Design of Case Report Forms

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Case Report Form

- CRF
  - Official clinical data-recording document or tool used in a clinical study

Purpose

- Collects relevant data in a specific format
  - in accordance with the protocol
  - compliance with regulatory requirements
- Allows for efficient and complete data processing, analysis and reporting
- Facilitates the exchange of data across projects and organizations especially through standardization
CRF Relationship to Protocol

- Protocol determines what data should be collected on the CRF
- All data must be collected on the CRF if specified in the protocol
- Data that will not be analyzed should not appear on the CRF

CRF Development

- Guidelines
  - Collect data outlined in the protocol
  - Collect data to support the analysis plan
  - Collect data required by the regulatory agencies
# CRF Development

- Guidelines (con’t)
  - Collect data with all users in mind
  - Be clear and concise with your data questions
  - Avoid duplication
  - Request minimal free text responses
  - Provide units to ensure comparable values
  - Provide instructions to reduce misinterpretations

- Provide “choices” for questions where possible
- Use of “None” and “Not done” for assessments
- Collect data in a fashion that allows for the most efficient computerization
- Collect data and formats that provides for pooling across studies
- CRF book needs to be finalized and available before an investigator starts enrolling patients into a study

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# Elements of the CRF

- Three major parts:
  - Header
  - Safety related modules
  - Efficacy related modules

<table>
<thead>
<tr>
<th>Module</th>
<th>block of specific questions</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRF</td>
<td>module(s) make up a single CRF page</td>
</tr>
<tr>
<td>CRF Book</td>
<td>series of CRF pages</td>
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</table>
Creating Safety Modules

- Ideally come from a standard library
- Select modules appropriate for your study
- Keep safety analysis requirements in mind
- Safety Modules usually include
  - Demographic
  - Adverse Events
  - Vital Signs
  - Medical History/Physical Exam
  - Concomitant Medications
  - Patient Disposition/Status at end of study

Efficacy Modules

- Designed for each therapeutic area based on the protocol
  - Primary and secondary efficacy endpoints/parameters
  - Health Outcomes Assessments/Questionnaires
- Considered to be “unique” modules and can be more difficult to develop
- Use existing examples from similar protocols where applicable
### Creating Efficacy Modules

- Follow general CRF design guidelines
- Include appropriate baseline measurements
- Repeat same battery of tests
- Define and identify
  - key efficacy endpoints
  - diagnostic tests for efficacy

### Importance of Standard CRFs

- Prepares the way for data exchange
- Removes the need for mapping during data exchange
- Allows for consistent reporting across protocols, across projects
- Promotes monitoring and investigator staff efficiency
- Allows merging of data between studies
- Provides increased efficiency in processing and analysis of clinical data

### CRF Development Process

- Drafts CRF from protocol
  - CRF Review Meeting
  - Comments back to designer
- Updates CRF to include comments
- Review and Sign off/approval
- Coordinate printing and distribution
## CRF Development Process

### Responsibility for CRF design
Responsibility for CRF design can vary between clinical research organizations (CRA, data manager, specialty role).

### Interdisciplinary review
Interdisciplinary review is necessary:
- Each organization has its own process for review/sign-off.
- Should include relevant members of the project team involved in conduct, analysis, and reporting of the trial.

### Begins
- As soon as possible in the study planning process (draft protocol).

## CRF Development Process

### Review Team (example)
- Clinician
- CRA
- Statistician
- Programmer
- Data Manager
- Others
  - Database Development, Dictionary Coding, Standards

## CRF Development Process

- **After the CRF book is approved**
  - Initiate the process for printing.
  
  *Note: the Protocol must be approved before the CRF book is approved and printed*

- **After it is printed**
  - Stored according to organizational guidelines.
  - Printed and distributed to research sites.
Properly Designed CRF

- Components/All of the CRF pages are reusable in future studies
- Saves time
- Saves money

Poorly Designed CRF

- Necessary data not collected
- Database may require modification
- Data Entry process impeded
- Need to review/clean data increases
- Target dates are missed
- Collected too much data – Wasted resources in collection and processing
- *Delay in getting study results and ability to adequately test the protocol objectives*

The Case Report Form

- How do we use it?
  - Collect data from the investigational sites
  - Helps project team and study site team
    - Reminder to investigator to perform specific evaluations
  - CRA uses to verify protocol is being followed and compare with source documents
  - Statistics and Programming groups use it to build database structures, develop edit checks and programming specs
The Case Report Form

- Data is Used for
  - Data analysis and reporting
  - Subject tracking
  - Reports to FDA on subject safety
  - Promotional materials
  - New Drug Application submissions
  - Support of labeling claims
  - Publication in medical journals

Electronic CRFs

- The use of RDC is increasing
- In general, the concepts for the design of electronic CRFs/RDC screens are the same as for paper CRFs
- Electronic CRFs will impact the following:
  - Review of CRF is different (screen review)
  - No need to print and distribute paper
  - Responsibility for Data entry
  - Data quality checks at source

Electronic CRFs and Data Capture

- Types of Systems
  - Direct entry into active database
  - Entry into local disc/holding file for later loading/transfer
  - Entry with second review necessary in order to change “status”
CRF Completion Guidelines

- Used to give both general and specific guidance to facilitate quality data collection
- Partial Dates
- Unknowns
- Missed Visits
- Unplanned visits
- Discontinued Subjects
- May also include navigation or technical instructions associated with an EDC system

Examples
### VITALS/TO DO

**Weight:**
- [ ] (1) lb
- [ ] (1) kg

**Height:**
- [ ] (1) in

**Blood Pressure:**
- [ ] (1) mmHg

**Heart Rate:**
- [ ] beats/minute

### IN PAIN DUE

<table>
<thead>
<tr>
<th>Date</th>
<th>Note</th>
<th>Time (hr:min)</th>
<th>Pain (0-10)</th>
<th>Units in Bottle</th>
<th>Comments (keep lid off right)</th>
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### PAST AND CONCURRENT MEDICATIONS

**YES**

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Initial Date</th>
<th>Dose</th>
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Questions ?