

## CHAPTER 6

### QUALITY CONTROL

During the first AFHS followup, stringent adherence to quality assurance (QA) was planned for and upheld throughout the study, from project initiation to final product delivery and acceptance by the Air Force. A quality program plan was developed for this study cycle, outlining all contract activities requiring periodic and/or systematic QA and quality control (QC) monitoring.

The purpose of this chapter is to provide an overview of the specific QA measures developed and used by the project team, specifically in the areas of administrative QC; questionnaire, physical, and psychological examination QC; laboratory QC measures; data base management QA; and statistical QC.

#### ADMINISTRATIVE QUALITY ASSURANCE

In recognition of the magnitude, complexity, and importance of the AFHS, a Quality Review Committee (QRC) was established at the initiation of the third-year followup for the purpose of providing general oversight to the AFHS QA Program and advice on the appropriateness of program management and QC actions. The QRC was composed of senior corporate personnel from the prime contractor. These independent reviewers remained separate from the project management staff. The QRC met formally each quarter to review recent study progress and any issues that either had an impact on study quality or were perceived as a potential problem.

Assisting the QRC in day-to-day oversight responsibilities was a QA officer responsible for reviewing procedures, performance, and work products from all task managers and key project staff. As part of the monitoring function, the QA officer received exception reports from project task managers whenever an incident occurred that appeared to affect study quality. Monthly reports were also prepared for the Air Force, documenting project compliance with project QA criteria and noting any instances of non-compliance.

An additional measure of corporate QC was implemented through independent QA audits of individual project tasks. Members of the QRC determined first-hand whether QA procedures for a particular task were being conducted, whether procedures were appropriate for the task, and whether QA was complete for all aspects of each task.

The remainder of this chapter comprises specific QA procedures followed for the individual tasks.

#### QUESTIONNAIRE QUALITY CONTROL

NORC used both onsite and home-office QA procedures to produce a comprehensive data set. All AFHS questionnaires were pretested to evaluate

their completion time and participant acceptability before they were used at the SCRF. Onsite QC procedures included weekly observation and rating of each interviewer, editing of every questionnaire at the completion of the interview, and monitoring of participant evaluations. The Air Force also continuously conducted QA observations of all onsite activities. QC of data processing included manually editing each questionnaire, including a 100-percent verification of critical items for each questionnaire, computerized cleaning (with both single item and interitem review for range and consistency), identifying outliers, and reviewing the actual questionnaire copy to reconcile or correct detected errors.

All telephone surveys were monitored for quality and accuracy of interviewer performance by NORC supervisors. The telephone survey supervisor monitored 3 percent of each interviewer's calls to assure an appropriate presentation and an accurate transcription of responses. An additional 5 percent of the participants were recontacted after the interview to evaluate interviewer performance and validate that the correct respondent had been contacted.

NORC recruited and trained interviewers according to the detailed procedures described in Chapter 3. A minimum number of interviewers was selected to reduce interviewer variability. Additionally, these individuals were blinded to the participants' exposure status to avoid any bias. Interviewers were required to ask questions exactly as recorded, and in the order in which they appeared. No personal interpretation was allowed.

An onsite field manager closely supervised each interviewer's work regularly, observing individual interviews weekly during the examination schedule. The field manager reported directly to the NORC Project Director weekly, and was reviewed by the Project Director during quarterly site visits, to ensure direct accountability by the home office and the field manager for promptly resolving any issues.

Specifically, interviewers were checked for accuracy in questionnaire skip patterns, probing, circling of the correct code, control of the interview, voice quality, reading, and use of associated documents. When called for, the onsite manager gave immediate retraining after each observation and documented the content of this training. At weekly meetings, held with all interviewers, the field manager used generalizations from individual interviewer performance observations to train an entire group of interviewers.

The NORC field manager also monitored participant evaluations of the study closely and used the information gathered to plan and implement retraining. The manager and staff edited each completed questionnaire before it was shipped to Chicago, attempting to retrieve missing data while the study participant was at the physical examination site. Missing or ambiguous data were also retrieved by telephone when necessary.

Spouse fertility data were obtained independently of the participant interview by sending the mail questionnaire while the study participant was at the examination site, and by having a group meeting for wives who accompanied their spouses to the clinic site, where they could complete their questionnaires in private. The Assistant Survey Director in Chicago supervised and edited all interviews conducted at home with participants and spouses.

