Out-of-(CSR)-Body Experiences – Tips on Assembling Appendices, Datasets, and CRFs

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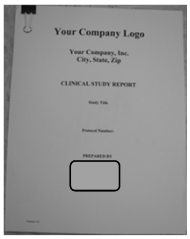
Views of a Clinical Study Report



OR

Photos courtesy of Leigh Vaughan and RAPS, 2008

Topics

- Process and timing for preparing appendices
- Format and contents of each appendix

Appendix Assembly Process

- When to start: At the protocol kickoff meeting, and make it a part of regular team meetings
- What: List of appendix items needed
- Who: Designate person responsible for each item, and for the QC process.
- How: Is there a template? If not, what is the format?
- Where: Need to know the source of the information as well as the storage location for appendix items in process, finished items, QCed, etc.
- When is it due (draft, final, QCed)?

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16.1 Study Information

16.1.1 Protocol and protocol amendments

- Provided by Trial Manager
  - Ensures that provided versions are:
    - Final
    - Signed-off
    - Most recent
- Include most current protocol and all amendments
- All versions of the protocol, if necessary for clarity
- Preferred document format:
  - Electronic

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16.1 Study Information

16.1.2 Sample case report form

- Provided by CRF Designer
- Include:
  - Unique pages only
  - Include diary cards and questionnaires
- Document format:
  - Electronic

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16.1 Study Information

16.1.3 List of IECs or IRBs and representative written information for patient and sample consent forms

- Provided by Trial Manager/CRA
- Include:
  - Names of Independent Ethics Committee(s) and/or Institutional Review Board(s)
  - Addresses of IECs/IRBs

Site Number	Investigator Name	Name and Address of Ethics Committee	Name of Chairman

- Document format:
  - MS Word (use standard template)

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TMF

16.1 Study Information

16.1.3 List of IECs or IRBs and representative written information for patient and sample consent forms

- Provided by Trial Manager/CRA
- Include:
  - Different versions if they varied considerably among sites
  - If not significant variation, include representative sample (usually the master) informed consent
  - All should be in English
- Document format:
  - Electronic

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16.1 Study Information

16.1.4 List and description of investigators and other important participants in the study…

- Provided by Trial Manager/CRA
- Includes names, affiliations, role in study, qualifications, and institution/address for:
  - All investigators
  - Any other person carrying out observations of primary or other major efficacy variables
- Check for completeness against the FDA Form 1572
- Cross-check against Item 19 (Financial Disclosure)
- Document format: MS Word (use standard template)

Site Number	Investigator Name	Sub-Investigator(s) Name	Affiliation	Investigator

Name	Title	Responsibility	Affiliation	Other Personnel

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16.1 Study Information

16.1.4 List and description of investigators and other important participants in the study, including brief CVs or equivalent summaries of training and experience relevant to the performance of the clinical study

- Provided by Trial Manager/CRA
- Brief CVs – options:
  - Original CVs – all or truncated
  - Templated CVs – how, who, etc?
  - May be electronic or scanned depending on approach
- Required for Investigators only
- Ensure CVs are in the same order as they appear in the "List of Investigators"

16.1 Study Information

16.1.5 Signatures of principal or coordinating investigator(s) or sponsor's responsible medical officer

- Provided by Trial Manager/CRA
- Identify this person early in the process (ie, as soon as last patient enrolled)
- Include this investigator in CSR review process
- Document format: scanned

16.1 Study Information

16.1.6 Listing of patients receiving test drug(s) from specific batches, where >1 batch was used

- Provided by Manufacturing/Trial Supply personnel (usually via Trial Manager)
- Include all test treatments (including positive and negative controls)

Subject Number	Drug	Batch Number
0001	Wunderdrug 20 mg capsules	1234
0002	Wunderdrug 50 mg capsules	1235
0003	Placebo capsules	2020

16.1 Study Information

16.1.7 Randomization scheme and codes (patient identification and treatment assigned)

- Provided by Statistician
- Includes
  - Detailed description of randomization method
  - Table of randomization codes, patient identifier, and treatment assigned.
    - For multicenter study, provide information by center.
- Document format: scanned (likely)

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16.1 Study Information

16.1.8 Audit certificates (if available)

- Provided by Quality Assurance
- Include
  - Description of auditing procedure
  - All certificates for audits conducted on the trial (eg, database, site, report)
    - Do not describe audit results.
- Document format: scanned (likely – signatures)

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16.1 Study Information

16.1.9 Documentation of statistical methods

- Includes:
  - Detailed documentation of **statistical methods**
    - Provided by Statistician
    - Document format: electronic, scanned (only if not otherwise available)
  - **Data monitoring group** meeting minutes (and data reports reviewed, particularly if meeting led to change in protocol or early termination of study)
    - Provided by Trial Manager/CRA
    - Document format: electronic or scanned

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16.1 Study Information

16.1.10 Documentation of inter-laboratory standardization methods and quality assurance procedures if used

- Provided by Trial Manager/Statistician
- Purpose: Required if more than one laboratory was used (ie, not one central lab)
  - Substantiation of comparability of results from different laboratories
- Document Format: electronic or scanned (only if not otherwise available)

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16.1 Study Information

16.1.11 Publications based on the study

- Provided by Trial Manager/CRA
- Document format: Scanned
- Include only:
  - If results of trial have already been published
    - Do NOT include abstracts or publications in preparation/submitted

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16.1 Study Information

16.1.12 Important publications referenced in the report

- Provided by "Librarian"
- Include:
  - All articles cited in the CSR
- Naming conventions
  - Last name of first author and year (Smith 2010)
  - Last name of first author, year, keywords from title or abbreviated journal name (Smith 2010 NEJM) (Smith 2010 Post-op ileus)
- Document format: scanned

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16.2 Patient Data Listings

- Provided by Statistician
- Statistical output listings of individual subject data arranged by variable
- Format: electronic SAS output

16.2 Patient Data Listings

16.2.1 Discontinued patients
16.2.2 Protocol deviations
16.2.3 Patients excluded from the efficacy analysis
16.2.4 Demographic data
16.2.5 Compliance and/or drug concentration data
16.2.6 Individual efficacy response data
16.2.7 Adverse event listings
16.2.8 Listing of individual laboratory measurements by patient

Process Issues

- Who provides each appendix?
- Who checks each appendix and when?
  - Before or after scanning?
- Who puts components into document repository or file structure and when?
- Who checks these in the published CSR and when?
  - When published or all at the end?
- How do reviewer comments get directed back to the responsible personnel for each appendix?

Planning/Tracking Tools

- Form/format for each document
- Tracking tool for all CSR components
- A TOC for appendices to be included in each CSR helps authors and publishers.
- Format: Word, Excel, MSProject, etc
- Responsible party
- Location at all parts of lifecycle
  - eg, assembly, review, QC, published, QCed published
- Checklist for QC between CSR body and the appendices.

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Summary

- Build appendices as they become available, ie, during the field portion of the trial.
- Use templates designed for the specific appendices and tailored to the trial.
- Map a process for assembling and quality checking the appendices prior to and/or during the CSR review periods.

Legible – Navigable - Interpretable

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Contact Information

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