



health care systems
research network

MULTI-SITE CLOSEOUT GUIDE

10-11-06

Acknowledgements: This guide was produced in collaboration with the following HCSRN sites:

- HealthPartners - Minnesota
- Harvard Pilgrim Health Care - Massachusetts
- Group Health Cooperative - Washington

The Coordinated Clinical Studies Network (CCSN) was a NIH Roadmap contract funded from 2004-2007. This guide was funded in whole with Federal funds from the National Institutes of Health, under Contract No. HHSN268200425212C, "Re-Engineering the Clinical Research Enterprise"

The CCSN Mission

Our mission is to foster a sustainable, shared research infrastructure to enhance collaborative multi-site clinical research in order to improve health care for our plan members, our communities, and our nation. The CCSN is committed to the principles of transparency, flexibility, innovation, and discovery.

TABLE OF CONTENTS

SPECIAL CONSIDERATIONS FOR MULTI-SITE STUDIES	4
IMPORTANCE OF DEVELOPING PROCEDURES	4
<i>Table 1. Closeout Responsibility Checklist Template</i>	5
PLANNING FOR CLOSEOUT	6
FINANCIAL AND INSTITUTIONAL REQUIREMENTS.....	7
STUDY DOCUMENT AND RECORD RETENTION.....	7
STUDY MATERIALS.....	7
<i>Table 2. Grid of document closeout responsibilities and retention periods</i>	8
ORGANIZING DATA DOCUMENTATION AND FILES	9
<i>Table 3. Data Retention Workplan: Template</i>	10
MANUSCRIPTS AND OTHER DISSEMINATION	11
NIH PUBLIC ACCESS POLICY	11
INTEGRATING RESEARCH AND PRACTICE.....	11
IRB AND RESEARCH REVIEW	12
SPECIAL CONSIDERATIONS FOR STUDIES INVOLVING PRIMARY DATA	12
PARTICIPANT COMMUNICATION	12
UNUSUAL BUT IMPORTANT SITUATIONS	13
EARLY CLOSEOUT.....	13
COMMERCIAL PRODUCTS	13
REFERENCES	14
ACKNOWLEDGEMENTS.....	14

INTRODUCTION AND PURPOSE OF THIS GUIDE

Project closeout is the administrative and scientific completion of a research project with attention to final participant contact (if applicable), finalizing of datasets, data archiving and destruction plans, and administrative considerations.

This guide was developed by members of the Health Care Systems Research Network (HCSRN), formerly known as the HMO Research Network (HMORN), to assist with multi-site study closeout. It is not intended to duplicate or replace funding agency or institutional requirements and procedures. Rather, we provide here a detailed discussion of those topics most relevant to multi-site studies and address the needs of different types of data collection. That is, those using primary data collection from volunteers and studies based solely on automated medical records.

Careful thought needs to occur long before the end of the study as to how to best set up systems and documentation for study closeout. This guide provides checklists and spreadsheets that staff can use as templates for their closeout process. The materials are meant to be used as a starting point or reference with the understanding that each study will have its own challenges and nuances. Please feel free to adapt the materials to your individual needs.

SPECIAL CONSIDERATIONS FOR MULTI-SITE STUDIES

A Steering Committee or Advisory Group which includes members from all study sites should have the responsibility for managing and overseeing all phases of the study. In this way all sites are invested, can give input, and a clear path of communication to each site is established and maintained. Project closeout should be one of the tasks of the Steering Committee. The group needs to delegate an individual, from the outset, who will create and monitor the timeline and process for addressing closeout-related issues. As with all studies, but especially for multi-site studies, including closeout considerations in initial project planning will make the project run smoother.

Importance Of Developing Procedures

Multi-site data studies pose a number of unique project closeout problems that need to be addressed. The participating sites' requirements and desires should be considered in the process of defining closeout procedures. Multi-site studies typically have some data residing within local environments at the individual sites (e.g., source files and documentation) and additional data stored at the primary site for analyses. The prime site has primary responsibility for implementing project closeout procedures, including archiving, establishing clear guidelines for data access and storage, authorship, and additional analyses.

The checklist that follows can be used to help guide discussion about assigning responsibility.

