SECTION 1
QUALITY ASSURANCE OVERVIEW

INTRODUCTION

The Women's Health Initiative (WHI) Quality Assurance (QA) Program consists of the implementation and routine use of various quality assurance methods in an organized, planned manner. It is an integral part of the WHI study protocol, procedures, and database. The program covers all aspects of WHI, from the development of the protocol to interpretation of results.

For WHI, QA methods and responsibilities include activities performed at the Clinical Centers (CCs) as well as activities initiated and coordinated by the Clinical Coordinating Center (CCC). Although the WHI QA Program is directed primarily at CC operations, it is based upon comprehensive, study-wide standards of quality. Clinical Center and CCC responsibilities and activities are based on a QA plan that establishes priorities for high quality data and conduct while preserving efficient and cost-effective operations. The basis of the QA program is to build quality into the system, ensure that all WHI staff are appropriately trained, set meaningful standards, use multiple methods to detect errors, provide feedback, and assure standards are maintained. Required and recommended QA activities for WHI balance what is necessary with what is possible and cost effective.

This manual includes the following sections:

Section 1 - Overview gives an overview of the WHI QA Program and summarizes its priorities.

Section 2 - Documentation describes the WHI Manuals, which contain the WHI protocol, forms, and documentation of WHI procedures. It also describes methods for providing documentation updates and answering procedural questions using the Inquiry Reporting System, and electronic files available to the CCs.

Section 3- Training and Certification describes training requirements and procedures for CC staff to certify the training activities.

Section 4 - Observations describes observations required for certification and other QA activities, gives the equipment monitoring schedule, and describes CC and CCC activities for CCC QA visits to the CCs.

Section 5 - Data Monitoring describes reports available for monitoring CC activities, including routine reports produced by the CCC, various types of reports CCs can run to monitor their activities, and gives CCs a schedule for running reports.

Section 6 - Performance Monitoring includes performance goals for various CC activities, and describes the performance monitoring plan and the functions of the Performance Monitoring Committee.

The Appendices in this volume contain specific QA resource materials, such as Certification Forms and Training/QA Checklists.

1.1 WHI QA Program Overview

The WHI QA program focuses on the following areas:

- Integrity of Primary Clinical Trial (CT) Results

The WHI Protocol (in Volume 1) describes the design and goals for both the Clinical Trial (CT) and the Observational Study (OS). Adherence to the CT design is essential for assuring the proper interpretation of the results, thus the QA Program includes monitoring the following essential CT activities:

  - Eligibility
  - Randomization
  - Blinding
  - Intervention, Adherence, and Retention
  - Outcomes

- Participant Safety

Quality Assurance procedures for ensuring participant safety include:

  - Procedures that are performed as specified in the WHI Manuals and in accordance with usual standards of medical care.
  - Potential problems, side effects, and adverse events that are managed appropriately.

- Ethical Conduct

Research involving human subjects must undergo a comprehensive review to assure ethical conduct. Study investigators at the National Institutes of Health (NIH), CCC, CCs, and the WHI Data and Safety Monitoring Board (DSMB) have reviewed the protocol, procedures, and participant materials and have approved the WHI model consent forms. (See *Vol. 1 - Study Protocol and Procedures, Section 2 - Consent Forms.*)

Model consent forms are included in the Protocol appendices. Each CC is responsible for keeping their consent forms up-to-date and for submitting them to the local IRB for approval. The Project Office centrally reviews new or revised CC consent forms for accuracy and completeness before the consent forms may be used.

Quality Assurance priorities for ethical conduct include:

  - Obtaining full, uncoerced, informed consent.
  - Collecting accurate participant information.
  - Preserving confidentiality of participant information.
  - Providing referrals and appropriate medical information to participants' health care providers.

- Valid and Reliable Data Collection

The WHI is a multicomponent, multicenter study of long duration that involves large numbers of women. These factors contribute to the unique nature of this research endeavor, and also increase the complexity of data collection and management activities.

Quality Assurance priorities for assuring valid and reliable data include monitoring that:

  - Data collected are complete and accurate.
  - Procedures used to collect, review, process, and enter data are standardized and consistent.
  - Procedures used to label and handle specimens are accurate, standardized, and consistent.
  - Data editing is accurate and appropriate.
  - Management of data is organized and timely.

1.2 Priorities

The WHI QA program seeks to balance the need to assure scientific quality of the study with available resources (time, money, and staff). The complexity, size, and fiscal responsibility of WHI necessitate establishing priorities to guide CC and CCC QA activities.

The WHI QA priorities were developed under the premise that aspects critical to the main components of WHI would be of highest priority. As the centerpiece of WHI, the fundamental elements of the CT are considered of highest priority. The next highest priority is given to key elements of the OS and elements of the CT that are important for interpretive analyses. The remaining elements are given a lower priority. *Table 1.1 - WHI QA Priorities* gives a basis for assessing the priorities of both CC and CCC QA activities for both the CT and OS.

The implementation of these priorities is manifested in the frequency and level of detailed QA methods applied to both CC and CCC QA activities.

- Priority 1 items receive rigorous routine review and monitoring, both centrally and locally.
- Priority 2 items receive review at a reduced level, often with only local monitoring or central review limited to data monitoring.
- Priority 3 items are addressed on a time available basis. Because the training and QA for some priority 3 items are identical to those of higher priority, there may be adequate carry-over effects from the higher priority activities to assure adequate performance. Continued monitoring of these areas is done to allow the detection of severe problems.

Table 1.1
WHI QA Priorities

Priority 1	CT Informed Consent CT Randomization CT Interventions, Adherence and Retention CT Safety CT Primary Outcomes
Priority 2	CT Blinding CT Eligibility OS Primary Outcomes OS/CT Biological Specimens OS/CT Baseline Predictive Data CT Follow-up Predictive Data
Priority 3	OS Informed Consent OS Enrollment OS Follow-up Predictive Data CT/OS Subsidiary Outcomes CT/OS Ancillary Study Interference

1.3 Quality Assurance Methods

The WHI QA responsibilities include study-wide requirements initiated and coordinated by the CCC as well as CC-established requirements and activities. The following standardized methods are used to maintain quality throughout the WHI :

- Document Procedures
- Train Staff
- Certify/Recertify Staff
- Observe Procedures
- Monitor Data (Completeness, Validity, Timeliness, Reliability)
- Establish and Monitor Performance Goals
- Provide Feedback

Each aspect of WHI can be evaluated using one or more of these methods. Clinical Centers and the CCC often share accountability for QA and each have specific responsibilities for assuring the quality of certain areas. The other sections in this manual give details of these responsibilities and methods. The WHI committee structure may prioritize QA activities so that multiple methods are used to assure quality in selected areas.

Section 1
Quality Assurance Overview

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