QUALITY ASSURANCE

A. INTRODUCTION

The UITN Study Investigators will assure for the standard administration of the study protocol and procedures by the UITN surgeons and research staff across all Continent Treatment Centers (CTC) through the implementation of a comprehensive Quality Assurance (QA) Plan. When properly implemented, the QA Plan protects the scientific integrity of the study by maximizing the reliability and validity of the treatments delivered and the evaluation measurements conducted. The accuracy of reports and results produced and published by the Investigators is dependent on the quality of the data submitted by the staff at the primary and satellite CTCs. The Biostatistical Coordinating Center (BCC) staff is also obligated to employ the highest standards for data processing and data analysis.

The main objective of the QA Plan is to provide a means by which Investigators can demonstrate that complete and accurate data are gathered and that the surgeries are conducted in a standardized manner. The QA Plan ensures that the surgical procedures and all critical study evaluation measurements are performed in a standard manner regardless of the CTC, Surgeon, Interviewer, Data Collector or Examiner.

Standard application of the protocol will be accomplished by the following methods:

1. Development of a study Manual of Operations as well as Procedures Manuals for the surgical procedures, urodynamic studies and other physical tests;
2. User-friendly Data Forms and Question-by Question (QxQ) Specification Guides clearly linked to the research objectives documented in the study protocol;
3. Steering Committee sign-off procedures for all study Data Forms;
4. Central training and certification of CTC Interviewers, Data Collectors and Data Managers using standardized QC checklists;
5. Certification of all participating Surgeons in the surgical procedures;
6. Certification of participating Examiners / Testers in the performance of urodynamic studies, staging of pelvic organ prolapse and other physical examination measures;
7. Verification of patient eligibility;
8. Regular, collaborative communications between the Site Coordinators and the BCC;
9. On-going monitoring of all protocols / data collection activities;
10. Regular QA site-visits to all CTC's to meet pre-specified monitoring goals.

Each of these methods as well as specific procedures for performance monitoring of data collection and surgical procedures are described in the following sections.

B. QA METHODS

B.1 Manual of Operations

The development of the Manual of Operations (MOO) takes place in three steps:

1. A working draft of the procedures is first produced as a Training Manual for use during baseline central training. This draft, with intermittent updates, is used as the primary reference manual for all data collection activities conducted in the earliest phase of patient recruitment, enrollment, baseline measurements and surgical interventions.

2. A final Operations Manual is produced, incorporating all revisions made in response to the findings and experiences of central training and subsequent to enrollment of the first several patients (e.g. one - two per site).
3. Subsequent revisions or updates should be minimal and consist of revised pages for replacement in the Manual.

The 'official' UITN Manual of Operations will be the complete reference for all study procedures. The Manual of Operations will consist of a primary volume containing the Study Protocol, Data Forms and QxQ Specification Guides, Surgical Procedures, and selected examination and testing procedures. A Data Management Manual will be the complete reference for all data entry, data cleaning, report generation, and other data management activities.

The BCC is responsible for updating study manuals, Data Forms and QxQ guides in collaboration with the UITN SC Investigators and/or assigned Work Groups. Selected Work Groups may assume primary responsibility for updates to assigned sections of the manual, e.g. UDS Working Group members will direct / approve changes or updates made to the UDS Procedures.

The 'current' version of the UITN MOO will be published on the UITN Website. Documents posted on the web are posted as pdf file documents to prevent alteration of master documents. A limited number of hard copies should be maintained locally in three ring binders such that updated instructions may be printed and inserted as replacement pages for all manuals study-wide. Notifications of updates to manuals will be distributed by the BCC as required. To ensure complete updating of all manuals in the field, Study Coordinators must keep a record of all 'official' manuals in use at their respective CTC. Notification of all updates will be distributed by the BCC to the Study Coordinators for internal distribution. Study Coordinators should conduct routine audits of all local copies of UITN study manuals to ensure that all are up-to-date and represent the most current version of study procedures for accurate reference during fieldwork. Audits of all CTC manuals by the BCC will be conducted during annual QC site visits.

