Quality Assurance Measures
DRCRnet Coordinating Center

In any multi-center study, extensive efforts are necessary to assure that the data collected are of high quality and that centers adhere to the protocol. This document summarizes the quality control procedures employed by the Coordinating Center for DRCRnet protocols. Separate Standard Operating Procedure documents provide details of the procedures described in the overview herein.

A. Training and Certification

1. Protocol Certification

Training and certification for a protocol will be accomplished through prestudy meetings of clinical center staff and, when indicated, prestudy site visits.

- For all major protocols, each investigator and coordinator will be required to either attend a protocol-certification meeting or participate in a protocol-certification conference call.

2. Certification for Study Procedures

Formal certification procedures exist for visual acuity testing, refraction, fundus photography, OCT, and fluorescein angiography. The procedures for obtaining and maintaining certification are detailed in separate documents. The Coordinating Center will track the certification status of site personnel and will provide reports of the frequency of performance of each procedure by each certified individual. The Coordinating Center review of certification status on an ongoing basis is detailed in the Protocol Monitoring Procedures. The Fundus Photograph Reading Center provides periodic monitoring reports of the quality of the photographs, OCT, and fluorescein angiography.

B. Measures to Verify Study Data

Data quality is assessed at multiple levels throughout the course of a study.

1. Case Report Forms

Data are directly collected in electronic case report forms, which are considered to be the source data.

The data are verified at the time of data entry. Checks on the data include out-of-range values and consistency checks with other data entered on the same form or entered at a previous visit.

2. Patient Eligibility

At the time of enrollment, patient eligibility is verified by a check of the entered data.

3. Visual Acuity Data

Visual acuity data are recorded electronically on the hard drive of the Electronic Visual Acuity Tester (EVA). Depending on the set up at the site, the visual acuity scores may be transcribed from the EVA or may be directly entered into the database from the EVA. With the former set up, the data are retrieved from the hard drive at intervals and compared with the data that were entered into the database.

4. Fundus Photograph, OCT, and Fluorescein Angiography Data

Data are transmitted from the site to the Reading Center either as digitized images or as hard copy photographs. Therefore, the Reading Center receives the source data from the sites. The Reading

Center quality control procedures are documented in its Standard Operating Procedures. The Reading Center transmits data electronically to the Coordinating Center.

5. Frozen Datasets

At periodic intervals, the dataset is frozen to generate data reports for the Data and Safety Monitoring Committee (DSMC). As part of the preparation of the report, the data are checked for errors and inconsistencies.

At the end of a protocol, a final complete check of the data is performed.

The procedures for freezing of datasets and verification of the data for DSMC reports and manuscripts are detailed in a separate SOP.

C. Editing

Once a record has been added to the patient database, all changes to that record are stored in an audit table which contains one record per change and the following fields: unique record identifier, old value, new value, date of the change, individual making the change, and the date/time the record was changed. Monthly, an audit report is generated listing all changes to the database that were made since the last report. This is reviewed by the Associate Director.

When a record is added to the study database, it is given a record identifying number that is unique for the study. This number is used to identify records for editing and other purposes.

D. Protocol Deviations

Adherence to the protocol by the clinics is monitored by the Coordinating Center in numerous ways. Where possible, computer programs are written to check the data and flag instances where the data indicate that a deviation from the protocol has or may have occurred.

Deviations from the protocol will be recorded in the database and included in monitoring reports. Deviations will be divided into major and minor issues. The personnel who identified the deviation will be tracked (e.g., CC, clinic, site visitor). In some circumstances, the Steering Committee may give pre-approval to a deviation and this will be noted.

E. Data Irregularities

A Coordinating Center must always be aware of the possibility of data fabrication. Although this is never expected and hopefully will never occur, awareness of the possibility is necessary. Depending on the form of the data, data may be assessed to see if the amount of variance is appropriate.

F. Quality Control Reports

Reports will be generated for internal Coordinating Center use and for review by the Steering Committee and the Data and Safety Monitoring Committee. Internal reports are used to track enrollments, visit completion, certification status, and protocol deviations, and other aspects of the study.

Each clinical site will have access at all times to monitoring reports for its site on the website. In addition, on a monthly basis, the coordinator at each site will be asked to print out monthly

monitoring reports for his or her center to review with the principal investigator.

For follow-up studies, the CC will proactively monitor visit completion and patient retention. A listing is maintained of all patients who have missed their last protocol visit and is reviewed during a monthly scheduled phone call with each clinical center coordinator.

G. Internal Operations Manual

An Internal Operations Manual will provide details of all Coordinating Center procedures.

H. Site Visits

Because CRF data are directly entered into the database via the network website, visual acuity data are electronically retrieved, photos, OCTs, and fluorescein angiograms are graded by a Reading Center, signed informed consent forms are sent to the Coordinating Center, and chart notes (when one exists for a visit) are sent to the Coordinating Center, there is limited value in conducting site visits with regard to verification of data.

Nevertheless, periodic site visits will be conducted. The primary purpose of the site visits will be to review the protocol and testing procedures with the site staff, rather than auditing the study patient charts.

The conduct of site visits is detailed in a separate SOP.