Case Report Forms
A Critical Link to the Success of Your Research Study

October 17, 2007

Alice Bisbee, MPH
Assistant Director, Data Management
BUSPH Data Coordinating Center

Outline
1. Introduction
2. Planning
3. Which data to include
4. The anatomy of a CRF
5. How to ask the questions
6. Examples
7. Review of general design principles
8. Final thought

1. INTRODUCTION

Why is this topic important?
- Sloppy CRFs... sloppy research
- Collect too much data... or too little... or the wrong data
- Study questions can’t be answered
- Annoyed Study Coordinator

What happens when you do it right?
Data will be:
- Complete
- Accurate
- Analyzable
- Answer the scientific questions

What makes a GOOD form?
1. User-friendly, uncluttered, well organized
2. Provides clear instructions for completion
3. Terminology familiar to person filling out
4. Reading level matches study participants and or evaluators
What makes a GOOD form?

5. Easy for subjects/clinic staff to fill out
6. Questions only asked in one place
7. Easy to refer back and clean data
8. Assists analyst in understanding data

2. PLANNING

Decisions

- Paper vs. web
- Spreadsheets vs. database
- Self-key vs. contract out vs. scan

Create draft versions

- Allow plenty of time
- Review the drafts with your study team
  - Investigators
  - Study Coordinator
  - Programmer
  - Data collectors (RA’s, interviewers, clinicians)
  - Clinical experts
  - Data Manager
  - Statistician

Example: draft #2

<table>
<thead>
<tr>
<th>MEDICAL HISTORY</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cardiovascular Status</strong></td>
</tr>
<tr>
<td>Documented CAD</td>
</tr>
<tr>
<td>Angina</td>
</tr>
<tr>
<td>MI (most recent)</td>
</tr>
<tr>
<td>Percutaneous Coronary Intervention</td>
</tr>
<tr>
<td>CABG</td>
</tr>
<tr>
<td>CVA (most recent)</td>
</tr>
<tr>
<td>CHF</td>
</tr>
<tr>
<td>Echocardiogram</td>
</tr>
</tbody>
</table>

Example: draft #99
Use your study team!

Data Management Team

CRFs

Clinical Investigators

Statistician

Keep the User in mind

- Data collectors: logical, accurate, etc.
- Database programmers: database structures, edit checks, etc.
- Data analysts: coding, reference
- Auditors: will use CRFs to assess quality assurance
- CRFs as archival documents

Pilot Forms

- Tested by intended study population/clinicians
  - Age group (elders, teenagers)
  - Language/Literacy level
  - Clinicians: can this form be used to report results?
- All corrections made prior to start of study
- Do not start data collection prior to finalizing study forms
- Pilot the data entry process

Re-evaluate: Adjust Accordingly

- Are any items generating a high non-response rate?
  - Reword/drop question
- Is useful information being obtained from open-ended questions?
  - Categorize/code
- Are the “skip” instructions being followed correctly?
  - Train clinic personnel/revise forms

3. WHICH DATA TO INCLUDE?

- Protocol dictates data collection
- Compliance with regulatory requirements
- Designed so that in 10 years you know what happened in your study
Types of Data to Include
- Collect data listed in protocol
- Regulatory data
  - Informed consent, adverse events, ...
- Administrative data
  - Sample tracking, visits missed, ...
- Should not include data that won’t be analyzed.
  - Clearly indicate which data will not be included in the database.

CRFs as Source Documents
- Controversial, but allowable
- Protocol must identify CRFs that are used as source documents (ICH GCP 6.4.9)

Read the protocol!
Know exactly what data need to be collected... and when.

VARIABLE 1M 3M 12M
- liver function tests  □   □   □
- HbA1c          □   □   □
- echocardiogram  □   □   □
- concomitant medications  □   □   □

4. THE ANATOMY OF A CRF
Anatomy of a CRF

Header

Modules
- Safety Data: demographics, AEs, medical history/physical exam, vital signs, concomitant meds, enrollment date
- Efficacy Data: baseline, 1° and 2° outcome variables

Footer
The confidentiality of records that could identify subjects should be protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirements (ICH GCP 2.11).

The sponsor should use an unambiguous subject identification code that allows identification of all the data reported for each subject (ICH GCP 5.5.5).

ID Assignment
- Needs to appear on every form & page
- Links paper form with specific record in database
- Multiple forms: ID="merge key" in database
- Must be UNIQUE for each subject
- May be multi-part: 100102
  1=female 001=unique subject # 02=site

Multiple Contacts

Example 1
DIFLUNISAL TRIAL: PHONE CONTACT
Contact Date: [DD/MM/YYYY] or [Month: 1 2 3 4 5 6 7 8 9 10 11 12]
Month: 1 2 3 4 5 6 7 8 9 10 11 12

Example 2
All patients: [Phone 3 month] [Phone 6 month] [Phone 9 month] [Phone 15 month] [Phone 18 month] [Phone 21 month]
Surgical only: [Visit 2: Pre-op] [Visit 3: Day 1 post-op] [Visit 4: Day]
1. During the past 30 days, how often did pain interfere with your daily activities?
   1) All of the time
   2) Some of the time
   3) A little of the time
   4) None of the time

1. During the past 30 days, how often did pain interfere with your daily activities? (select one)
   ☐ All of the time
   ☐ Some of the time
   ☐ A little of the time
   ☐ None of the time