Study Coordinators, Interviewers and other Data Collectors should review the training manual, including Data Forms and QxQs, after central training, intermittently as needed, and when questions regarding protocol implementation arise.

UITN study manual materials and Data Forms should not be reproduced or distributed, in whole or in part, beyond the UITN study staff without Steering Committee approval.

B.2 User Friendly Forms and Question by Question Specification Guides

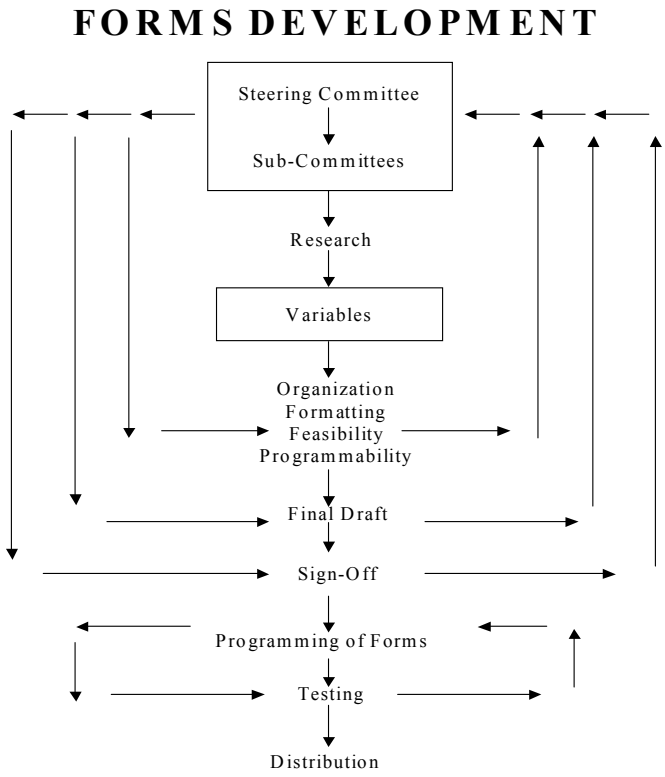
Most importantly, study Data Forms and QxQ Guides are developed to address the study's scientific aims. Of equal importance, forms are designed to be user-friendly for the study staff and, in the case of the self-administered instruments, the research patients. Every effort is made to design forms that are essentially 'fail-safe'; that is, to minimize data collection, data recording, scoring, and data entry errors. Key formatting issues that help to ensure high quality data include: minimal use of open-ended questions; clear skip patterns; standard typeset conventions to distinguish verbatim questions from interviewer instructions; standard introductions and transitions within interviews; subsections organized by topic, and standard coding conventions.

Sign-Off Procedures: All Data Forms and QxQ Guides have been developed, reviewed and

approved by the SC Investigators. UITN forms development included the following activities:

a. Staff of the BCC drafted Data Forms in accordance with the scientific protocols developed by the UITN Steering Committee.
b. The Forms Work Group members reviewed and revised draft forms in preparation for SC review;
c. Final drafts were distributed to SC members for review and **sign-off** prior to the start of study data collection.

This process is summarized in the figure below.



B.3 Baseline Central Training of Study Coordinators, Interviewers and Data Collectors

A major contributor to data quality and consistency across multiple clinical sites is centralized training at start-up. In the best of circumstances, all Study Coordinators, Data Collectors and Data Managers from all CTCs attend a central training program to complete training in the study procedures including study design, required measurements and standards, forms completion, editing procedures and data management. Sessions at central training include a didactic review and discussion of the study protocol including all primary and secondary outcome measures. Following this didactic review, the group reviews each measure and data form in detail.

Demonstrations are conducted wherever possible. Several videotapes will be employed to augment central training. UITN central training will include demonstration and return demonstration sessions for the Preliminary Screening Interviews, the Voiding Diary and the Pad Test.

