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

PAPER

RDC/RDE (Remote Data Capture, Remote Data Entry)
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
Protocols and Analysis Plan:

- **Protocol**
  - Describes Study Conduct
    - purpose
    - objectives
    - operational aspects

- **Analysis Plan**
  - Describes Analysis
    - data presentations
    - key endpoints
    - statistical methods

- **Case Report Form**
  - Collects data to support the above
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
CRF Development

Guidelines (con’t)

- 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
Elements of the CRF

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

- Module: block of specific questions
- CRF: module(s) make up a single CRF page
- CRF Book: series of CRF pages
Header Information

- Key identifying Information
- **MUST HAVES**
  - Study Number
  - Site/Center Number
  - Subject identification number
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 can vary between clinical research organizations (CRA, data manager, specialty role)
- 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
<table>
<thead>
<tr>
<th>CENTER</th>
<th>SUBJECT ID</th>
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<tbody>
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<th>DATE OF VISIT</th>
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<td>YYYY - MM - DD</td>
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Subject Initials: [ ] [ ]

Please print all details, and INITIAL and DATE all corrections. Indicate [ ] where applicable.
DATE OF BIRTH: (yyyy-mm-dd)  

SEX AT BIRTH:  
☐ (1) Male  
☐ (2) Female  

RACE:  
☐ (1) White  
☐ (2) Black  
☐ (3) Asian  
☐ (4) Other
<table>
<thead>
<tr>
<th>IF SUBJECT IS FEMALE, HORMONAL STATUS:</th>
<th>(1) Premenarchal</th>
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<tbody>
<tr>
<td></td>
<td>(2) Premenopausal</td>
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<td>(3) Postmenopausal</td>
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<tr>
<th>SMOKING STATUS:</th>
<th>(1) Current Smoker</th>
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<td>(2) Ex-Smoker</td>
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<td>(3) Non-Smoker</td>
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### SIGNIFICANT MEDICAL/SURGICAL HISTORY:

- [ ] (1) NOT DONE
- [ ] (1) No Significant History

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<th>Specify:</th>
<th>Past (1)</th>
<th>Present (2)</th>
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<td>Blood Pressure, (1) Sitting:</td>
<td>Systolic / Diastolic mmHg</td>
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<td>Heart Rate, (1) Sitting:</td>
<td>beats/minute</td>
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<td>Date (yyyy-mm-dd)</td>
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<td>Time Post Dose (Hours)</td>
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Body Fluid/Matrix: SERUM

(1) PK NOT DONE
PRIOR AND CONCOMITANT MEDICATIONS:

<table>
<thead>
<tr>
<th>Drug Name (Generic preferred but use brand name for combination product)</th>
<th>Start Date (yyyy-mm-dd)</th>
<th>End Date (yyyy-mm-dd)</th>
<th>Continuing (1)</th>
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Questions ?