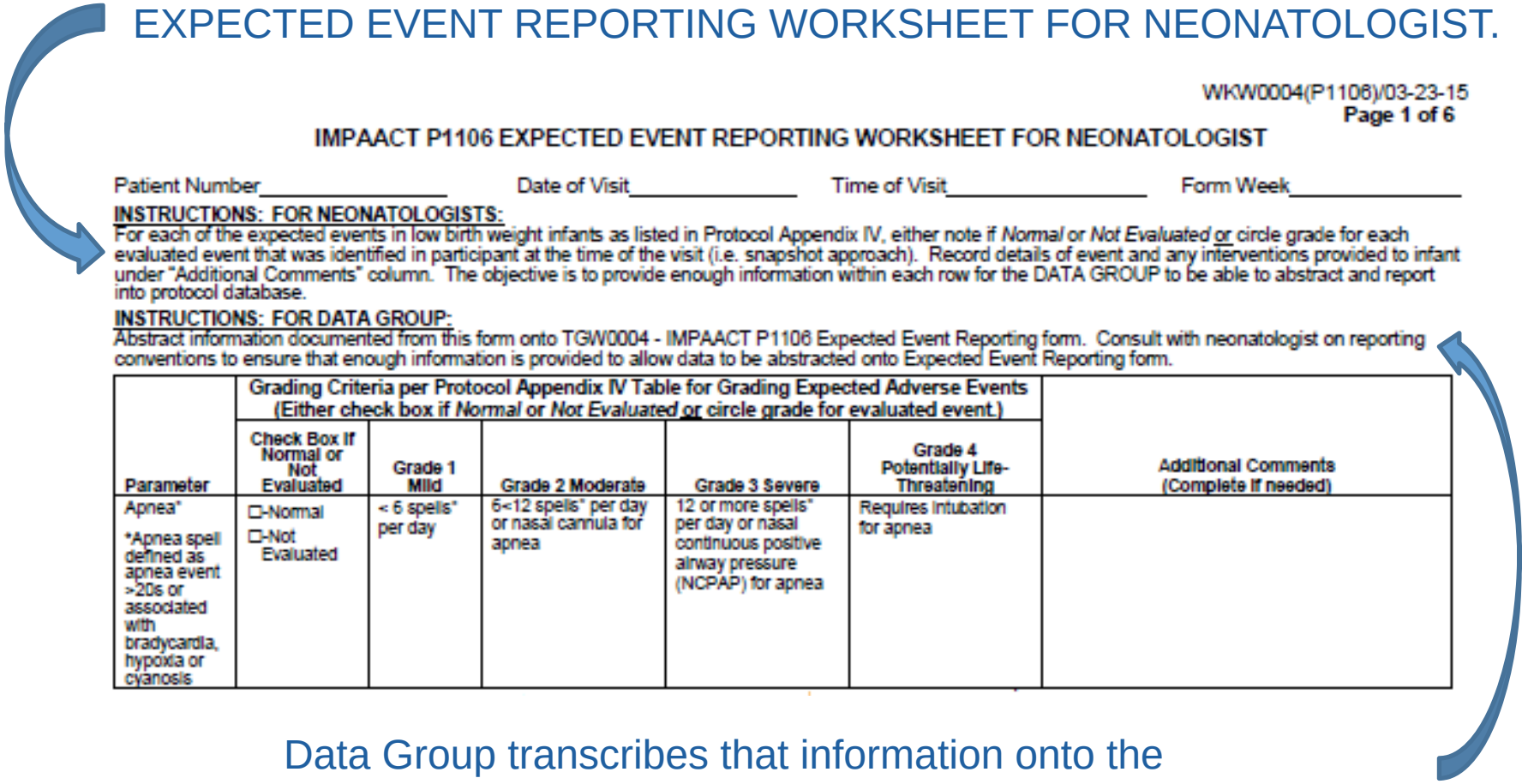
- Expected Events: Defined as those limited events listed in Protocol Appendix IV.
- Unexpected Events: Defined as all other events outside the scope of Protocol Appendix IV. The term SUSAR (Suspected Unexpected Serious Adverse Reaction) is used throughout CRFs.