B.4 Certification Activities

UITN study staff must complete certification requirements before they begin enrolling patients. Research staff's ability to meet minimum standards is assessed using pre-determined criteria established by the QC Work Group (for Surgeons) and by the BCC in accordance with prevailing performance standards utilized in NIH Clinical Trials. Separate criteria have been developed for Surgeons, Interviewers and Data Collectors, PE Examiners and UDS Testers. These criteria are summarized below and can also be found in the Certification Modules for each performance category attached here and published on the UITN Web page.

To achieve baseline certification, staff must complete certification requirements and submit all related materials to the BCC for review and registration. The BCC reviews these materials for quality and completeness and notifies the CTC of the results within 3 business days of receipt.

B.4.1 Baseline Interviewers and Data Collectors

After central training, Interviewers and Data Collectors complete baseline certification activities at the CTC where they continue to practice completion of the study interviews (Baseline Data Forms 01, 02, 03) and other required measurement protocols including the Pad Test, Voiding Diary and any record abstraction that may be required to complete the Physical Exam (Form 04), Stress Test (Form 13) and UDS (Form 05).

To achieve certification as a UITN Interviewer, an individual must meet the minimal requirements for certification listed below and documented in the Attestation of Compliance for Interviewers and Data Collector included in the Certification Module for Interviewers and Data Collectors attached here and published on the UITN Web page.

Baseline Certification Requirements for UITN Interviewers / Data Collectors:

1. Attend central training;
2. After central training, complete a review of all study training materials including the Study Protocol, Data Forms, QxQ Specifications Guides, Chapter 6, etc;
3. After central training, review all patient educational videos including the Study Introduction for use in completing consent procedures and the Voiding Diary and Pad Test video;
4. Practice UITN interviewing procedures with volunteers;
5. Demonstrate competence in the conduct of a research interview through successful completion of an observed mock interview. QC observations will be completed by BCC staff using the QC Observation Checklist for Interviewers /Data Collectors (see attached). This standard can be met either through an in-person observation of a mock Preliminary Screening Part I interview (completed at central training or at the time of a QA Site Visit) or through the submission of an audiotape of a mock Preliminary Screening Part I Interview completed with a CTC volunteer. BCC staff will evaluate Interviewer competence through a review of the live or audiotaped interview and completed Data Form. The BCC reviewer will provide a written report of his/her evaluation and contact

the Interviewer to review the outcome of the review. Additional practice and/or a repeat mock demonstration may be recommended.

6. Demonstrate compliance in the performance of Voiding Diary and Pad Test Procedures per UITN protocol, as observed by a CTC colleague using the QC Observation Checklist for the Voiding Diary and Pad Test. (See the QC Observation Checklist included in the Certification Module for Interviewers and Data Collectors attached.).
7. Practice completion of data collection procedures using clinical records of patients likely to meet eligibility criteria for enrollment in the study;
8. Using medical records referenced in # 7 above, compare abstracted data across data collectors within each CTC to achieve high inter-abstractor agreement;
9. Submit to the BCC all baseline visit Data Forms and copies of source documentation to the BCC for the first two UITN enrollees [Form 01 (Preliminary Screening Part I); Form 02 (Preliminary Screening Part II); Form 03 (Medication Audit); Form 04 (Physical Exam); Form 13 (Stress Test), Form 05 (UDS); Form 06 (Voiding Diary and Pad Test); Form 07 (Baseline Patient Survey Part I), Form 08 (Baseline Patient Survey Part II), Form 09 (Randomization Assignment); Form 10 (Operative Measures), and Form 11 (Immediate Post-Operative Measures).
10. Submit an Attestation of Compliance for attainment of certification to the BCC.

If an Interviewer/Data Collector joins the study after central training has taken place, an alternative training plan must be established in conjunction with the BCC.

Elements of the QC Observation Checklist for Interviewers / Data Collectors

Quality Assurance Observation Checklists have been developed to standardize the assessment of research staffs' compliance with various study procedures. Two checklists have been developed for Interviewers and Data Collectors, specifically the QC Observation Checklist for Interviewers and Data Collectors and the QC Observation Checklist for Voiding Diary and the Pad Test. The Checklist for Interviewers and Data Collectors includes minimal standards for completion of the Preliminary Screening Interview Part I and Part II. Certification is achieved through the demonstration of competence in the performance of the Preliminary Screening Part I interview. The QC Checklist for the Voiding Diary and Pad Test contains the minimal standards for completion of the Voiding Diary and Pad Test measures including precise standards for the weighing procedures for the incontinence protective pads used in the Pad Test. See the QC Observation Checklists included in the Certification Module for Interviewers and Data Collectors attached here and published on the UITN Web page.

