

Chapter 14

COORDINATING CENTER PROCEDURES

14.1 STAFFING AND ORGANIZATION

The Coordinating Center for AREDS is located at The EMMES Corporation in Potomac, Maryland. The staff at the Coordinating Center include the following:

- ! Co-directors
- ! Statisticians
- ! Administrative Coordinator
- ! Database Administrator
- ! Protocol Monitor
- ! Computer System Group.

The Co-directors are in charge of the Coordinating Center and work closely with the Administrative Coordinator who is responsible for all logistic and administrative support and for project statisticians who assist in protocol development and report generation. The Database Administrator is responsible for maintaining the accuracy and integrity of the AREDS database and for training and certifying clinic personnel in the use of the Interactive Data Entry System. The Database Administrator is also available for support, directly or as a liaison, in defining and solving problems associated with data entry. The Protocol Monitor assists in training and certifying clinic staff to perform participant examinations and participates in periodic Protocol Review Visits (Section 12.5). The Protocol Monitor also serves as a staff specialist for dealing with problems associated with participant accrual. The Computer System Group is responsible for the design, development, installation, and maintenance of the AREDS Interactive Data Entry System. The hardware and software components of the AREDS Interactive Data Entry System are located at the Coordinating Center and are linked to similar components at the participating Clinical Centers.

14.2 COORDINATION AND ADMINISTRATION

One of the routine functions of the Coordinating Center is to meet the many administrative, logistic, and communications requirements of AREDS.

14.2.1 Roster of AREDS Personnel

To maintain efficient communication among the participating Clinical Centers, the Reading Center, the various AREDS committees, and the NEI, the Coordinating Center maintains a roster of all AREDS personnel (Appendix A). This roster lists the names and addresses of all participating

units, the names and telephone numbers of all AREDS staff members, and the names and telephone numbers of current committee members by committee designation.

14.2.2 Committee Support

AREDS is supported by a network of committees. For most committee meetings, the Coordinating Center provides logistic support. The Coordinating Center collaborates with AREDS leadership to:

- ! Determine optimal meeting dates
- ! Select meeting sites based on cost and convenience
- ! Reimburse DSMC members for expenses and provide honoraria
- ! Communicate information about meetings to committee chairpersons and meeting participants
- ! Prepare meeting materials
- ! Provide logistical support onsite
- ! Duplicate and distribute materials prior to each meeting
- ! Prepare and distribute minutes of the meetings
- ! Followup on all action items after each meeting
- ! Coordinate conference calls.

14.2.3 Documentation

The Coordinating Center supports the preparation, duplication, and dissemination of administrative and technical reports and manuscripts. These documents include:

- ! Manual of Operations
- ! Participant recruitment materials
- ! Meeting minutes
- ! Newsletter
- ! Ancillary study protocols
- ! Statistical reports
- ! Bibliographies
- ! Abstracts
- ! Manuscripts for publication
- ! Roster of AREDS personnel.

Coordinating Center staff work closely with clinicians, statisticians, writing committees, protocol development committees, and scientists and authors. The staff routinely help to:

- ! Compile and organize materials
- ! Coordinate reviews and incorporate comments
- ! Summarize background materials
- ! Write administrative reports

- ! Edit technical language to accommodate lay readers
- ! Ensure that presentations are effective visually.

14.2.4 Equipment Purchase and Maintenance

The Coordinating Center purchases and maintains the hardware and software for each Clinical Center and the Reading Center.

The Coordinating Center also purchases light boxes and charts for each center.

14.3 STUDY PLANNING

The design of AREDS is a collaborative venture that involves the Clinical Directors, biostatisticians and epidemiologists from the Coordinating Center, Reading Center staff, and the NEI.

Coordinating Center staff participate on various AREDS committees involved with the design of the study. The Coordinating Center has primary responsibility for (1) evaluating the impact of protocol decisions on the scientific integrity of the study (eg, integrity of randomization, potential for unmasking of observers or participants, and feasibility of obtaining and maintaining participant compliance with study procedures); (2) determining the minimum required sample size, confidence limits, and power (to the extent that protocol decisions affect sample size requirements); and (3) establishing resource (personnel and equipment) requirements.

Each page of the Phase II Manual of Operations is dated so that subsequent changes can be identified readily. The Coordinating Center distributes and maintains the Manual of Operations.

The Coordinating Center also prepares and distributes revisions and modifications of the manual and will maintain a chronology of these changes as part of the AREDS library at the Coordinating Center.