Once the participant and spouse questionnaires were received in Chicago, they were edited for completeness by a coding supervisor and staff dedicated to the AFHS for the entire project. Resolution of inconsistencies was accomplished by staff members, who standardized all responses prior to keypunching. Questionnaires were then coded, and a 10-percent recode was done on open-ended items. When a batch failed the 10-percent recode, the entire batch was recoded and the coding staff was retrained. One hundred percent quality control was accomplished by the Air Force.

During data entry, range validity checks were performed and 10 percent of the most important items in each questionnaire was verified. Data were then passed through a computer program that checked for inter- and intra-column errors. When errors were detected, the questionnaires were reviewed and the errors corrected. The process continued until no errors were detected by the cleaning program. Then, frequencies were reviewed and any anomalies or errors previously undetected were corrected by reviewing the questionnaires on a case-by-case basis. All corrections were entered into the data tape, but no changes were made to the data recorded in the questionnaires. QA reports were generated monthly, detailing the summary statistics on the number of questionnaires reviewed, the number and types of transcriptions failing QC checks, and the average number of coding errors per batch processed.

#### **PHYSICAL EXAMINATION QUALITY CONTROL**

QC was emphasized in the physical examination, as this data source provided most of the medical information for clinical and epidemiological analyses.

Initial concern for a high-quality physical examination was addressed by a stringent SCRF selection process for all personnel who were to directly interact with the participants. Each staff member was hand-selected for the AFHS on the basis of expertise, experience, and a commitment to remain with the study throughout the examination cycle. Further, the Air Force Technical Team reviewed the credentials of all key staff members and approved their participation in the study.

A complete pretest physical examination, interview, psychological test, and laboratory workup was done for 10 volunteers several weeks before the scheduled start of the study. Refresher training was given to the dermatologists to enhance their skill in diagnosing chloracne, techniques for detecting specific heart sounds were reviewed with the internists, and diagnosticians were reminded of the need to review Baseline examination data as they formulated all diagnoses. Further, all aspects of patient contact were reviewed: the initial inbriefing of the participants, the logistics of transportation and patient flow within the clinic, and the final outbriefing by the diagnostician.

During the examinations, refinements continued whenever operational problems were detected by the SCRF staff and the Air Force onsite monitor, or when participants identified areas requiring improvement. Both of these types of information were addressed during the weekly clinical QA meeting of key SCRF staff, chaired by the SCRF Medical Project Director and attended by an Air Force representative. In addition, written critique forms submitted by all participants were reviewed in detail at the SCRF weekly meetings,

providing additional insight to both temporary shortcomings of the entire logistic process as well as the numerous strong points of the programs.

Following examination of each participant group, all physical examination forms were reviewed by the SCRF staff for omissions, incomplete examinations, and inconsistencies. The examiners or technicians were quickly contacted to correct the data. Special effort was made to complete this review while the participants were at the examination site. In all cases of data correction, a complete audit trail was maintained. Finally, all mark-sense physical examination forms were read by an optical scanner to ensure total continuity and sensibility of the final examination contents. (This subject is discussed in more detail in the Data Management Quality Control section of this chapter.)

Compliance with all aspects of the physical examination was monitored daily by the Air Force onsite monitor and the SCRF Medical Project Director. Additional periodic inspections were conducted by the SCRF Chief of Medicine and the SAIC Principal Investigator. All such clinical reviews were done unobtrusively, and with the full consent of the participant; suggestions or corrections to the examination procedure were always discussed privately with the attending physician. These inspections emphasized aspects of clinical techniques, sequencing and completeness of the clinical data with respect to the examination forms, and the total blindness of the examinations. Of particular note were the detailed daily log entries of the five Air Force monitors. These entries ensured continuity of knowledge (the monitors rotated approximately every 2 weeks) by documenting examination procedural changes and recording events requiring followup by either the Air Force or the prime contractor.

Establishment of rapport with each study participant was a primary goal of all organizations involved in this study. Although "rapport building" may not be a traditional QA parameter in most research studies, it is paramount in the AFHS because maintaining the satisfaction of participants encourages them to continue in the study, and thus a significant reduction in future statistical power or bias, or both, is avoided. Every staff member, therefore, from the initial telephone recruiter to the nurse coordinator and the Project Manager, emphasized courtesy, empathy, assistance, and personalized treatment of each participant.