B.4.2 Baseline Certification of Surgeons

Recognizing the need for both internal and external validity, the UITN Steering Committee has adopted a set of standard elements for the conduct of the 2 surgical procedures under study, specifically the Burch modified Tanagho and the autologous fascia sling procedures. These standard elements are documented in detail in the UITN Surgical Procedures Manual (Chapter 7). Surgeons participating in the Trial will be required to 'certify' their commitment to comply with these standard elements through a certification process completed at baseline. All documents and materials related to the Certification of UITN Surgeons are included in the Surgical Certification Module attached here and published on the UITN Web page. A master set (in hard copy) of all required documents and materials will be provided to each Principal Investigator and Co-Principal Investigator (two sets per CTC) by the BCC.

To achieve certification as a UITN Surgeon, the physician must 'certify' that s/he met the minimal requirements as listed below and documented in the Attestation of Compliance for Surgeons included in the Certification Module for Surgeons attached here and published on the UITN Web page.

Baseline Certification Requirements for UITN Surgeons performing the Burch Procedure

1. Named as a Principal Investigator, Co-Principal Investigator or Co-Investigator on the UITN Study at his/her respective CTC;
2. Board Certified in Urology or Obstetrics/Gynecology;
3. Licensed as a physician by the state in which s/he practices;
4. Holds hospital privileges at a participating UITN Institution;
5. Regularly and frequently performs the Burch modified Tanagho procedure in his/her clinical practice;
6. Reviewed the final version of the UITN Protocol;
7. Reviewed the final version of the UITN Surgical Procedures Manual for the Burch modified Tanagho procedure;
8. Reviewed the UITN videotape of the Burch modified Tanagho procedure;
9. Demonstrated compliance in the performance of the Burch modified Tanagho procedure per UITN protocol as observed by a UITN Principal Investigator or Co-Principal Investigator completing the Burch QC Observation Checklist; and,
10. Submitted an Attestation of Compliance for attainment of certification in the performance of the Burch Modified Tanagho to the BCC.

Surgeons who are **not** named on the UITN Grant as a Principal Investigator, Co-Principal Investigator or Co-Investigator may be Board-eligible in Urology or Obstetrics /Gynecology rather than Board certified and must also:

11. Meet with a UITN Principal Investigator to discuss the protocol and standards set for the Burch modified Tanagho procedure for the UITN Trial; and
12. Receive UITN Steering Committee approval to participate in the UITN.

Baseline Certification Requirements for Surgeons performing the Sling Procedure

1. Named as a Principal Investigator, Co-Principal Investigator or Co- Investigator on the UITN Study at his/her respective CTC;
2. Board Certified in Urology or Obstetrics/Gynecology;
3. Licensed as a physician by the state in which s/he practices;
4. Holds hospital privileges at a participating UITN Institution;
5. Regularly and frequently performs autologous fascia sling procedures in his/her clinical practice;
6. Reviewed the final version of the UITN Protocol;
7. Reviewed the final version of the UITN Surgical Procedures Manual for the autologous fascia sling;
8. Reviewed the UITN videotape of the autologous fascia sling procedure;
9. Demonstrated compliance in the performance of the autologous fascia sling procedure per UITN protocol as observed by a UITN Principal Investigator or Co- Principal Investigator completing the Sling QC Observation Checklist; and,
10. Submitted an Attestation of Compliance for attainment of certification in the performance of the autologous fascia sling procedure to the BCC.