14.4 DATA MANAGEMENT

Data management is one of the main functions of the Coordinating Center. In collaboration with the Operations Committee, the Coordinating Center plays a primary role in designing, developing, and pretesting AREDS forms to meet the requirements of the clinical study.

Pretesting the study forms involves the testing of the forms and the accompanying instructions at a suitable number of participating units. Persons completing the forms are asked to comment on its clarity and ease of use and on the time required to complete it. Item analyses of the completed forms will be done and followup telephone interviews will be conducted with the participants as needed.

When a final format is accepted, the forms will be generated by computer and, when approved for use, will be distributed electronically to all participating units.

14.4.1 Interactive Data Entry System Design and Operation

AREDS uses an Interactive Data Entry System (AIDES) that has a centralized capability for data evaluation. Each of the Clinical Centers and the Reading Center have a self-contained data entry facility for recording and controlling the data generated onsite. The Coordinating Center maintains a central master database and receives copies of changes in the local master databases, which it then consolidates for review, evaluation, and summarization. The Clinical Centers and the Reading Center "own" the data they generate locally (ie, the Clinical Center and the Reading Center are the only units of the AREDS network that can enter or modify data). AREDS hardware or software can be modified and the standard prescribed method for using the system can be modified or circumvented by the Coordinating Center, but *not* by the Clinical Centers or Reading Center.

A schematic diagram of the AREDS data flow is provided in Exhibit 14-1. A more detailed review of the entire AREDS Interactive Data System is given in the AREDS Clinical Center Data Management Handbook.

The AREDS Interactive Data Entry System is configured as a star network. All data changes are transmitted electronically and periodically to the Coordinating Center, where the data are reviewed and consolidated into a central database containing data from all units. No data changes are made at the Coordinating Center. Errors detected in the data must be corrected at the site of origin and then retransmitted. The Clinical Centers and Reading Center initiate data transfer to the Coordinating Center, ensuring that only logically complete sets of data are used to update the Coordinating Center master files. The Clinical Centers and the Reading Center are responsible for timely data entry and transmission. Lapses in responsiveness are determined at the Coordinating Center and are reported to the unit, the Study Chairperson, and the NEI.

The Coordinating Center trains and certifies authorized users, including the coordinators of the Clinical Centers and the Reading Center, who are trained to instruct other users. All users must be certified, however, by the Coordinating Center before being permitted to use the system. Certification requires that the new user:

- ! Read the relevant user's guides.
- ! Complete the training practicum under the direction of the Coordinating Center or certified user. This practicum, which usually takes less than 1 day to complete, is divided into two parts: use of the computer system and data entry procedures.
- ! Operate the system under the close supervision of a certified user until he or she is thoroughly familiar with all aspects of the system.

14.4.2 Changing the AREDS Data System

During AREDS, it is anticipated that modifications to the hardware and software will be necessary. These changes will be strictly controlled by the Coordinating Center. Changes in hardware and basic system software will be made deliberately and under the exclusive control of the Coordinating Center. Changes required by the Coordinating Center will be announced in sufficient time for the Clinical Centers and the Reading Center to respond. Change requests initiated by the Clinical Centers and/or Reading Center will be reviewed based on need and impact by the Coordinating Center in collaboration with the Operations Committee.

At the beginning of the study, each Clinical Center will be supplied with identical hardware configurations and system software. To ensure that the Clinical Centers continue to operate effectively and that the Coordinating Center can support each system, no changes may be made to any system without first requesting and receiving permission from the Coordinating Center. There are no exceptions to this requirement, no matter how trivial the change may appear. Any hardware modifications will be made to all systems to retain uniform site configurations.

14.4.3 Installing New AREDS Software Versions

Periodically, the Coordinating Center will distribute new AREDS software via diskettes or electronically during regular communication sessions. If the Clinical Centers and Reading Center are to receive new software via an electronic download, they will be notified in advance and given instructions on when the new software or tables will be loaded for operational use. If the software upgrade is distributed on diskettes by mail or courier, instructions will be enclosed in a cover memorandum.

14.4.4 Computer System and Software Configurations and Maintenance

The microcomputer hardware and software used for data entry are the same at each AREDS location. These systems represent the source of AREDS data for the Coordinating Center, and their continuous operation is a fundamental requirement. No changes to any of these systems is permitted without prior approval by the Coordinating Center. Specifically, the Clinical Centers and Reading Center must have prior Coordinating Center approval to:

- Add or remove hardware
- Install new software packages
- Make modifications to the directory structures
- Modify the boot-and-install parameters.