#### **LABORATORY QUALITY CONTROL**

Before the study was begun, specific QC laboratory procedures were designed, developed, and implemented to rapidly detect problems related to test/assay performance, validity of reagents, analysis of data, and reporting of results. All laboratory assays for the study were done with state-of-the-art laboratory equipment and techniques. Laboratory facilities all had the equivalent of National Institutes of Health Biosafety Level 2 (BSL-2) approval ratings and were certified by the College of American Pathology (CAP).

Hematology assays were performed on Coulter S Plus® equipment; sedimentation rate determinations were performed using the large-tube Westergren method. The Dupont Automated Chemical Analyzer® (ACA) was used to perform the biochemical assays; radioimmunoassays (RIA) were done with standard test kits; and porphyrin was assayed by high-performance liquid

chromatography at the Mayo Clinic in Rochester, Minnesota. Hepatitis B tests were performed using Abbott kits, and manually performed electrophoresis and monospecific antibodies were used for immunoglobulin assays. Blood-cell counts were performed with standard microscopy, and Clinitek, a reflectance spectrometry urinalysis, was used for all urinalyses. All other assays were done using industry-approved equipment and techniques.

All laboratory operations were controlled with the use of an integrated medical laboratory management information system that incorporated direct device to data base interfaces for automated testing equipment, and data entry for manual tests was performed by the laboratory technologists. An automated audit trail and a set of comments for technologist entries were kept for each test so that any QC results could be retraced.

Procedural QC included using instrumentation and reagents from one lot number throughout the study. Strict standards of calibration for all automated laboratory equipment were maintained at all times.

Trilevel or bilevel controls were used as the primary means for monitoring the quality of all tests. On every group of participant samples, one control (low, medium, or high) was run at the start, after every ninth sample, and at the end of each test run. Each trilevel control was used before repeating it in the run, when more than 18 experimental samples were analyzed. In addition, split aliquots were made from every tenth patient sample and were analyzed separately to measure test reproducibility.

All QC data were analyzed and summarized in formal QC reports generated weekly. QC data were subjected to independent statistical analysis to produce and analyze time-dependent trends. For all equipment malfunctions or other exceptions, a formal QC exception report was prepared by the responsible individual and forwarded to the QA officer and the project management team.

An additional measure of quality control introduced during the study was the CUSUM tests run with trilevel controls. In particular, the fast initial response cumulative sum (FIR CUSUM) QC technique was used. It has an advantage in detecting long-term subtle drift that could have substantial adverse analytical consequences.<sup>2</sup> FIR is a special case of the CUSUM QC scheme that increases the overall effectiveness of the QC procedure. Unlike QC procedures using standard control charts, which compare each observation to designated limits, these tests utilize the cumulative sum of deviations from a target value.

CUSUM statistics were accumulated for each of the trilevels to quickly detect instrument calibration problems as identified by excessive drift. If an out-of-control situation was indicated, the graph showed when the change first occurred. Coefficient of variation (CV) standards were established before the study for each test. All adjacent patient samples were reanalyzed after the equipment was thoroughly checked and fresh controls were run.

FIR CUSUM generally has been applied to QC in industry, particularly in high-volume, high-precision applications. To our knowledge, FIR CUSUM has not generally been applied in a biomedical setting. According to SCRF laboratory personnel, this procedure proved so successful in the AFHS that most of the SCRF clinical laboratory will begin using it in the near future.

As the examination portion of this study ended, all laboratory outliers were analyzed for logical validity by an independent clinician. All out-of-range test results were examined and scored as clinically explainable, clinically possible, or clinically unexplained.

### Quality Control Procedures for the Immunology Laboratory

The QC procedures for the Cellular Immunology section of the AFHS were structured to rapidly detect any problems in four major test parameters: (1) assay performance, (2) reagent validity, (3) data analysis, and (4) results reporting. The QC measures were detailed in the Quality Procedures Plan and documented before testing started. Compliance was monitored daily by the Cellular Immunology laboratory supervisor. Key aspects of the program included instrument and equipment calibration and maintenance, assay controls, accuracy and precision determination, and system failure checks.