Surgeons who are not named on the UITN Grant as a Principal Investigator, Co-Principal Investigator or Co-Investigator may be Board-eligible in Urology or Obstetrics /Gynecology rather than Board certified and must also:

11. Meet with a UITN Principal Investigator to discuss the protocol and standards set for the autologous fascia sling procedure for the UITN Trial; and
12. Receive UITN Steering Committee approval to participate in the UITN.

Elements of the QC Observation Checklist for Surgeons

To satisfy certification requirements, Surgeons will be observed during the completion of each of the UITN surgical procedures prior to study start-up, i.e. criterion # 9. Observations must be completed by a CTC Principal Investigator using the QC Observation Checklist of pre-determined criteria established by the UITN QC Working Group and approved by the UITN Steering Committee. Criteria are scored on a yes / no scale with opportunity for comments available for each criterion. The criteria included on the QC Observation Checklists for both surgical procedures follows here and can be found in the Certification Module for Surgeons attached here and published on the UITN Web page.

B.4.3 Baseline Certification of Examiners and Testers

Similarly, certification standards have been identified for UITN Physical Examiners and UDS Testers, respectively. Specialty certification is required for the performance of the Pubococcygeus Contraction (PC) Assessment, the Pelvic Organ Prolapse Quantification (POP-Q) examination, the Stress Test and the Q-tip test, as well as the Urodynamics Studies (UDS) procedures. Physicians and others will certify in the exam and UDS procedures in a manner similar to that described above for Surgeons. UITN Examiners and Testers must complete the specified self-directed certification modules to obtain certification as a UITN Examiner and /or UDS Tester. While none of the exams/test is experimental, the procedures have been standardized by the Steering Committee to maximize the quality of eligibility and outcome measurements for this Study. Furthermore, standard procedures are designed to minimize variability between Examiners / Testers at the various CTCs.

The Physical Exam Procedures Manual (including a separate Manual for the Stress Test Procedures), and the UDS Testing Procedures Manual are included in Chapter 7. A certification module has also been developed for each; these are attached here and published on the UITN Web page. All documents and materials related to the certification of Examiners and Testers are included in these certification modules and a master set (in hard copy) of all required documents and materials will be provided to each Principal Investigator and Co-Principal Investigator (two sets per CTC) by the BCC.

To achieve certification as a UITN Examiner and / or Tester, an individual must ‘certify’ that s/he met the minimal requirements as listed below and documented in the related Attestation of Compliance documents, i.e. Attestation of Compliance for Physical Examiners and Attestation of Compliance for UDS Testers, which can be found in the certification modules attached here and published on the UITN Web page.

Physical Examinations: Certification will be required for the performance of the Pubococcygeus Contraction (PC) Assessment, the Pelvic Organ Prolapse Quantification (POP-Q) examination, the stress test and the Q-tip test.

Baseline Certification Requirements for Physical Examiners

1. Registered / licensed to meet State requirements for clinicians completing physical examination procedures (e.g. MD, NP, PA, RN, other technician category, etc.);
2. Regularly and frequently performs **PC assessments** in his/her clinical practice;
3. Regularly and frequently performs **stress tests** in his/her clinical practice;
4. Regularly and frequently performs **POP-Q exams** in his/her clinical practice;
5. Regularly and frequently performs **Q-tip tests** in his/her clinical practice;
6. Reviewed the final version of the UITN Protocol;
7. Reviewed the final version of the UITN Physical Examination Procedures Manual, the UITN Physical Examination Data Form (Form 04) and the Form 04 QxQ Specifications Guide;
8. Reviewed the final version of the UITN Stress Test Procedures, the Stress Test Data Form (Form 13) and the Form 13 QxQ Specification Guide;
9. Reviewed the ICS POP-Q standards published in the *Am J Obstet Gynec (1996) 175:10-17;*
10. Reviewed the Duke University Medical Center POP-Q videotape;
11. Demonstrated compliance in the performance of the PE measures per UITN procedures as observed by a CTC Principal Investigator or Co-Principal Investigator completing the PE Examiner QC Observation Checklist;
12. Demonstrated compliance in the performance of the Stress Test per UITN procedures as observed by a CTC Principal Investigator or Co-Principal Investigator completing the Stress Test QC Observation Checklist; and
13. Submitted an Attestation of Compliance for attainment of PE Examiner certification to the BCC.