INSTRUCTIONS:

- Record the expected events routinely noted in low birth weight infants as listed in Protocol Appendix IV on this form. Abstract information collected by neonatologist from the "Expected Event Reporting Worksheet for Neonatologist" (WKW0004) onto this form. This provides a snapshot (i.e. whether the event was identified in the infant at the time of the visit) check of those expected events as listed in Protocol Appendix IV.
- Record unexpected (SUSAR) events and protocol required hematologies/chemistries on appropriate form.
  - Diagnoses III - (PE6852)
  - Signs and Symptoms - III - (PE6832)
  - IMPAACT P1106 Hematologies and Chemistries - (LBW0143)

Reporting Expected Events

Neonatologist report findings on the WKW0004-IMPAACT P1106 EXPECTED EVENT REPORTING WORKSHEET FOR NEONATOLOGIST.



WKW0004(P1106)/03-23-15
Page 1 of 6

IMPAACT P1106 EXPECTED EVENT REPORTING WORKSHEET FOR NEONATOLOGIST

Patient Number_____ Date of Visit_____ Time of Visit_____ Form Week_____

INSTRUCTIONS: FOR NEONATOLOGISTS:
For each of the expected events in low birth weight infants as listed in Protocol Appendix IV, either note if *Normal* or *Not Evaluated* or circle grade for each evaluated event that was identified in participant at the time of the visit (i.e. snapshot approach). Record details of event and any interventions provided to infant under "Additional Comments" column. The objective is to provide enough information within each row for the DATA GROUP to be able to abstract and report into protocol database.

INSTRUCTIONS: FOR DATA GROUP:
Abstract information documented from this form onto TGW0004 - IMPAACT P1106 Expected Event Reporting form. Consult with neonatologist on reporting conventions to ensure that enough information is provided to allow data to be abstracted onto Expected Event Reporting form.

	Grading Criteria per Protocol Appendix IV Table for Grading Expected Adverse Events (Either check box if *Normal* or *Not Evaluated* or circle grade for evaluated event.)					
Parameter	Check Box If Normal or Not Evaluated	Grade 1 Mild	Grade 2 Moderate	Grade 3 Severe	Grade 4 Potentially Life-Threatening	Additional Comments (Complete if needed)
Apnea* *Apnea spell defined as apnea event >20s or associated with bradycardia, hypoxia or cyanosis	☐-Normal ☐-Not Evaluated	< 6 spells* per day	6<12 spells* per day or nasal cannula for apnea	12 or more spells* per day or nasal continuous positive airway pressure (NCPAP) for apnea	Requires intubation for apnea	

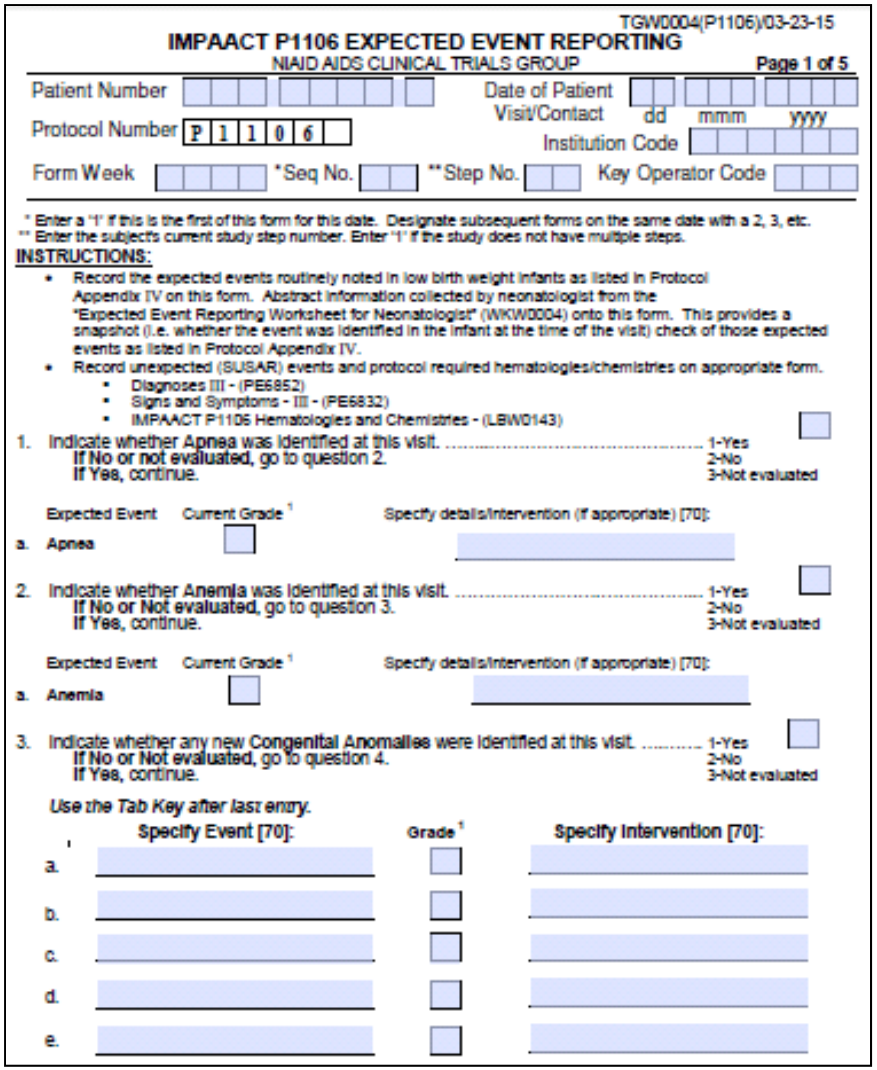
Data Group transcribes that information onto the TGW0004-IMPAACT P1106 EXPECTED EVENT REPORTING.