QC measures followed in all Cellular Immunology assays included:

- Blood sample from a normal, healthy control individual with each group of AFHS patient samples
- Duplicate testing of one random patient sample in each assay
- Quadruplicate testing of each patient sample for each variable in each of the functional assays (e.g., PHA stimulation, natural killer cell effector/target ratios)
- Parallel testing and monitoring reactivity of various lots of reagents when appropriate
- Verification of patient and specimen identification by at least two individuals before final reporting to the data base
- Note codes attached to any data point with a detected deviation from normal due to procedural setup error, assay malfunction, equipment malfunction, or assay technical error
- Review of all final assay reports by the Cellular Immunology laboratory supervisor prior to entry into the data base.

QC for each functional assay including phytohemagglutinin (PHA), pokeweed, mixed lymphocyte culture (MLC), and natural killer cell consisted of monitoring assay controls, duplicate sample reproducibility, and any trends in reagent reactivity. Assay precision was determined by calculating the CV of the quadruplicates for each variable tested. Also, a mean value of the CV for each assay was calculated. Individual CV's of 15 percent or less were the target values for the stimulated samples in the mitogen and natural killer cell assays. The Student's t-test was applied to duplicates to determine if there was a significant difference in sampling for the functional assays. Critical t-values at the 0.05 significance level were used to determine if duplicate sample results varied significantly. Grubbs' statistical test<sup>3</sup> was used to identify any statistically significant outlier. This test was applied only to samples whose CV's were greater than 20 percent at a p-value of 0.01. The mitogen stimulation (PHA, pokeweed) effect was

followed by daily evaluation of the radioactive counts in counts per minute (cpm) for each mitogen. When counts fell below expected values, suggesting that reagent deterioration had occurred, new aliquots were used.

QC measures for the cell surface marker assays were calculation of  $T_4+T_8/T_{11}$  cell ratios, evaluation of flow cytometer computer outputs (cytograms and histograms), and duplicate sample testing.  $T_4+T_8/T_{11}$  cellular ratios should approximate the value 1.0 for a normal population. Validity of cytogram and histogram distributions generated by the flow cytometer was confirmed by the Cellular Immunology laboratory supervisor for each sample analyzed. The percent positive cells for each surface marker was determined in the duplicates and viewed graphically using a microcomputer program. Any significant differences between duplicates were noted and followed for abnormal trends.

On completion of this followup effort, the entire cellular immunology data base was reviewed by the Air Force team, laboratory staff, and consultants. Comments attached to the data points were also reviewed. Any data point that appeared unusual was reviewed and identified as an unexplained outlier. Unexplained outliers were deleted from the data base as errors of an unknown nature. This review was conducted without knowledge of exposure status.

## **DATA MANAGEMENT QUALITY CONTROL**

### **Overview of Quality Control Procedures**

The QC program for the data management activity consisted of multiple checks at all steps of the examination, data collection, and data processing cycle. Data QC procedures for data collection, conversion, and integration were developed before the clinical examinations began. Pretesting of all forms, procedures, and logistic arrangements was conducted 3 weeks before the examinations actually began. Additionally, during the first 2 months of the clinical examinations, all data collection activities were intensely scrutinized to detect and correct procedural deficiencies.

QC activities also included automated QC techniques applied to laboratory data, clinical evaluations of all laboratory outliers, review of all physical examination findings by an independent diagnostician, and automated and manual data quality checking of hard copy against transcribed computer files for all questionnaire, physical examination, and medical coding data streams.

Five interwoven layers of QC were instituted to ensure data integrity. Efforts focused on (1) data processing system design, (2) design and administration of all exams or questionnaires, (3) data completeness checks, (4) data validation techniques, and (5) quality control of medical records coding. In some cases, the QC procedures about to be described were implemented throughout the data management task rather than assigned to a particular activity. These comprehensive QC procedures will be mentioned where appropriate throughout the remainder of this section.

## Data Processing System Design

For each data stream, standards were set to establish data element format (character or numeric), data element naming conventions, data element text labels, numeric codes for qualitative responses and results, QC range checks for continuous data elements, and QC validity checks for categorical data. A data dictionary provided detailed information on each data element.

A systems integration approach was applied to the design and implementation of data collection procedures and techniques so that data emanating from the various study sources (physical examination, questionnaire, laboratory) were consistent in file format and structure. This was necessary to ensure that all data could be integrated into a single data base management system for analysis. Figure 6-1 provides an overview of the QC activities used in the data base management process.