Table 1. Closeout Responsibility Checklist Template*

TASK	RESPONSIBLE PARTY		NOTES
	PRIME	SUBS	
<input type="checkbox"/> Closeout considerations discussed at study outset			
<input type="checkbox"/> Closeout meeting held			Typically led by prime site or administrative core
<input type="checkbox"/> Financial and institution-specific requirements complete			
<input type="checkbox"/> Study documents file complete			Typically responsibility of prime site or coordinating center/core
<input type="checkbox"/> Data documentation and files in order			Note owner(s), location(s), retention and access information
<input type="checkbox"/> Planned manuscripts and other dissemination in progress and tracked			
<input type="checkbox"/> Final report sent to IRB and sponsor			Prime site and subs will have different requirements
For primary data collection from human subjects...			
<input type="checkbox"/> Consent/authorization forms are filed			
<input type="checkbox"/> If drugs are used, dispensing forms are complete and remaining drugs have been returned/destroyed			

* Based on Woodin and Schneider 2003

PLANNING FOR CLOSEOUT

A study is ready for closeout when

- the scope of work is complete,
- the study is terminated due to problems, or
- a clearly and previously defined phase is completed in studies with multiple assessments; for example, after an initial assessment in a long-term follow-up study.

Certain closeout topics warrant attention at the very beginning of the study. These are much easier to incorporate into initial procedures than to add on later. Additionally, partnerships with operational leaders from the beginning will help improve the opportunity to have the results obtained from the research implemented in clinical practice. Below are advantages to addressing closeout issues at an early stage in planning.

- Ensures responsibility for tasks is clear and nothing falls through the cracks, thereby increasing efficiency and compliance.
- Minimizes length of closeout period; this is essential for maximizing limited funding available per site for multi-site studies.
- Improves data quality.
- Allows efficient access to data and documents if needed for any reason (e.g., audit, manuscript revisions, additional analyses, or development of new grant submissions).

Topics to discuss early in the lifecycle of a project might include:

- Intellectual property.
- Authorship and presentation policies.
- Likelihood of auxiliary studies.
- Likelihood of producing public use datasets.
- Potential for integrating findings into clinical practice.

FINANCIAL AND INSTITUTIONAL REQUIREMENTS

Each institution should ensure the study is closed out according to their requirements. These include financial, IRB, staffing and other considerations. For multi-site studies it is especially important that the prime site understands the specific requirements of each participating site.

In addition, the prime site or administrative core has the responsibility to communicate information regarding any information it needs to closeout the project with the sponsor as well as notifying sub-recipients of no-cost extensions.

STUDY DOCUMENT AND RECORD RETENTION

Study documentation will be different depending on the type of study, who funded it, and the policies of individual institutions. The following are general guidelines.

Study Materials

All investigators should have a copy of, or web-based access to, the following study materials:

- The final study protocol (including the analytic plan).
- Study instruments.
- Data tables.

Study files, including such things as study consents, IRB submissions and approvals, protocols, reports, and financial information should be retained for a minimum of three years, per OMB circular A-110, which states that,

"Financial records, supporting documents, statistical records, and all other records pertinent to an award shall be retained for a period of three years from the date of submission of the final expenditure report or, for awards that are renewed quarterly or annually, from the date of the submission of the quarterly or annual financial report, as authorized by the Federal awarding agency.."

Study files related to FDA regulated clinical trials must be retained for at least two years after notification from the sponsor that the drug/device has been approved for the indication that was investigated or it is determined that development has been discontinued. These files should be kept for a longer period if indicated by contract. (ICH Guidelines 4.9.5).

Studies must retain HIPAA-related documentation, as required by 45CFR164.316, for 6 years from the date of its creation or the date when it last was in effect, whichever is later. This would include such things as IRB-issued HIPAA waivers, signed authorization forms, business associate agreements, and so on.