14.4.5 Local Hardware Malfunction and Maintenance

The microcomputers installed at the Clinical Centers may malfunction from time to time. Such malfunctions may result in failures that can cause the system to become unavailable or, in extreme cases, data to be lost. It is critical that there be a well-defined plan to recognize system

problems and to identify, isolate, and resolve them quickly. The Coordinating Center maintains a spare-parts depot in Potomac, Maryland, from which any suspected malfunctioning component can be replaced overnight.

When a problem occurs at a Clinical Center or Reading Center, the user and computer staff at the Coordinating Center will collaborate on diagnosing the problem. The types of problems that can occur include:

- ! Communications
- ! Hardware (processor, keyboard, disk, etc.)
- ! Data file corruption
- ! Software malfunction.

Problems will most often be first detected by the user during normal use. Because the operation of the system is procedural, it will usually be clear when there is a problem. When a problem occurs, the user should immediately notify the Coordinating Center so that prompt action can be taken to identify and resolve the problem and to restore any lost data. Coordinating Center staff will be available to deal with problems at all times during normal business hours. Calls will be logged at the Coordinating Center and will be summarized periodically.

Regardless of whether the user or the Coordinating Center detects the problem, the user with the problem will be asked to perform basic diagnostic operations and to examine specific log files maintained to track the operation of the system. Using this approach, Coordinating Center staff will usually be able to pinpoint the cause of the problem and to resolve it immediately or suggest a "work-around" procedure that enables the user to continue working until a permanent solution is obtained.

In more severe cases in which the system is totally disabled and onsite, end-user diagnostics cannot be performed, a local hardware specialist will be called in to provide service on a "per-call", "time-and-materials" basis. The Coordinating Center will help each site identify a local source for this service through related organizations or from a private company. Only service organizations that can provide responsive onsite service will be considered. Coordinating Center staff will work directly with the service representative, if necessary, to help resolve more difficult problems.

To support this activity, the Coordinating Center maintains a standard hardware and software configuration of the basic remote system at the EMMES facility for testing new software and diagnosing remote-site problems. This system, or "PAL" unit, will be used by Coordinating Center staff to duplicate problems and to test methods for resolving them quickly.

For software-related problems, the Coordinating Center will develop a "fix" to the current release of the system, test it to ensure that the change resolves the problem, and download the new software or table to the remote site. Before the fix is distributed to other sites, however, it will be tested at the site that reported the problem. All other sites will receive the software update as soon as it is certified, even though they may not have experienced the problem.

When a hardware problem is detected and can be identified with a specific component, the Coordinating Center will immediately ship a working replacement for that component and request

that the malfunctioning hardware be returned immediately to the Coordinating Center in the same box. The Coordinating Center periodically tests its spare parts for functionality and will retest any part before shipping it to a user site. The returned malfunctioning component will be repaired, recertified, and placed in the spare-parts inventory. If a component cannot be repaired, it will be replaced immediately to ensure that a full complement of spare parts is always available.

14.5 QUALITY ENHANCEMENT PROGRAMS

The Coordinating Center will be directly involved in ensuring the quality of the data collected, helping to fulfill the principles cited for the AREDS quality enhancement program (Section 12.1). Detailed descriptions of the editing process can be found in Section 11.2.

Coordinating Center staff plays a major role in designing the study and presenting materials, particularly those relating to methodologic issues, data collection, and training and certification of clinic staff. The Coordinating Center collaborates in the training and certification process as it pertains to:

- ! Clinical measurements (eg, visual acuity, blood pressure)
- ! Fundus photography
- ! Participant registration and data entry
- ! Data transmission.

14.6 DATA ANALYSIS AND REPORTING

In providing statistical support for AREDS, Coordinating Center biostatisticians are responsible for developing the analysis plan for Phase II (Chapter 11) which provides for the monitoring of participant accrual, participant eligibility rates, adverse reactions, visual function parameters, and other outcomes. Detailed analyses of studies will be performed periodically, and the progress of the study will be monitored continuously. The biostatisticians will play a key role in reviewing the findings of the study and defining ancillary studies. They are fully trained and understand the medical aspects of AREDS. They are expected to help ensure that AREDS is conducted properly, progresses appropriately, and establishes accurate results based on the data gathered.

AREDS requires continuous and comprehensive technical and administrative reporting which will be overseen by the Coordinating Center. AREDS reports will constitute important interim and final products of the scientific effort.

Database assessments conducted by the Coordinating Center will be targeted at maintaining the integrity of the database, monitoring adherence of the clinics to the protocol, and developing cumulative baseline and outcome assessments.

Exhibit 14-1. SCHEMATIC DIAGRAM OF AREDS DATA FLOW

