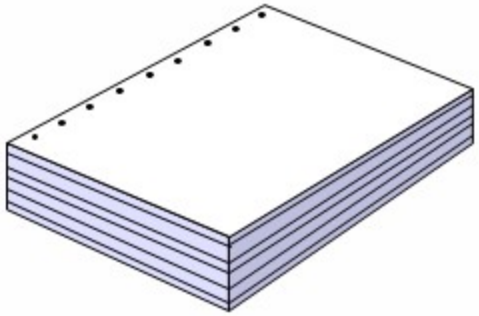
Design of Case Report Forms

Module 10 Topic 5.2

Case Report Form

- 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 esp. 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 with all users in mind
  - Collect data required by the regulatory agencies
  - Collect data outlined in the protocol
  - 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 (contd)

- Guidelines (contd)
  - Provide "choices" for each questions
    - allows for computer summarization
  - Use "None" and "Not done"
  - Collect data in a fashion that:
    - allows for the most efficient computerization
    - similar data to be collected across studies
  - CRF book needs to be finalized and available before an investigator starts enrolling patients into a study
  - Take the time to get it right the first time

Elements of the CRF

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

Elements of the CRF

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

- Module Block of specific questions
  ↓

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

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

- Usually 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

Efficacy Modules

- Designed for each therapeutic area based on the protocol
- Considered to be “unique” modules and can be more difficult to develop
  - Use existing examples from similar protocols where applicable
  - Consider developing a library of efficacy pages
- Design modules following project standards for data collection

Creating Efficacy Modules

- Follow general CRF design guidelines
- Use pages or modules from the therapeutic library
- Define diagnostics required
- Include appropriate baseline measurements
- Repeat same battery of tests
- Define and identify
  - key efficacy endpoints
  - additional 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 of clinical data

CRF Development Process

CRF Designer

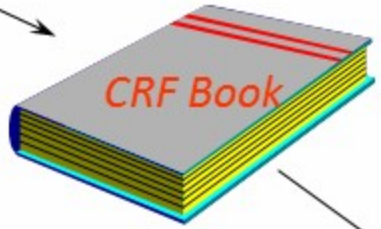
- **Drafts CRF from protocol**

Reviewers

- **CRF Review Meeting**
- **Comments back to designer**

CRF Designer

- **Updates CRF to incl. comments**
- **Review and Sign off**
- **Coordinate printing and distribution**



Site

CRF Development Process (contd)

- Responsibility for CRF design can vary between clinical research organizations (CRA, data manager, specialty role)
  - Include all efficacy and safety parameters specified in the protocol using standards libraries
  - To collect ONLY data required by the protocol
  - Work with protocol grid/visit schedule
- 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 in the study prep process as possible

CRF Development Process (contd)

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

CRF Development Process (contd)

- 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

CRF Development Process (contd)

- 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

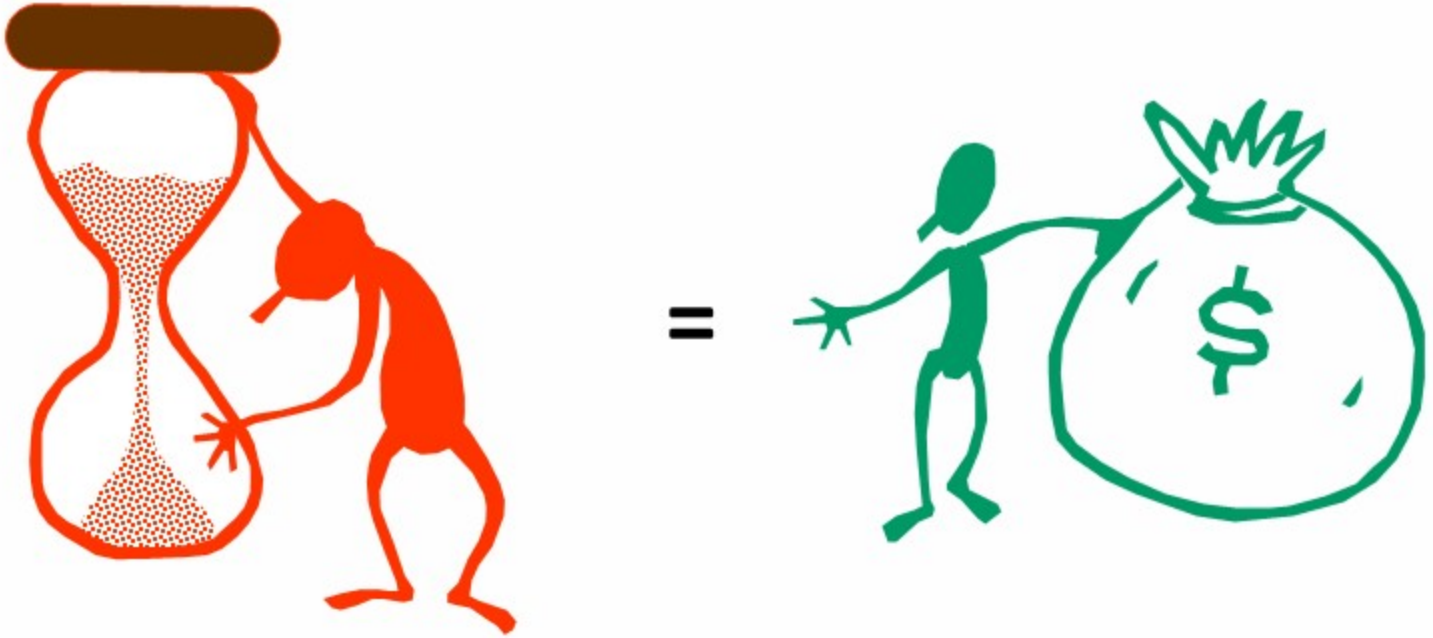
- Components/All of the CRF pages are reusable
- Saves time
- Saves money