Urodynamic Studies: Certification will be required for the performance of urodynamic studies completed on all UITN patients to determine eligibility and to determine the prognostic value of one or more of these test.

Baseline Certification Requirements for UDS Testers include the following:

1. Registered / licensed to meet State requirements for clinicians completion UDS testing procedures (e.g. MD, RN, NP, PA, other technician category, etc.);
2. Regularly and frequently performs UDS testing in his/her clinical practice;
3. Reviewed the final version of the UITN Protocol;
4. Reviewed the final version of the UITN UDS Procedures Manual, the UDS Data Form (Form 05) and the Form 05 QxQ Specification Guide;
5. Met with a UITN Principal Investigator to discuss the UITN UDS Procedures and QC Standards;
6. Demonstrate compliance in the performance of UDS Testing per the UITN procedures observed by a CTC PI or Co-Principal Investigator completing a UDS QC Checklist; and,
7. Submitted an Attestation of Compliance for attainment of UDS certification to the BCC.

B.4.4 Baseline Certification of Data Managers and Data Entry staff

Data managers and data entry personnel will also be required to complete baseline certification exercises in keeping with the standards established for surgeons, interviewers, examiners and testers. These standards are described in detail in the Data Management Manual.

B.4.5 Maintenance of Certification Status through Re-certification

Standards for the ongoing maintenance of research staff proficiency in the conduct of procedures and measurements are designed to prevent/minimize "drift" in the performance of the various techniques over time. The Steering Committee has established a requirement for **annual** re-certification for most staff categories to prevent/minimize drift and maintain consistency across CTCs. To achieve re-certification status, research staff must demonstrate compliance with UITN protocols and procedures during observed sessions at 12-month intervals from the date of their initial certification for each respective procedure or measure. Qualified observers must complete a QC Observation Checklist at the time of the observation. Here follows a list of staff by category and their respective re-certification obligations.

1. Surgeons named on the UITN Grant are e**xempt from the requirement for re-certification for surgical procedures.**
2. Surgeons not named on the UITN Grant must be re-certified annually in **surgical procedures.** The PI or Co-PI must observe the 'peripheral' surgeon completing each of the surgeries under study. The UITN patient(s) should be randomly selected and the QC Observation Checklist(s) should be completed.
3. Examiners must be re-certified annually for Physical Examination procedures including Stress Testing.
4. UDS Testers must be re-certified annually for UDS Procedures.
5. Data Collectors must be re-certified annually for Pad Test/Voiding Diary procedures.

The completed QC Observation Checklists should be sent to the BCC once completed. Re-certification observations should be completed in advance of the anniversary date to avoid expiration of certification status as data from non-certified staff cannot be entered into the UITN data management system.

B.4.6 Summary of UITN Staff Certification Standards

Minimal performance standards have been established for virtually every UITN study staff personnel category in an effort to address the deficiency identified in previous surgical studies of urinary incontinence as described by others and summarized in the UITN study protocol, (UITN Study Protocol, page 7);

> *The 1996 Clinical Practice Guidelines in Urinary Incontinence (Fantl et al., 1996), issued by the Agency for Health Care Policy and Research (AHCPR), concluded that the surgical literature was deficient "in describing the patient population, the type of incontinence, the methods for accurate diagnosis, the techniques of the surgical procedure, or the outcome in different domains." Two other major reviews substantiate these findings. Black and Downs' (1996) exhaustive review of the surgical literature documents the extant methodological flaws including variability of case definition,*

failure to account for known confounders, variability in duration of follow-up, poor generalizability, inadequate power to detect clinically important differences, lack of assessment of complications, and marked variability in outcome assessment. The American Urologic Association (AUA) in 1996 undertook a comprehensive review of relevant surgical procedures, and this organization similarly concluded that most studies did not contribute to our understanding of the problem of incontinence, which evaluations were meaningful, and how a cure is defined clinically (Leach et al., 1997)

While none of the exams/test is experimental, the procedures have been standardized by the Steering Committee to reduce variability in the performance of surgical and evaluation measurement procedures. UITN study staff is obligated to complete certification requirements before they engage in any study activities with UITN patients.