Avoid Open-ended & Include Response Measure

1. What is your date of birth? _________________
2. How much do you weigh? _________
3. How tall are you? ________
4. Record subject’s temperature ___

Avoid Open Ended

Frequency

1. How often do you use an inhaler? (Choose one.)
   ☐ QD (daily)
   ☐ QAM (every AM)
   ☐ BID (2x/day)
   ☐ PRN (as needed)
   ☐ If none of the above, how often?: ___________

Include Clear Instructions

What is your race/ethnicity? (Check one)
☐ Caucasian
☐ African American/Black
☐ Asian, Pacific Islander
☐ Native American
☐ Other (specify): __________

What is your race/ethnicity? (Check all that apply)
☐ Caucasian
☐ African American/Black
☐ Asian, Pacific Islander
☐ Native American
☐ Other (specify): __________
1. Have you been treated in the past for any of these medical problems?

   Read each condition, then select Yes or No.

   a. High Blood Pressure  
   b. Heart Disease  
   c. Diabetes  
   d. Cancer  
   e. Lung Disease  

   Yes  No

   a. [ ]  
   b. [ ]  
   c. [ ]  
   d. [ ]  
   e. [ ]
**Item In-a-Series Format:**
Long, wordy

1. To what extent do you consider a lack of rental housing to be a problem in this community?
   - □ Not a problem
   - □ Small problem
   - □ Moderate problem
   - □ Serious problem

2. To what extent do you consider poor road and street repair to be a problem in this community?
   - □ Not a problem
   - □ Small problem
   - □ Moderate problem
   - □ Serious problem

**Revised To...**

1. Do you consider each of the following to be a Serious problem, Small Problem, or Not A Problem in this community? (Please check one answer for each)

<table>
<thead>
<tr>
<th>Serious Problem</th>
<th>Moderate Problem</th>
<th>Small Problem</th>
<th>Not A Problem</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. A lack of rental housing</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>b. Poor road and street repair</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
</tbody>
</table>

**Always Consider the “Other” Category**

1. Major admitting diagnoses (Check all that apply)
   a. □ Post Operative
   b. □ Trauma
   c. □ Neurological
   d. □ Cardiovascular
   e. □ Respiratory
   □ Other

**Inclusion of “OTHER”**

- Might cut down on items left blank
- Position “Other” last in list of possible responses
  - Ensures all anticipated responses considered 1st
- Continue to monitor “Other”
  - Was common response category overlooked?

**Missing Responses**

What level of precision is needed?

<table>
<thead>
<tr>
<th>Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not Available</td>
</tr>
<tr>
<td>Not Applicable</td>
</tr>
<tr>
<td>Not Done</td>
</tr>
<tr>
<td>Refuse</td>
</tr>
</tbody>
</table>

**Illustrate Skip Patterns**

15. Do you work out every day?
   - □ Yes (Go to Q.16)  □ No (Go to Q.18)

16. About how many minutes per day do you workout?
   ___ ___ ___ minutes per day

15. Do you work out every day?
   - □ No (Skip to Q.18)
   - □ Yes

16. About how many minutes per day do you workout?
   ___ ___ ___ minutes per day

"Skip to Question 18" NOT "Skip questions 16 and 17."
When Open Ended Cannot Be Avoided:

- Check data as it comes in
- Create new categories where appropriate
- Re-evaluate continuously
- May require new versions of forms

Coding Manuals: Open Ended

1. In what country were you born (check one)?
   - USA
   - Guatemala
   - Mexico
   - Dominican Republic
   - Other

Coding Manuals: Open Ended

1. After 10-20 forms completed, compile list of open-ended responses to open-ended question
2. Group into common themes, categories (e.g., countries)
3. Assign numeric code to each of these categories to create a "coding scheme" or codebook

6. EXAMPLES

Anatomy of a CRF

Header
Modules
- Demographics
- Screening / IC
- Adverse events
- Labs
- Medical history
Footer

Demographics

1. Gender:  □ Male  □ Female
2. DOB:   /   /   (MM/DD/YY)
3. Ethnicity: Is the patient of Hispanic/Latino/Hispanic Puerto Rican/Central or South American origin or descent?
   - Yes, not Hispanic  □ Yes, Hispanic  □ Don't Know / No Response
4. Race (check all that apply)
   - American Indian/Alaskan Native
   - White
   - Asian
   - Other (Specify)
   - Black
   - Don't Know / No Response
   - Native Hawaiian or other Pacific Islander
7. REVIEW OF GENERAL DESIGN PRINCIPLES

Review of design principles #1
- Modular design
- Follow the flow of the treatment schedule of the protocol
- Define the data entry (units)
- Data entry instructions/tips (supplementary documentation?)
- One page forms
- Subject identifiers on every page

Review of design principles #2
- Ask questions in only one place
- Ways to opt out: none / not done / NA
- Instructions (‘see protocol’ vs. most recent HCT ≥ 38%)
- One form per contact
- Consistent coding; coding marks

Review of design principles #3
- Uses data entry boxes as visual clues
- Use italics for instructions (& bolding)
- Avoid free text
- Skip patterns:
  - Don’t use “Skip question X”
  - Use “Skip to question Y”
- Be consistent in positioning data entry fields
8. FINAL THOUGHT

“Perfection is attained by slow degrees; it requires the hand of time.”

- Voltaire