Forms and questionnaires were carefully designed to ensure that all required data elements would be collected according to the Study Protocol. The design of these instruments was such that they reflected the order in which the examination itself would be administered and provided for the sequential recoding of information to streamline remaining data management activities.

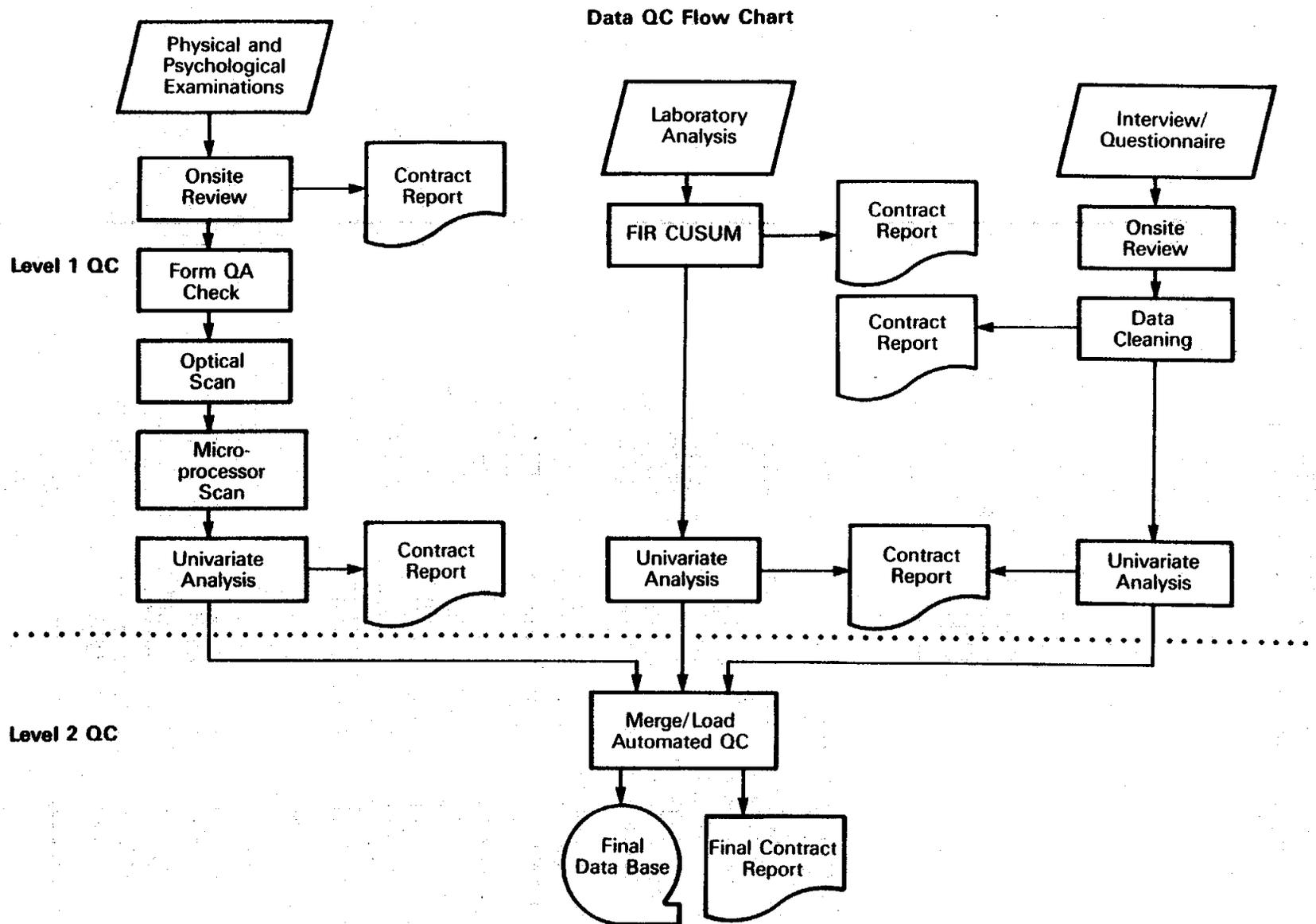
Completed medical records and questionnaires were converted from hard copy to machine-readable images using customized data-entry systems or state-of-the-art optical mark reading equipment. Verification procedures were performed to ensure that a uniquely identified participant record existed within each data file, and that the appropriate number of responses for each applicable field was provided. Data files were then verified against original data sheets and corrected as necessary.

