IMPAACT 2000 CRF Overview

Data Management Center
Alex DiPerna
September 2014
Agenda

- Review the Data Collection Forms Schedules (DCFS)
- Examine specific CRFs
- Study notes
- Questions
What is the meaning of X?
• Forms are required for that visit

What is the meaning of V?
• Data collection on these forms may be required; “event directed”
• In this study, the Study Event Tracking form directs completion of the V’d forms, when appropriate
• Collect the information for the visit week
• Record data from the week on ONE CRF
• Key to the database on the last day of the visit week, unless otherwise specified

SVW0262
• Tracks study visits and events
• Directs completion of other CRFs
• Complete on every visit day and/or visits marked with an X

ADM0040 and F3008
• Complete on in-person visit days, any other visit marked with an X, and if directed by Study Event Tracking form

TRK0144
• Tracks episode(s) of fever
• Completion directed from the Study Event Tracking

PRN Section
• Location for forms that should be completed only as needed
Sick Visits:

Visit that takes place outside of a regularly scheduled clinic visit

To calculate the Form Week for the Header:

Form Week = Form Week of the last visit + the number of weeks since that visit

The following forms are required at a Sick Visit (X):
- Visit Status Report
- Master Specimen Tracking
- Study Event Tracking

The following forms may need to be completed and are directed from the Study Event Tracking:
- Non-ARV Concom Meds
- Signs and Symptoms
- Diagnoses
- Episodic Fever Tracking

### DATA COLLECTION FORMS SCHEDULE

**IMPAACT 2000**

**BOOK 4 - WEEK 4, WEEK 5, and WEEK 8**

<table>
<thead>
<tr>
<th>Administrative Forms</th>
<th>WEEKS</th>
<th>ON STUDY</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DAYS 3</td>
<td></td>
</tr>
<tr>
<td>F1601(2000)</td>
<td>Off Study - Revised 5</td>
<td>X</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study Forms</th>
<th>WEEKS</th>
<th>ON STUDY</th>
</tr>
</thead>
<tbody>
<tr>
<td>F3099(2000)</td>
<td>Master Specimen Tracking - Revised</td>
<td>X X X</td>
</tr>
<tr>
<td>PE0414(2000)</td>
<td>Non-Antiretroviral Concomitant Medications/Therapies - IV 5</td>
<td>V V V</td>
</tr>
<tr>
<td>PE0332(2000)</td>
<td>Signs and Symptoms - III 5.7</td>
<td>V V V</td>
</tr>
<tr>
<td>PE882(2000)</td>
<td>Diagnoses - III 5.7</td>
<td>V V V</td>
</tr>
<tr>
<td>TRK0114(2000)</td>
<td>IMPAACT 2000 Episodic Fever Tracking 5</td>
<td>V V V</td>
</tr>
</tbody>
</table>

1. Form Week of Sick Visit = Form week of the last visit + the number of weeks since that visit.
2. Key into the database, even if there are no data to record.
3. If in-person visit is moved by ± 1 day, then telephone visit is moved to replace in-person visit date.
4. Located in the section labeled "PRN." Use only as needed.
5. Located in the section labeled "Off Study".
6. Located in the section labeled "Event Directed Forms".
7. Complete Event Evaluation form if necessary.
“For Protocol” Notes

PLEASE:
• Make sure to read ALL of the instructions on each form
• Be sure to pay attention to ALL study specific notes on the CRFs

The following CRFs are just a few of the forms that contain important instructions specific to the IMPAACT 2000 study:
• Visit Status Report and Master Specimen Tracking forms
• Non-ARV concomitant Medications
• Signs and Symptoms
• Diagnoses
• Event Evaluation
• Chemistry/Hematology

For Protocol 2000:
Please refer to Table 5 in Protocol Section 7.2 for Adverse Event Signs and Symptoms CRF Recording Requirements.
Use only one PE6832 for each visit week. Complete an additional form if the number of signs and symptoms entered for the visit week exceeds lines a-g.
The header date of the form should be the date the form is keyed.
Record all signs and symptoms of any grade, but only evaluate:
• Any SAE, LRI, Grade 4 Fever, and any Grade ≥ 3 Solicited or Unsolicited AEs that occur during the first 28 days on study (Acute Phase).
• Any SAE or LRI that occurs between days 29-56.
• After Day 56, any SAE that meets study recording criteria listed in Table 5.

For Protocol 2000:  
At Inoculation:  Does the study participant have any current or ongoing signs and/or symptoms?
### Sick Visit Instructions

- Complete this form at each clinic visit.
- For Protocol 2000: For sick visits that occur outside of a regularly scheduled visit, use code 8.
- If Q1 is 1, 3 or 4, complete 2 and go to question 3.
- If Q2 is 2, complete 3 and go to question 3.