Table 2. Grid of document closeout responsibilities and retention periods

TYPE OF DATA	WHO HAS A COPY	WHERE ORIGINAL RESIDES	RETENTION PERIOD
Report of Project Status: A record of project summaries or evaluations prepared during the course of a study or at the end of a funding period.	PI-individual sites	Prime	3 years after study termination if research is not grant/contract funded; transfer to Archives for review
Research Data -- Exempt from Human Subjects Review:	PI-individual sites	HS office-individual sites	Check requirements for individual sites.
HIPAA Related Documentation	PI-individual sites	Individual site	6 years from the date of its creation or the date when it last was in effect, whichever is later.
Human Subjects Review Committee Applications -- Approved	PI-individual sites	HS office-individual sites	Check requirements for individual sites.
Financial Records	Typically, Project Coordinator at each site	Typically, Grants and Contracts office at each site	Minimum of 3 years, per OMB Circular A-110.
Data Analysis Files	Depends	Depends	Determined according to analysis and writing plans and data protection protocols. See Data Retention Section for more details.

The HCSRN web portal is an option for storing shared documents. Private, secure access to each site within the portal is granted to a specific set of users.

ORGANIZING DATA DOCUMENTATION AND FILES

The guiding principle of good programming documentation is that project investigators should be able to recreate final analyses without difficulty. This is regardless of whether the source data were stored centrally or locally at the participating sites. Understanding the data process from beginning to end should be simple and everything needed to understand the process should be in one place.

The first step towards organizing data for closeout is establishing and following a protocol to ensure that analyses are complete and that any study files are complete before closeout. Especially when data collection is decentralized, auditing procedures should be established and the appropriate de-identification procedures should be implemented.

Any dataset used to generate the final analytic files (intermediate datasets) should be retained until scheduled destruction. Final datasets should be clearly designated by name and described in a separate document; for example, with a printed PROC CONTENTS if using SAS.

Data documentation should specify every step of the data creation and analytic process, including the location of all project datasets, who has access to the data, relevant local contacts for data access, storage procedures, and the location of relevant programs and related output. This documentation should be stored centrally and available to all investigators.

Often in multi-site studies, instructions or code will be sent from one site to others to guide programming and analyses (often referred to as workplans). The prime site and all participating sites should:

- Retain all workplans and programs.
- Keep all final versions and all related output returned by sites.
- Include a header with information such as the programmer, dates, datasets used, and output generated on all final programs.

The final programs should be fully annotated to allow a different programmer to understand the steps taken in the programming. If the output from a program is used to create specific tables in a report or publication, it should be noted in the program (e.g., this program generates the data for Table 4 of the XXX manuscript). Some of the descriptive detail in the programs can't be done until the end of the project.

The analyst(s) should create a final program documentation and flowchart document that lays out the process used to create the final results. Often analyses involve multiple steps, programs and datasets - all of which should be clearly described to show how the project proceeded from raw data to the final results tables in a publication/report.

If public use datasets are created, both internal and external documentation may be required.

Documented data destruction procedures must describe who will oversee the process and who will destroy files. The procedures set up for each study must be carefully followed.

Table 3. Data Retention Workplan: Template

	WHO IS RESPONSIBLE	SENT TO SHARED FILE YES/NO & WHERE	WHERE STORED? COMPUTER & HARDCOPIES	FILE NAME	DATE TO DESTROY	COMPLETED YES/NO
Regulatory Files (IRB), HIPAA						
IRB applications						
Continuation Reports						
Subject Research Files*						
Study Protocol and Related Docs						
Questionnaires						
Data Dictionary						
Analysis Plan						
Final Data Set Files and documentation						

*If the study involves an Investigational New Drug, or if the trial may be used in support of a licensing application to the FDA, all records pertaining to the trial must be maintained for the longer of:

- 1) two years after the FDA approves the marketing application in the last country seeking approval, or
- 2) two years after FDA notification that a trial has been discontinued at all sites.

Studies for which a signed HIPAA authorization to use or disclose protected health information is obtained must be retained for minimum of six years.

MANUSCRIPTS AND OTHER DISSEMINATION

Typically, a project's steering committee or executive committee oversees the manuscript writing process or assigns a subcommittee. The committee brainstorms or solicits ideas for manuscripts and oversees and tracks the designation of lead and co-authors. Publication committees should make an effort to ensure that all key contributors join writing groups, especially if they are junior investigators.

The publication committee or central staff should maintain a log of manuscripts in progress or published, including status and authors.