Data files were then subjected to validity checks. Any potentially conflicting results as well as any data values falling at the extremes of expected ranges were manually reviewed. Extreme values were reverified against the original raw data copies and either corrected or documented as valid results. Potentially conflicting results were returned to the examiners for review. These results were then documented as correctly recorded, corrected, or flagged for exclusion from analysis because of unresolvable examiner errors or omissions.

Once the edits were completed and the data reverified, the "cleaned" files or tapes were transferred to the data analysis center for final inspection and integration into the study data base. For this QC measure, each data file was loaded into a Statistical Analysis System (SAS®) data set, and descriptive analyses were run. The validation, correction, transmission, and analysis QC procedures were repeated as necessary to ensure that all extreme or suspicious values had been validated.

## Design and Administration of Physical and Psychological Examination Forms

As mentioned, the examination forms were designed to solicit all required data such that recording time was minimized, comprehension was enhanced, and data input could occur with a minimum of transcription errors. Optical Mark Recognition (OMR) technologies were selected to eliminate the risk of transcription errors and were applied to all psychological tests.



**Figure 6-1.**  
**Two Levels of Quality Control Applied to All Collected Data Prior to Statistical Analysis**

Customized mark-sense forms were also developed and OMR technology was used to achieve these same objectives for segments of the physical examination and the self-administered questionnaires. The use of mark-sense forms allowed the creation of computerized data files directly from the raw data recorded on these forms.

QC procedures for all data collection instruments began with a review of all forms immediately as they were completed. Any forms containing missing examination results were returned to the examining physician for completion before the participants left the site. Any questionable results or "hard-to-diagnose" conditions (such as heart sounds or peripheral pulses) were verified by the diagnostician at the outbriefing. All examination forms were signed by the examining physician, and the examiner identification number was coded in the data base so that interexaminer variation could be analyzed. Detailed QC records were maintained, which indicated the examining physician and the type of deficiency detected. Deficiency reports were reviewed by the study coordinator to detect any patterns of physician data entry error. A final level of QC audit was accomplished by Air Force statisticians, who conducted a detailed screening of the data and checked for errors.

### Data Completeness Checks

Customized programming of the OMR allowed for the identification of those forms (and their corresponding data records) with missing responses, as well as those with multiple responses to questions that required a single response. The OMR scanner was programmed to reject forms that failed completeness and multiple response checks and to output a control code for each rejected form. The control code identified the location of the first three verification checks failed for a given form.

When a raw data form was rejected, the reason for the rejection was determined and the exact data element was corrected by comparing the rejected raw data form to the values recorded in the data record created by the scanner. A customized set of rejection and resolution codes was developed for the study to describe all the reasons for a form's rejection and any subsequent reasons for changing a data value. Various codes identified values recovered from light marks, missing marks explained by examiner comments, and missing comment flags resolved by the presence or absence of text in the comment areas. These codes ensured data completeness by accounting for all questionable or missing responses. (See examples of mark-sense forms in Figures 4-3 and 4-4.)

Some of the rejected forms did not contain actual data errors but rather anomalies created in using mark-sense cards for data collection. For instance, incompletely erased responses and responses marked with too little carbon or graphite were incorrectly counted or missed, respectively, by the scanner. Examiners also tended to clearly mark responses for abnormal findings while bypassing or lightly marking responses for expected or desired findings. Failure of the form to provide the correct number of expected responses always resulted in rejection. These technology-based errors were resolved, as were the anticipated, more traditional errors.

The rejection code, data location code, resolution code, data inspector's initials, and correct data value were directly posted to a

participant's data record. This innovative technique not only effectively maintained a comprehensive audit trail of all record manipulations, it also provided a mechanism for measuring the frequency of specific errors.

Careful monitoring identified trends where individual data values were missed as well as the frequency with which individual examiners incorrectly marked their examination forms. Statistics were compiled on out-of-range results and data omissions that had been accepted in the previous QC audits. The results were monitored to detect trends, possible bias situations, and other data quality problems. This information was reviewed and relayed to examiners and internal auditors to assist in preventing or correcting chronic, but avoidable, problems.