### Complete and Key Both Forms at the Same Visit

Complete and key both forms at the same visit for 2000.

### Always Answer Q2 as “2-No” for 2000

Ensure to always answer Q2 as “2-No” for 2000.
If there are no other assays to record after Question 4b3, eData will take you to Question 5.
At each visit during a visit week, collect the data on ONE CRF. ONE CRF will be completed for each visit week.

If the data exceeds the available space (a-i), continue onto an additional form (call sequence 2).

Each additional form should have the same header date (date of last visit day of visit week).

Even if there are no data to record for the visit week, answer Q1 as “2-no” and submit the form.

Example for Header Date:
You have recorded data on two Non-ARV Concomitant Medications forms (sequence 1 and 2), and the last visit day of the visit week is 27-September-2014, the Header Date on EACH form will be 27-SEP-2014.
At each visit during a visit week, collect data on ONE CRF (One CRF for each visit week).

If the data recorded for the week exceeds lines a-g, continue to record on an additional CRF.

All forms for a visit week will have the same Header Date (date of the last visit day of a visit week).

Even if there are no data to record, answer Q1 as “2-no” and submit the form.

Notice instructions for recording data, evaluating and grading AEs.
PE6852: Diagnoses → The instructions for Signs and Symptoms also apply to Diagnoses

Instructions for data collection, and recording and evaluating AEs

Instructions for grading fever and AEs

Question 1 for Protocol 2000
Table 5: AE CRF Recording Requirements

<table>
<thead>
<tr>
<th>Study Phase at the Time of Event Onset</th>
<th>Calendar Date</th>
<th>AEs to Record on CRFs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days 6 to Day 28 Visit (Acute Phase)</td>
<td>ANY</td>
<td>- All SAEs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- All solicited AEs that meet Appendix 4 criteria</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- All unsolicited AEs (Grades 1 to 4), with the exception of the following conditions if not treated with prescription medication or OTC medications with antipyretic properties: fever, URI, otitis media, diarrhea, tachypnea, and vomiting.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Note: SAEs and LRIs must be reported via DAIDS Adverse Experience Reporting System (DAERS) (see Section 7.3).</td>
</tr>
<tr>
<td>Day 29 to Day 56 Visit (Post-Acute Phase)</td>
<td>ANY</td>
<td>- All SAEs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- LRIs that meet Appendix 4 criteria</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Note: SAEs and LRIs must be reported via DAERS (see Section 7.3).</td>
</tr>
<tr>
<td>Day 57 and until RSV Season Surveillance Period</td>
<td>Up to October 31st in year of inoculation</td>
<td>NONE except Grade ≥ 3 AE or SAE that are probably or definitely related to Pre-RSV Season Study Visit procedures. Note: During this period, there will be no vaccine shedding; therefore, no new events will be related to the study product.</td>
</tr>
<tr>
<td>RSV Season Surveillance Period</td>
<td>November 1st to March 31st following inoculation</td>
<td>- Fever, URI, and otitis media that meet SAE definitions</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Medically attended:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- URI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- LRI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- otitis media</td>
</tr>
<tr>
<td>Post-RSV Season</td>
<td>April 1st to April 30th in the year after the inoculation</td>
<td>NONE except Grade ≥ 3 AE or SAE that are probably or definitely related to Post-RSV Season Study Visit procedures.</td>
</tr>
</tbody>
</table>