B.5 Verification of Patient Eligibility and Currency of Measures

Accuracy of patient eligibility determination will be verified using the UITN web-based Data Management System (DMS). Initially, a patient's eligibility status will be determined by CTC staff during completion of UITN screening measures, including selected measures that require manual scoring. But the UITN DMS will not issue a Randomization Authorization number for a patient until all of the required screening forms are data entered and the patient's eligibility status is confirmed by the DMS.

In addition, the DMS will verify that all measures are current. The Steering Committee has categorized several measures as 'expiring measures', that is, if more than 6 months transpires between completion of the measure and the expected date of surgery, the measure must be repeated to ensure current eligibility for the trial as well as to obtain current baseline values for critical measures that would be subject to change over a 6-month period. These measures are listed in Section H5 in the UITN study protocol. All measures must meet this currency standard prior to the issuance of the patient's Randomization Authorization number.

Once all baseline forms are entered and the eligibility status is confirmed by the DMS, CTC staff may print out the Patient's Authorization for Randomization Report that will allow randomization in the surgical suite just prior to UITN surgery using UITN Data Form 09: Randomization Assignment Form.

Note, at study start-up, each Data Collector is required to submit copies of all baseline visit Data Forms for their first 2 UITN patients to the BCC prior to randomization. The BCC will confirm eligibility status and assign the Randomization Authorization Number for these first 2 patients upon confirmation of the patient's eligibility. Patients may not be randomized without a Randomization Authorization number.

B.6 Study Coordination and Communications

Each primary CTC will employ/appoint a Study Coordinator who acts as a key staff person in assisting the PI to ensure quality implementation of all study protocols at the primary CTC and at all satellite Centers affiliated with the primary site. Study Coordinator responsibilities include: communications with the BCC for all protocol issues; informing CTC Surgeons, Interviewers, Data Collectors, Examiners, Testers and Data Managers, of protocol updates; supervising the completion of all training activities required for Interviewers, Data Collectors, Examiners, Testers and Data Managers; coordinating submission of all required certification materials and

documents for all research staff including Surgeons, Examiners, Testers, Interviewers and Data Collectors and Data Managers; supervising recruitment, enrollment and study visit scheduling of all patient appointments; supervising baseline and follow-up measurement activities; coordinating all surgical intervention activities; completion of or supervision of local QA activities including observation and critique of all data collection activities and review of completed Data Forms and data edits; and supervising all data transfers to the BCC as required.

The BCC will schedule regular conference calls among all UITN Study Coordinators. The Study Coordinator conference calls will be used to discuss questions and issues regarding field procedures. Frank discussion of problems early in the process of data collection can improve the quality of the data dramatically and accelerate the learning curve.

Communication and correspondence between the BCC and the CTCs must be documented across all sites in a standard manner. Study-wide Operations Memos will be distributed to Coordinators for internal distribution to appropriate staff at their Centers. Operations Memos will be numbered to ensure that the Coordinators have received all of them. They should be kept in a Communications Log Book in a central location that is accessible to all study staff. Staff are obligated to read and initial all new memos to document they have read them. The purpose of the Communications Log Book is to provide a single, reliable location for all updates and protocol changes that occur throughout the study. The Operations Memos will be distributed by the BCC simultaneously to all centers via the UITN Web site for review and site distribution.

Throughout the data collection phase, Interviewers and Data Collectors may have specific questions about protocols and procedures. Study Coordinators should review the manuals, forms and QxQs to determine if the question can be answered in the currently published materials. If the question cannot be answered by referencing the manuals, the Principal Investigator or Site Coordinator should not attempt to clarify the procedure locally. All questions regarding study protocols and procedures must be directed to Kim Dandreo at the BCC, (617) 923-7747 x 219. The BCC is responsible to investigate and communicate the appropriate approach and determine if the inquiry has study-wide implications. In some instances, Steering Committee and/or Work Group members will be contacted to determine the proper approach. Site inquiries should be forwarded to the BCC in writing.

