Development of Case Report Forms

Introduction to the Principles and Practice of Clinical Research

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Diane St. Germain, RN, MS
Nurse Consultant
Division of Cancer Prevention
National Cancer Institute
Objectives
Name 3 key factors to consider during case report form development
Describe the typical data elements captured on case report forms
Describe how data is submitted electronically
Discuss what constitutes a poorly designed case report form
Use of Data
Data analysis and reporting
Subject tracking
FDA safety reporting
New Drug Application submissions
Support of labeling claims
Reviewed by Data Safety Monitoring Boards
Publication in medical journals
Data Management Reporting
Outcomes of a clinical trial dependent on data that is collecting accurately and is verifiable
Data must reflect the aims of the clinical trial
Collection must comply with regulatory agencies
Adequately designed case report forms is essential
Investigator Recordkeeping and Record Retention
21 CFR Sec. 312.62

“An investigator is required to prepare and maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual administered the investigational drug or employed as a control in the investigation. Case histories include the case report forms and supporting data...”
Case Report Form
A pre-printed form developed by the sponsor or PI to document the data elements outlined in the protocol
  Gathers all necessary information to test the hypothesis
  Ensures standardization and consistency of data collected
Case Report Form
Design impacts the quality of data collected
Properly designed CRFs = streamlined audits, data analysis and reporting
Users of the Case Report Form

Investigator: to recall tests/evaluations to be performed according to the protocol
CRA: to verify protocol requirements and required source documentation
Statistician: to ensure data requested will answer the aims of the study
IT: to develop database
Descriptions of protocol, analysis plan and case report form
Methods of Data Collection
Different methods of data collection
Developing Case Report Forms
When will data be available?
Where will the data be collected?
Who will be completing the forms?

(McFadden, 2007)
Considerations During CRF Development
Involve members of the research team
  - Research nurse
  - Data manager
  - Statistician
Review the analysis plan
Determine if there are suitable, existing forms
Develop standardized forms
Considerations During CRF Development
Data to be collected and forms to be used should be clearly outlined in the protocol
Data requested should be unambiguous
Data requested should correlate with statistical software
Table: Study Plan Table
The following forms need to be completed online at time points specified

Form
Considerations During CRF Development
Generate user friendly forms
Avoid lengthy text
Collect essential data only
Number data elements for easy reference
Number each version generated
Form showing Significant medical/surgical history

D. Mailhot
Considerations During CRF Development
Consider use of common data elements
Consider piloting forms
Complete CRF development prior to study activation
Common Data Elements
Standardized, unique terms and phrases that delineate discrete pieces of information used to collect data on a cancer clinical trial
Uniform representation of demographics and data points to consistently track trends
Elements define study parameters and endpoints
B. Meadows
Format of Questions
Consider the following:
  Recording data in a paper form
  Data entry into the computer
  Data retrieval for analysis

McFadden (2007)
Consistency!
Layout, design and coding

Form

D. Mailhot
Considerations During CRF Development
Request data consistently!
  Dates
  Decimal points
  Units of measurement
  Unknown/not applicable/not available/not done
  Other
Case report form

D. Mailhot
Header
Standardize!
Identifies the patient
  Unique patient identifier (do not use initials, DOB)
Identifies the trial
  Study number
  Name of institution
Typical Data Elements Captured on CRF: On Study Forms

Demographic data
Eligibility criteria
Family history
Patient history, physical exam including PS
Surgical history
Prior treatment
Concomitant medications
Laboratory and radiology results
Pathology
Review of current symptoms
Typical Data Elements Captured on CRF During the Study
Study treatment
Laboratory & radiology results
Concomitant medications
Adverse events
Toxicities
Hospitalizations
Treatment response
Follow-up
Disease status
Non-protocol treatment
Long term adverse events
Date of death
Cause of death
Autopsy results in performed
CRF Development Process

Graphic: CRF development process
Basic Rules for CRF Completion
Always use ink
Avoid extraneous writing in the margins/ outside of the text boxes
Data added in response to a query is initialed and dated
Basic Rules for CRF Completion

Correction of an error

Never obliterate an entry: do not erase, use whiteout
Cross out with a single horizontal line and initial and date
Should be performed by person who entered the data initially
Electronic Data Capture

Graphic: Woman sitting at computer doing data entry
Advantages: Electronic Data Capture
Shortened time from subject visit to data entry
Rules/edit checks will decrease queries
Errors in input can be identified in real-time
No need to decipher handwriting
Decreases transcription error
Real-time data collection

Ryan, J (2008)
Advantages: Electronic Data Capture

- Rapid and timely data transmission from multiple sites simultaneously
- Generate reports more rapidly
- Manageable audit trail
- May be able to download data from other sources (labs)
Designing Electronic CRF
The method of data collection will impact the design of the data entry screens
Same considerations for designing electronic forms as for paper forms
Consider volume and frequency of data submission
Avoid excessively detailed screens
Thoroughly test data capture screens
Develop detailed user instructions

McFadden (2007)
How is Data Submitted Electronically
Paper version of CRF, then entered electronically
Entered directly into an electronic device
On-line entry
  Virtual private network (VPN)
  Via a web application
  Electronic gathering at the site

Razvillas (2008)
Graphic of EDC-Electronic Data Capture process
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*

D. Mailhot
Additional Methods to Capture Data
Patient Diaries
Calendars
Questionnaires
Phone logs
Mail surveys

Data Submission

“Data must be treated with a scrupulousness that exceeds the care with which we treat most information in daily life”.

(Whitebeck, 2006)