+

Poorly Designed CRF

- Data not collected
- Database may require modification
- Data Entry process impeded
- Need to edit data
- Target dates are missed
- Collected too much data – Wasted resources in collection and processing

Poorly Designed CRF Issues



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 evaluation
    - CRA uses to verify protocol is being followed and compare with source documents
    - Biometrics uses it to build database structures, develop edit checks and programming specs

The Case Report Form (contd)

- ...Used for
  - Subject tracking
  - Data analysis and reporting
  - Reports to FDA on subject safety
    - e.g.. APR
  - Promotional materials
  - New Drug Application submissions
  - Support of labeling claims
  - Articles 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 covered for paper
- Electronic CRFs will impact the following:
  - Review of CRF is different (screen review)
  - No need to print and distribute paper

Protocol ID:

CENTER | SUBJECT ID

DATE OF VISIT

YYYY - MM - DD

Visit: Screening

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

IF SUBJECT IS FEMALE, HORMONAL STATUS:

- ☐ (1) Premenarchal
- ☐ (2) Premenopausal
- ☐ (3) Postmenopausal

SMOKING STATUS:

- ☐ (1) Current Smoker
- ☐ (2) Ex-Smoker
- ☐ (3) Non-Smoker

SIGNIFICANT MEDICAL/SURGICAL HISTORY:

☐ (1) NOT DONE

☐ (1) No Significant History

	Past (1)	Present (2)
Specify:	☐	☐
Specify:	☐	☐
Specify:	☐	☐

VITALS NOT DONE:	☐ (1)
Weight:	☐☐☐.☐☐ ☐ (1) lb ☐ (2) kg
Height:	☐☐☐.☐☐ ☐ (1) in ☐ (2) cm
Blood Pressure, (1) Sitting:	☐☐☐ / ☐☐☐ mmHg Systolic Diastolic
Heart Rate, (1) Sitting:	☐☐☐ beats/minute

Body Fluid/Matrix: SERUM

Analyte:

☐ (1) PK NOT DONE

Date (yyyy-mm-dd)	Not Done	Time Post Dose (Hours)	Actual Time (24 hour clock)	Unique Sample ID	Comments (Keep brief and legible)
☐☐☐☐ - ☐☐ - ☐☐	☐ (1)	0	☐☐ : ☐☐		
☐☐☐☐ - ☐☐ - ☐☐	☐ (1)	0.5	☐☐ : ☐☐		
☐☐☐☐ - ☐☐ - ☐☐	☐ (1)	1	☐☐ : ☐☐		
☐☐☐☐ - ☐☐ - ☐☐	☐ (1)	2	☐☐ : ☐☐		

PRIOR AND CONCOMITANT MEDICATIONS:

☐ (1) NONE

Drug Name (Generic preferred but use brand name for combination product)	Start Date (yyyy-mm-dd)	End Date (yyyy-mm-dd)	Continuing (1)
	☐☐☐☐-☐☐-☐☐	☐☐☐☐-☐☐-☐☐	☐
	☐☐☐☐-☐☐-☐☐	☐☐☐☐-☐☐-☐☐	☐
	☐☐☐☐-☐☐-☐☐	☐☐☐☐-☐☐-☐☐	☐
	☐☐☐☐-☐☐-☐☐	☐☐☐☐-☐☐-☐☐	☐
	☐☐☐☐-☐☐-☐☐	☐☐☐☐-☐☐-☐☐	☐

Questions ?