The HCSRN web portal is an option for storing shared documents.

NIH Public Access Policy

The National Institutes of Health (NIH) Policy on Enhancing Public Access to Archived Publications Resulting from NIH-Funded Research (Public Access Policy), which took effect on May 2, 2005, requests and strongly encourages all investigators to make their NIH-funded peer-reviewed, author's final manuscript available to other researchers and the public through the NIH National Library of Medicine's (NLM) [PubMed Central](#) (PMC) immediately after the final date of journal publication. The NIH has developed a password-protected, Web-based, [NIH Manuscript Submission](#) (NIHMS) system to implement the NIH Public Access Policy. Submitting a publication through this system fulfills the grant requirement that all NIH-funded manuscripts be submitted to NIH.

Integrating Research and Practice

Hopefully, operational leaders of health care delivery systems and/or health plans have been involved as partners from the beginning of the research and are ready to implement lessons learned. If not, developing such partnerships should be a priority. This could be accomplished, for example, via presentations to operational leaders and clinicians (if applicable) within your organization and community.

IRB AND RESEARCH REVIEW

Final human subjects, Data Safety Monitoring Board (DSMB) and sponsor reports should be submitted by the prime site. Sub-recipients should furnish any requested information to the prime site and comply with institutional requirements.

SPECIAL CONSIDERATIONS FOR STUDIES INVOLVING PRIMARY DATA

Participant Communication

Plan a final communication for studies where participants have repeated contact with study staff (e.g., a thank you letter). Discuss up-front if volunteers will be notified of study findings. If so, how will they be notified and by whom? Options include:

- personalized letter,
- generic letter with preliminary results in lay language, and
- copy of eventual published articles.

Also, make sure to discuss early on whether participants or providers will be notified of the original randomization assignment or continuing treatment options. If so, determine when and by whom they will be notified.

UNUSUAL BUT IMPORTANT SITUATIONS

There are situations which either cause early closeout or require a closed-out study to be reopened. Should one of these situations occur, careful consultation with IRB and other compliance expert sites and affected sites is recommended. However, with successful planning and archiving, a study team will be reasonably well prepared for unusual scenarios, regardless of whether final data and documentation are retained entirely by the lead site or not.

Early Closeout

Early closeout can happen if a study is terminated early due to a safety or efficacy problem.

After studies are closed, they may be reopened for various reasons. Study information can be required to be shared subject to a Freedom of Information Act request. Also, new research questions or findings may arise that warrant secondary data analysis or even recontacting a study cohort. The possibility of reopening a study depends on its consent and confidentiality procedures. If investigators think that secondary or other future analyses are likely for a research study, they should give careful thought to procedures that enable this at the outset. Maintaining careful records of data destruction dates and study procedures will allow the study team to determine feasibility of secondary data analysis and recontacting the cohort. Take note of relevant state privacy laws.

Commercial Products

If the research study has the potential to yield a commercial product, it is essential that the research team agree, ideally at the contracting stage of the project, on terms for intellectual property and technology transfer.

REFERENCES

Dinnett EM, Mungall MB, Kent JA, Ronald ES, Gaw A. Closing out a large clinical trial: Lessons from the prospective study of pravastatin in the elderly at risk (PROSPER). *Clinical Trials* 2004; 1: 545-552.

<http://publicaccess.nih.gov/> Policy on Enhancing Public Access to Archived Publications Resulting from NIH-Funded Research.

Woodin KE and Schneider JC. *The CRA's Guide to Monitoring Clinical Research*. Boston: CenterWatch, 2003.

Friedman LM, Furberg CD, DeMets DL. *Fundamentals of clinical trials*. St. Louis, MO: Moby-Year Book, Inc., 1996.

ACKNOWLEDGEMENTS

We thank the following individuals for their participation in developing this Multi-site Closeout Guide:

Jeff Brown, Harvard Pilgrim Health Care Institute

Betty Jo Haggerty, HealthPartners Institute for Education and Research

Mark Hornbrook, Kaiser Permanente Northwest

Karin Johnson, Group Health Research Institute

Barb Monsey, Group Health Research Institute

Ella Thompson, Group Health Research Institute