### Data Validation Techniques

QC activities also included data validation techniques. As mentioned earlier, data files were examined in a series of verification and validation procedures developed to check the results within each participant's record for logical consistency and abnormal findings. Any records noted to have ambiguous findings, incongruent observations, extreme results, or nonobvious errors or omissions were listed and submitted for review to a physician.

Again, clinical judgments were made by the auditing physician in assigning a validation code for each extreme or questionable data result. The validation codes allowed for indicating that data were deciphered from examiner comments or from related findings from another specialty area, or were accurately recorded and logically consistent with other findings for the participant. Data points that could not be definitively validated or recovered through clinical judgment and consultation with the original examiner were assigned codes noting missing or invalid data values. These unrecoverable data points were excluded from subsequent analysis.

### Medical Records Coding Quality Control

Upon completion of the NORC data processing, all AFHS questionnaires were forwarded to SAIC for the medical coding of reported conditions. The International Classification of Diseases, 9th Revision, Clinical Modification (morbidity); International Classification of Diseases, 9th Revision (mortality); Systematized Nomenclature of Medicine (anatomic site); and American Hospital Formulary Service (medications) coding schemes were used, suitably modified. Each questionnaire was coded by two coders working independently. The results of the two coders were forwarded to the USAF for 100-percent QA/QC and final adjudication. The information from the physical examination was coded similarly.

After the coding data were adjudicated, they were returned to SAIC for data entry. The coding sheets were batched, key entered, verified, and corrected. The corrections were also verified. The key entry and verification functions were performed by various operators. Five percent, or 100 records of each batch (whichever was larger), was randomly selected and subjected to manual reverification. An error rate of greater than 1 percent of this sample mandated reverification of the entire batch. In this final QA/QC check, the automated files were reviewed and compared to the hard copy by trained medical record coders, all of whom satisfied the minimum requirement of Accredited Record Technician or Registered Record Administrator eligibility.

A manual tracking system was used to retrieve medical records. A chronological log was maintained to track participant requests for authorization to obtain medical record(s), receipt of the authorizations, requests for records from the provider, and receipt of the records from the provider. Identifying information in these logs included participant name, case number, date of action, condition(s) to be verified, dependent name (if appropriate), and type of medical provider (Federal/non-Federal).

Due to the intricacies of obtaining medical records from Federal facilities, this task ultimately became the responsibility of the Air Force.

#### STATISTICAL ANALYSIS QUALITY CONTROL

Specific QC measures were developed for activities falling within the statistical analysis task: construction of data bases for the statistical analysis of each clinical chapter, the statistical analysis itself, and the production of statistical reports to serve as the basis for the clinical chapters.

Each specialized statistical data base was constructed by defining and locating each variable within the many subparts of the composite followup data base. Lists of variables and their data sources were submitted to the Air Force for approval. Although the data had been subjected to QC procedures during collection, statistical checks for outliers and other improbable values were conducted; anomalies identified by the statisticians were discussed with those responsible for the data collection, i.e., either NORC or SCRF.

QA largely depended on regular communication and general agreement among statisticians. Several meetings and consultations among the Air Force team, the Principal Investigator, the SAIC statisticians, and the University of Chicago staff members were held in conjunction with the development of the data analysis plan. During the course of the analysis there were frequent telephone conversations. Any problems arising in the statistical analysis were resolved by team discussion. The software was checked by comparing results from analyses on the same variable by different programs (for example, BMDP®-LR [logistic regression] and BMDP®-4F [log-linear model] will give the same results for dichotomous variables when the program options are chosen properly). The statisticians frequently checked that the number of observations used in an analysis was correct, and peer review ensured that the program code was appropriate for the chosen procedure. The analyses were conducted in accordance with the data analysis plan which was reviewed extensively. Throughout the study, duplicate data bases were maintained by the USAF and SAIC. Upon completion of the analyses, SAIC delivered all analysis software and SAS data sets for each clinical area to the USAF for final review and archiving.

All tables and statistical results were checked against the computer output from which they were derived, and all statistical statements in the text were checked for consistency with the results given in the tables. Additionally, drafts of chapters in the report were reviewed by the USAF and SAIC investigators, and the QRC.

## CHAPTER 6

### REFERENCES

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