APPENDIX 4: DEFINITIONS OF SOLICITED ADVERSE EVENTS

<table>
<thead>
<tr>
<th>Event</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>Temperature ≥100.0°F, or rectal temperature of ≥100.4°F</td>
</tr>
<tr>
<td>Acute Otitis Media¹</td>
<td>Loss of tympanic membrane landmarks, accompanied by erythema and loss of mobility. May or may not be associated with fever or other respiratory symptoms. Confirmed with tympanometry if possible.</td>
</tr>
<tr>
<td>Upper Respiratory Tract Illness (URTI)</td>
<td>Two or more consecutive days of sneezing, coughing, and/or a runny nose, or a sore throat.</td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>Two or more consecutive days of pharyngeal erythema accompanied by edematous, and/or enlarged tender lymph nodes. Note: May be associated with sore throat, or painful or difficult swallowing.</td>
</tr>
<tr>
<td>Cough without LRI</td>
<td>Two or more consecutive days of 3 or more episodes of cough during a 15-minute timed observation period, or cough awaken child from sleep. Note: Not associated with eating, drinking, or choking.</td>
</tr>
<tr>
<td>Hoarseness</td>
<td>An unusually deep or rough quality of voice.</td>
</tr>
<tr>
<td>Lower Respiratory Tract Illness (LRTI)</td>
<td>Lower Respiratory Tract Illness (LRTI)</td>
</tr>
<tr>
<td>Wheezing²</td>
<td>Sustained, high-pitched, musical breath sounds, especially during the expiratory phase, which do not clear with cough.</td>
</tr>
<tr>
<td>Pneumonia²</td>
<td>Rales and crackles, originating in the lower respiratory tract, usually accompanied by tachypnea, which do not clear with cough. May be confirmed by x-ray showing areas of consolidation.</td>
</tr>
<tr>
<td>Laryngotracheobronchitis (croup)¹²</td>
<td>Barking cough, hoarseness, and inspiratory stridor.</td>
</tr>
<tr>
<td>Rhonchi²</td>
<td>Course breath sounds which are not transmitted noises from the upper airway and do not clear with cough.</td>
</tr>
<tr>
<td>Rales²</td>
<td>Abnormal breath sound heard through a stethoscope. Rales may be absent (whistling), dry (crackling) or wet (more slisly) depending on the amount and density of fluid refluxing back and forth in the air passages.</td>
</tr>
</tbody>
</table>

¹ Diagnosis must be made by a medical professional.
² Must be confirmed by auscultation.
³ Clinical assessment must be made by a medical professional and confirmed by a second medical professional, if possible.

NOTE: Solicited AEs will only be recorded on CRFs according to criteria defined in Section 7.2.
Grading Tables for AEs and Fever from Protocol Sections 7.151 and 7.152 (referenced on CRFs)

### 7.151 Solicited AE Grading

#### Table 3: Grading Table for Solicited AEs

<table>
<thead>
<tr>
<th>Severity</th>
<th>Defined</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade (0) None</td>
<td>No medical intervention required; may include over-the-counter medications managed by the subject or caregiver for treatment of symptoms</td>
</tr>
<tr>
<td>Grade (1) Mild</td>
<td>Outpatient medical intervention by a health care provider required; may include use of over-the-counter and/or prescription medications</td>
</tr>
<tr>
<td>Grade (2) Moderate</td>
<td>Prolonged medical intervention and/or hospitalization required</td>
</tr>
<tr>
<td>Grade (3) Severe</td>
<td>Life threatening illness requiring hospitalization with intensive care</td>
</tr>
<tr>
<td>Grade (4) Life threatening</td>
<td>Event resulting in fatal outcome to the subject</td>
</tr>
</tbody>
</table>

### 7.152 Fever Grading: Temperature Measurement

#### Table 4: Fever Grading: Temperature Measurement*

<table>
<thead>
<tr>
<th>Severity</th>
<th>Defined</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade (0)</td>
<td>≥100.0°F but &lt;100.4°F (≥37.8°C but &lt;38°C)</td>
</tr>
<tr>
<td>Grade (1)</td>
<td>≥100.4°F but ≤101.4°F (≥38°C but ≤38.6°C)</td>
</tr>
<tr>
<td>Grade (2)</td>
<td>≥101.5°F but ≤102.4°F (≥38.7°C but ≤39.1°C)</td>
</tr>
<tr>
<td>Grade (3)</td>
<td>≥102.5°F but ≤104.8°F (≥39.2°C but ≤40.5°C)</td>
</tr>
<tr>
<td>Grade (4)</td>
<td>≥104.9°F (≥40.0°C)</td>
</tr>
</tbody>
</table>

*Applies to any modality of temperature measurement
SVW0262 - Study Event Tracking:
Required at EVERY visit (every day)

Enter the appropriate visit type depending on which Data Collection Forms Schedule the participant is following at that visit:
- Days 0-56 (Books 1-4)
- Pre-RSV Season, Seasonal Surveillance, and Post-RSV Season (Book “5”)

For Question 1a, which only applies if the participant is within study days 0-56, the “visit day” is the study visit day listed on the Data Collection Forms Schedule (0-56).

This form directs the completion, or continued completion of the:
- Signs and Symptoms
- Diagnoses
- Non-ARV Concomitant Medications
- IMPAACT 2000 Episodic Fever Tracking form
Be sure to complete the F3008-Master Specimen Tracking form for:

- samples obtained for immunologic assays
- nasal wash for viral detection and quantification

If an adventitious virus assay was required at a visit, remember to complete the F3008 CRF, including question 4b3.
EVENT EVALUATION - V
NIH AIDS CLINICAL TRIALS GROUP Page 1 of 4

Patient Number: [ ]
Date of Patient Visit/Contact: [ ]
Protocol Number: [ ]
Form Week: [ ]
Protocol Code: [ ]
Institution Code: [ ]

1. Did the primary event meet the International Conference on Harmonization (ICH) definitions of a Serious Adverse Event?