B.7 Ongoing Monitoring of Data Collection and Intervention Activities

B.7.1 CTC Certification at Start-up

Each CTC is required to submit to the BCC for QA review, all pertinent documentation relevant to the enrollment, randomization and surgical intervention of its first 2 UITN patients.

B.7.2 Local QA Activities

Local QA activities must be in place from the first day of data collection. Study Coordinators or other designee must supervise all local data collection activities. CTCs must assure that all local research activities are in compliance with all the QA elements described herein. At a minimum, sites should implement a QA Plan that will ensure their personnel attain and maintain a minimum level of proficiency in data collection, examination and testing skills as well as data entry and data management. Baseline certification and re-certification standards are documented above.

The CTC Study Coordinator or designee will be responsible for local QA activities such as monitoring the completion of outstanding training and certification activities completed at the CTC, and completing ongoing local QA audits and observations in accordance with the master QA Plan.

B.8 QA Site Visits

The BCC is obligated to conduct QA site visits to each CTC at least once a year to review site staffing and administrative procedures; observe consent procedures, interviewing, data collection and testing; review corresponding forms completion; as well as to check for correct filing of forms and data corrections including maintenance of patient confidentiality standards. NIH Program Staff and DSMB members may also attend QA Site Visits. In most instances, site visits will be coordinated in advance with each PI and Study Coordinator. However, site visits may be conducted without notice for good cause. Center PIs and Study Coordinators must be available, in person, during a planned site visit. At a planned QA site visit, the BCC monitoring staff will review selected CTC study materials, tour center facilities, meet with center staff, conduct an audit of administrative files, patient research files and medical records, and make direct observations of interviewers, data collectors and examiners in the clinical setting. The QA site visit observations will provide data to evaluate the quality of data being collected and the standardized administration of study protocols in realistic settings. Site visitors will use a standardized QA Site Visit Guide. A copy of the Guide is published on the UITN Web page.

A summary of site visit activities and materials required appears below. At the end of the visit, Site Visitors will meet to debrief with the Center's PI and Study Coordinator. A written site summary report will be submitted to the PI and NIDDK.

B.8.1 Materials Required

The following materials will be reviewed prior to, or during, the QA site visit:

1. A list of all study staff, their responsibilities, percent effort devoted (not budgeted) to the UITN study, and currency of certification status.
2. Site organizational chart delineating lines of authority and communications.
3. Record(s) of staff meetings and attendance.
4. A written description of local recruitment procedures.
5. Copies of current approved informed consent documents.
6. Copies of all recruitment materials and standard correspondence in use.
7. A list of all satellite and secondary practice sites used for patient recruitment, screening, testing and study follow-up sessions.
8. All standard study materials including all copies of all Procedures Manuals, Communications Log memos, study-wide minutes of meetings and conference calls, all master Data Forms, etc.

B.8.2 Site Visit Activities

During a site visit, QA Site Visitors will:

- Meet with senior CTC staff, including Principal Investigators and Study Coordinator. Site Visitors will always include members of the BCC monitoring team and may include NIH Project Officers and members of the UITN Data Safety and Monitoring Board.

- Tour study facilities including clinical areas used to complete study visits, videotape viewing, staff work and equipment storage areas, team meeting rooms and data management area, as well as the surgical areas where the UITN surgical staff complete the surgeries under study.
- Complete an organized, comprehensive audit of study files, including patient consent forms, data files and related source documents.
- Observe recruitment, screening, testing and surgical activities at all primary and satellite centers.
- Talk with Investigators, Interviewers, Data Collectors, Examiners, and data management staff regarding pertinent research study procedures as appropriate.
- Audit all materials and Data Forms from several randomly selected patients. The BCC staff will select IDs and DMS data shortly prior to the site visit.
- Complete a de-briefing meeting at the end of the site visit with the Center's Principal Investigator(s) and others as arranged.
- Complete a site visit report forwarded to the PI and the NIDDIC Program Officers.