

## **Quality Control**

Quality control occurs on several levels: the scientific review of new protocols, the design of new forms, the review of data by study coordinators, and the review of each submitted data form for consistency and completeness.

### **Protocol Development and Review**

The first step to ensure quality control in clinical trials is to develop protocols that are clearly stated and exhaustively inclusive of all criteria and procedures necessary for conduct of the study. The protocols are the standard against which the Group measures the conformance of the investigators. Most importantly, protocols reflect the scientific direction and standards of the group.

The Statistical Center is intimately involved in the development of protocols, from the capsule stage through to activation. The Committee Statistician works closely with the Study Coordinator(s), the Disease Chair, and the Protocol Coordinators to develop the protocol design. Statisticians collaborate with their medical colleagues to determine appropriate scientific questions, correct endpoints, and feasible accrual goals. During the protocol development, the Data Coordinator for each committee may provide critiques and recommendations to eliminate ambiguities. Each protocol is reviewed for protocol consistency via a Protocol Review Committee in the Statistical Center and a Protocol Consistency Checklist in the Operations Office.

These aspects of each protocol have been designed to enhance the quality of the data. The first is the eligibility section, which assures eligibility of all patients at the time of registration. This section must be confirmed by the physician and the clinical research associate prior to the placement of the registration call to the Statistical Center. The second is a study parameter calendar for each arm of a study, detailing the data to be collected at each patient encounter, and treatments to be delivered at each treatment visit. This is not only essential at the institution level to assure conformance to standards, but is useful in quality control review of the submitted record. Finally, study data collection forms are designed to provide efficient data collection and study analysis.

### **Initial Quality Control Review**

The initial forms set (IFS) consisting of the completed eligibility worksheet, and any other forms required by the protocol are reviewed by the data coordinator to ensure protocol compliance. All data are assessed to confirm that prestudy information pertaining to stratification variables is the same as that given at registration; that the patient's body surface is calculated correctly; that the required protocol tests were performed; and that initial treatment was given as per the protocol. Results of quality control are communicated to the registering institution via an evaluation status report. If a documentation error or discrepancy is noted, the institution may correct the error by submitting the appropriate amended form. Evaluation status reports are mailed to institutions regardless of the quality control outcome.

## **Data Entry**

Data entry of prestudy information and other data on data collection forms is accomplished through scanning and entry via Teleform<sup>®</sup>. Extensive range and logical error checks are incorporated.

## **Patient Evaluations**

A summary of the data for each patient is mailed to the study coordinator for review and evaluation. This summary includes preliminary evaluation information, entered by the Statistical Center data coordinator on eligibility, protocol deviations, toxicity grades, and response. These judgments are preliminary until reviewed and confirmed by the study coordinator. In the case of a disagreement, the disease committee statistician may become involved. Continuing disagreements are adjudicated by the disease committee chair or in rare instances, the Group Chair.

## **Data Coordinator Quality Assurance (DCQA)**

The DCQA program was implemented in August 2000 as an internal audit mechanism to monitor and maintain the quality of data evaluations conducted by data coordinators. Each data coordinator is audited every three months by the quality assurance coordinator, with respect to coding of: eligibility; disease status, treatment; reason off treatment, toxicity; notes; other (second primaries, etc). If necessary, further instruction and education is provided to the data coordinator to ensure that errors are not repeated.

## **Study Coordinator Evaluation Monitoring System**

Study Coordinator Evaluation Forms (SCEFs), are generated by the disease site data coordinator at certain key points after patient registration to a Southwest Oncology Group protocol, e.g., following completion of treatment, relapse, and death. For some protocols, it may be appropriate for the study coordinator to evaluate patient data every three months during treatment.

The Evaluation Monitoring System tracks all SCEFs generated after June 1995. Each time a SCEF is generated, the patient number, study number, registration type, and date of generation are automatically recorded as a row in the SCEVAL database table. This row also includes fields indicating the SCEF returned status and the study coordinator evaluation date (generally the date the study coordinator completes and returns the form). Upon return of each SCEF from the study coordinator, any coding changes made by the study coordinator are entered into the database by the data coordinator.