Reporting Expected Events

TGW0004-IMPAACT P1106 EXPECTED EVENT REPORTING

TGW0004 is laid out to mirror the reporting on the WKW0004.
[NOTE: This makes the transcription process easier!]

The transcribed information is what gets keyed into the database.
[TIP: Make sure there is good communication between neonatologist and data group to ensure accurate reporting.]



TGW0004(P1106)/03-23-15

IMPAACT P1106 EXPECTED EVENT REPORTING

NIAID AIDS CLINICAL TRIALS GROUP

Page 1 of 5

Patient Number | Date of Patient Visit/Contact dd mmm yyyy

Protocol Number P 1 1 0 6 | Institution Code

Form Week | *Seq No. | **Step No. | Key Operator Code

* Enter a '1' if this is the first of this form for this date. Designate subsequent forms on the same date with a 2, 3, etc.
** Enter the subject's current study step number. Enter '1' if the study does not have multiple steps.

INSTRUCTIONS:

- Record the expected events routinely noted in low birth weight infants as listed in Protocol Appendix IV on this form. Abstract information collected by neonatologist from the "Expected Event Reporting Worksheet for Neonatologist" (WKW0004) onto this form. This provides a snapshot (i.e. whether the event was identified in the infant at the time of the visit) check of those expected events as listed in Protocol Appendix IV.
- Record unexpected (SUSAR) events and protocol required hematologies/chemistries on appropriate form.
  - Diagnoses III - (PE6852)
  - Signs and Symptoms - III - (PE6832)
  - IMPAACT P1106 Hematologies and Chemistries - (LBW0143)

1. Indicate whether **Apnea** was identified at this visit. ..... 1-Yes 2-No 3-Not evaluated
   If No or not evaluated, go to question 2.
   If Yes, continue.

	Expected Event	Current Grade [1]	Specify details/intervention (if appropriate) [70]:
a.	Apnea		

2. Indicate whether **Anemia** was identified at this visit. ..... 1-Yes 2-No 3-Not evaluated
   If No or Not evaluated, go to question 3.
   If Yes, continue.

	Expected Event	Current Grade [1]	Specify details/intervention (if appropriate) [70]:
a.	Anemia		

3. Indicate whether any new **Congenital Anomalies** were identified at this visit. ..... 1-Yes 2-No 3-Not evaluated
   If No or Not evaluated, go to question 4.
   If Yes, continue.