- [ ] Yes
- [ ] No

Indicate which criteria were met by answering '1-Yes' or '2-No' to each of the following:

- [ ] Results in death
- [ ] Life threatening
- [ ] Inpatient hospitalization or prolongation of existing hospitalization
- [ ] Persistent or significant disability/incapacity
- [ ] Congenital anomaly/birth defect
- [ ] Other important medical event

* Enter a '1' if this is the first of this form for this event. 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. All instructions and codes are located at the back of this form in the PE5895 Appendix A.

2. Did this primary event meet Expedited Adverse Event (EAE) reporting requirements?

- [ ] Yes
- [ ] No

Refer to the EAE Manual and Protocol.

3. Did this primary event meet other protocol reporting requirements for

   For Protocol 2000: Did this primary event meet the criteria for evaluation as described in the instructions on the Signs and Symptoms of Diagnoses forms?

If all criteria as 1, 2, and 3 are answered No, STOP. Do not complete this form.

6. Continued

   a. Diagnosis Code: [ ]
   Body Site Code: [ ]
   Grade: [ ]
   Date of Onset (dd/mm/yyyy): [ ]
   Specify Diagnosis, Organism and Body Site (and other relevant information): [ ]

   b. Specify Sign/Symptom and Body Site (and other relevant information): [ ]

   Grade: [ ]
   Date of Onset (dd/mm/yyyy): [ ]

   c. Lab Test Code: [ ]
   Value: [ ]
   Limit of normal: [ ]
   Grade: [ ]
   Specimen Date (dd/mm/yyyy): [ ]

7. Is this adverse event associated with the study participant or the study participant's fetus or neonate?

   a. Study participant AE: [ ]
   b. Study participant's fetus or neonate: [ ]

Events associated with a fetus or non-enrolled neonate are recorded under the mother's PID number with Question 7 marked "Study participant's fetus or neonate". Events associated with an enrolled neonate or infant must be recorded under the infant's PID number with Question 7 marked "Study participant AE".

EVENT EVALUATION - V

4. Describe the primary event [280]:

__________________________________________________________

5. Enter the status code of the primary event at the time of this report:

- Recovered/resolved
- Recovering/resolving
- Not recovered/not resolved (ongoing)
- Recovered/resolved with sequelae

Describe sequelae [70]:

__________________________________________________________

6. Indicate the primary event being evaluated:

- 1-Diagnosis: Complete 'a' and go to question 7.
- 2-Sign/Symptom: Complete 'b' and go to question 7.
- 3-Chemistry or Hematology result: Complete 'c' and go to question 7.

NOTE: Any event reported here must also be recorded on the appropriate diagnoses, signs and symptoms, chemistry or hematology form and identified as a primary event.

HEMATOLOGIES - III

INSTRUCTIONS:

- Required tests are those:
  - Specified by the protocol.
  - Caused a treatment modification.
  - Required an Expected Adverse Event (EAE) report to be filed.
  - Met International Conference on Harmonization (ICH) reporting guidelines.

- Any hematology associated with a primary event must be completed on this form regardless of grade.

For Protocol 2000: Complete this form if a hematology result associated with a primary event is obtained, and an Event Evaluation form (PE6865) has been completed.

CHEMISTRIES - III

INSTRUCTIONS:

- Required tests are those:
  - Specified by the protocol.
  - Caused a treatment modification.
  - Met International Conference on Harmonization (ICH) reporting guidelines.

- Any chemistry associated with a primary event must be completed on this form regardless of grade.

For Protocol 2000: Complete this form if a chemistry result associated with a primary event is obtained, and an Event Evaluation form (PE6865) has been completed.
This form is V’d on the Data Collection Forms Schedules because...

completion of this CRF is directed from the Study Event Tracking form.

Only complete if an EPISODE of fever has RESOLVED:

- Record the start and stop date of the EPISODE of fever
- Record the MAXIMUM temperature of the fever that occurred during the episode

The occurrence of a fever will be recorded and on the Signs and Symptoms CRF (new, ongoing, and resolved).

Should the participant have more than one fever episode during a visit week, then complete an additional form.

The Header Date of the form is the date of the visit.
VAC0003-Nasal Vaccine Record

Only required at the Inoculation Visit (Day 0)

Only information regarding the study product (RSV LID ΔM2-2 vaccine/placebo) should be recorded on this form.
Questions?

Alexandria DiPerna
diperna@fstrf.org
716-834-0900 ext. 7266

Linda Marillo
marillo@fstrf.org
716-834-0900 ext. 7257