A Study Coordinator Evaluation Report is generated and sent to the Group Chair, the disease committee chairs, and to individual study coordinators. This report contains information on the number of evaluations generated for a particular study, the number of evaluations returned, and the length of time since outstanding evaluations were generated. These and other reports are used to monitor study coordinator workload and to evaluate compliance with study coordinator responsibilities.

## **Expectation System**

The Statistical Center expectation system is the structure within which quality control functions are implemented. The primary focus of the current version is data submission timeliness. The expectation system notifies institutional clinical research associates what and when specific submissions or tasks are due; when a submission becomes overdue, the notifications become insistent. It also generates timeliness data on each institution, which can then be used to provide feedback on performance.

Expectations are entered into the Study Description File (SDF) and are posted automatically at the conclusion of the registration process. Expectations are highly study dependent and may additionally depend on registration-specific factors such as treatment assigned, applicable stratum, registering institution, type of institution, prior treatment, and/or prior pathology reviews. Expectations to be generated are specified in the SDF corresponding to that study registration using a simple procedural language to implement the logic necessary for deciding whether an expectation of a specific type is to be posted. For example, SWOG 9917 is a placebo-controlled study of L-Selenium based chemoprevention of prostate cancer among men with high grade prostatic intraepithelial neoplasia. The study requires a repeat biopsy only for those patients whose initial biopsy included fewer than 10 cores or was performed more than 6 months prior to registration. Materials from the repeat biopsy, if required, must be submitted for central review within 14 days of the repeat biopsy to confirm absence of cancer prior to randomization. Therefore, pathology submission expectations associated with the repeat biopsy are posted only for a subset of patients.

An expectation is resolved when the Statistical Center has received the submission or has been provided evidence that the task has been performed. In most cases, the resolution of an expectation is an automatic process resulting from data entry of the submission. Remote data entry, for forms submitted on-line, includes automatic resolution of the data expectation item. Lists of expectations are posted monthly for the institutions, on the CRA Workbench.

### **Institutional Performance Review (IPR)**

In conjunction with the monthly expectation report, the Southwest Oncology Group summarizes monthly statistics that are used to assess institutional performance. These standards assess data submission based on four criteria: submission of initial forms sets, follow-up for alive patients, submission of pathology materials, and submission of radiation therapy materials. Data items that are overdue on any of these categories are starred on the institutions' expectation reports, to aid in identification of cases requiring immediate attention. The monthly IPR statistics are reported to the institutions, and monitored at the Statistical Center by the Coordinating Statistician. Institutions that are out of compliance for two months in a row receive a warning letter. Any institution that is out of compliance with the standards of the Group for three months in a row will lose registration privileges until the deficiencies are corrected.

### **Serious Adverse Event Reporting System (SAE)**

Serious adverse events are reported in several ways. If an SAE occurs that is reportable per protocol, investigators are expected to call the Operations Office to report it. AdEERS (Adverse Event Expedited Reporting System) may also be required. If the investigator fails to report an SAE, the study coordinator may ask that the event be reported. Certain toxicities, including fatal toxicities for all treatments and life threatening nonhematologic toxicities for investigational treatments, are subject to an automatic Serious Adverse Events Reporting System.

For studies with flow sheets, data coordinators at the Statistical Center grade and enter all toxicities for patients undergoing evaluation. Toxicities for many studies are also entered via toxicity forms submitted by institutions. If a Grade 5 (fatal) toxicity is entered for any patient or a Grade 4 (life threatening) toxicity is entered for patients receiving investigational treatment, the computerized Serious Adverse Events Reporting System checks the database to determine if the event has been reported. If the event has been previously reported, no further action is taken. If the event has not been previously reported, the patient number, study number and registration type will appear on a report that is routed to the SAE coordinator and to the Operations Office SAE coordinator. This allows the SAE coordinator to contact the institution to ask that the event be reported.

Serious adverse events reported to the Operations Office in any of above ways receive an SAE number and are entered into the tracking system by the SAE coordinator. The Operations Office will notify the Statistical Center when a final determination has been made as to whether an SAE is attributable to protocol treatment.