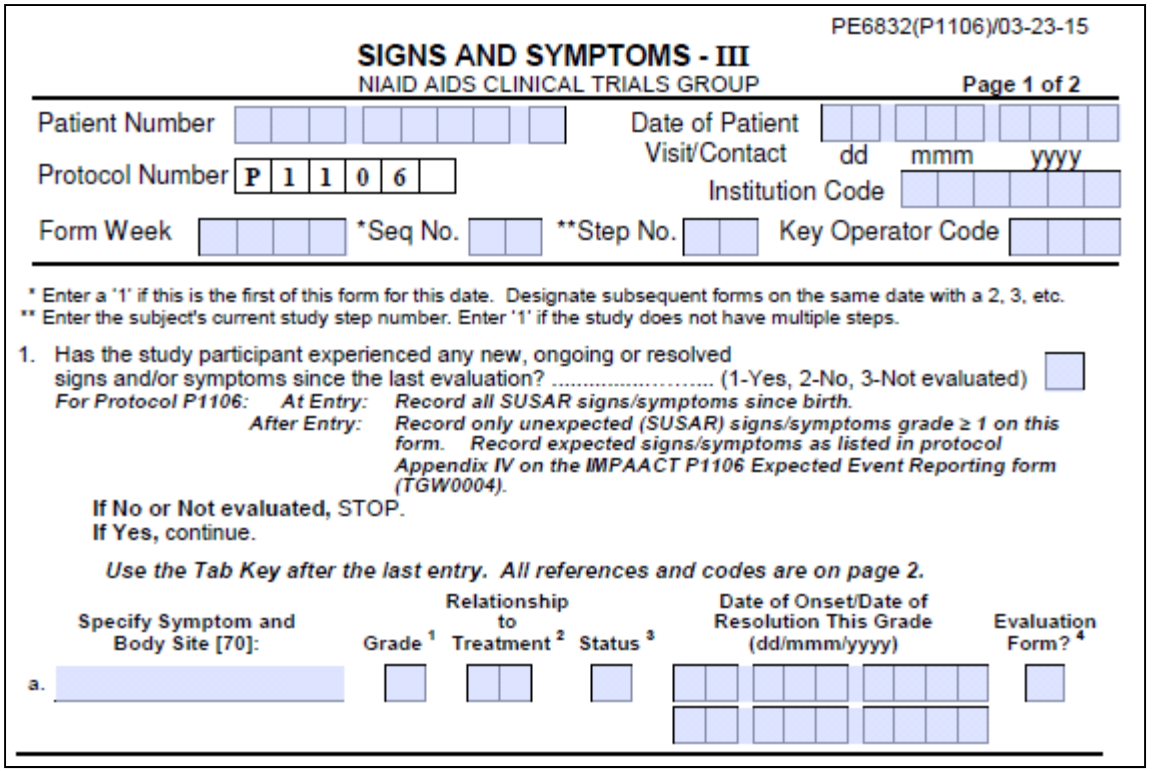
Use the Tab Key after last entry.

	Specify Event [70]:	Grade [1]	Specify Intervention [70]:
a.			
b.			
c.			
d.			
e.			

Reporting Unexpected Events

Unexpected events reported on the primary safety CRFs:

- LBW0143-IMPAACT P1106 Hematologies and Chemistries
- PE6832-Signs and Symptoms-III
- PE6852-Diagnoses - III



PE6832(P1106)/03-23-15

SIGNS AND SYMPTOMS - III

NIAID AIDS CLINICAL TRIALS GROUP

Page 1 of 2

Patient Number | Date of Patient Visit/Contact dd mmm yyyy

Protocol Number P 1 1 0 6 | Institution Code

Form Week | *Seq No. | **Step No. | Key Operator Code

* Enter a '1' if this is the first of this form for this date. Designate subsequent forms on the same date with a 2, 3, etc.
** Enter the subject's current study step number. Enter '1' if the study does not have multiple steps.

1. Has the study participant experienced any new, ongoing or resolved signs and/or symptoms since the last evaluation? ..... (1-Yes, 2-No, 3-Not evaluated)

For Protocol P1106: At Entry: Record all SUSAR signs/symptoms since birth.
After Entry: Record only unexpected (SUSAR) signs/symptoms grade ≥ 1 on this form. Record expected signs/symptoms as listed in protocol Appendix IV on the IMPAACT P1106 Expected Event Reporting form (TGW0004).

If No or Not evaluated, STOP.
If Yes, continue.

Use the Tab Key after the last entry. All references and codes are on page 2.

Specify Symptom and Body Site [70]:	Grade [1]	Relationship to Treatment [2]	Status [3]	Date of Onset/Date of Resolution This Grade (dd/mmm/yyyy)	Evaluation Form? [4]
a.					

Questions?