Manual 12
Quality Assurance and Quality Control
Visit 5/NCS

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Study website - http://drupal.cscc.unc.edu/aric/

Quality Assurance and Quality Control

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1. INTRODUCTION

1.1. Quality Assurance and Control Procedures

The distinction between quality assurance and quality control is both arbitrary and philosophical. The former is considered here as relating to activities to assure quality of data which take place prior to collection of data, while the latter relates more to efforts during the study to monitor the quality of data at identified points during data collection and processing. It is quality control on which this manual focuses, whereas quality assurance is the essence of the entire Manual of Operations, and includes the following activities:

1) Detailed protocol development. A clear description of the study design, training, certification, and the various data collection activities provides the blueprint for the study. Each protocol is a written reference for staff and researchers. Procedures for handling the routine, as well as the exceptional, are given. Those protocols constitute the ARIC Visit 5/NCS Manuals of Operation.

2) Training. Training is the transfer of the study plans in the protocol to the research staff. The process has resulted in clarification and revision of the protocol. Special materials for this purpose have been developed for ARIC and are the basis for continuing education during the study.

3) Certification. Criteria to examine the adequacy of an individual's training have been established. Individuals meeting these criteria are qualified to execute a protocol or a segment of it. Certification indicates that an acceptable performance standard has been mastered or an adequate knowledge of material has been achieved. The Coordinating Center (CC) monitors the study to ensure that the research staff performs only those functions for which they are certified.

Quality control procedures involve monitoring data collection by observation (directly and by audio or video tape recording) and quantitative assessment (using repeated measurements and statistical analysis of study data). Monitoring is performed both by personnel within the field centers and by monitoring visits from the CC. A summary of selected aspects of ARIC Study quality control follows.

1) Observation monitoring. Over-the-shoulder observations of staff by supervisors are made to identify techniques that need improvement and points where the protocol is not being followed. Also, periodic monitoring visits by CC staff are made to observe clinic activities. Immediate feedback is given on issues related to protocol adherence, and recommendations for improvements are given to the field center Principal Investigator for action.

2) Quantitative monitoring. Repeat measurements taken by the same and different technicians are used as quality control tools. Randomly re-doing a fraction of an individual's work may not only stimulate better overall quality of data, but also allows estimation of measurement reliability. At the time of reporting the results of the study, it is important to establish that the “error” in the data is not so large as to threaten the validity of conclusions. In addition, descriptive statistics and graphical representation of study variables by technician and month are monitored to identify differences among technicians or trends over time.

3) Reporting results. Two aspects of the reporting of quality control monitoring should be emphasized. First, the results must be timely. When remedial action is required, reporting must be prompt so that a return to an acceptable level of performance is not

unnecessarily delayed. Second, the reporting format must be easily understood. Tabular presentations are accompanied by clear graphical displays.

4) Action on results. With conscientious and trained staff, quality control reports provide an opportunity to praise a job well done. On the other hand, a poor performance is the basis for some remedial action. Depending upon past performance, the amount of error, and the appropriate action may be a simple discussion to encourage a better performance. Re-training may also be appropriate at times.

1.2. Monitoring of Data Quality and Implementing Corrective Action

The subsequent sections of this Manual describe the reports used to monitor quality control. These reports are designed to be clearly understandable and to lead to corrective actions. A Quality Control Committee (QCC) is designated by the ARIC Steering Committee to coordinate and direct the quality control activities. This committee will have monthly conference calls to discuss issues that arise and review QC reports.

The QCC is charged with establishing the content of the quality control reports and reviewing them with specific attention given to deviation from protocol, and trends or shifts in data over time. The QCC prepares recommendations to the Steering Committee in matters of quality assurance, and contacts field centers, reading centers, or laboratories as needed, to advise them of a problem and to discuss the mechanism for correction. The QCC has representation from the CC, field centers, reading centers, laboratories, and NHLBI.

As the repository for ARIC Study data, the CC is responsible for preparation and dissemination of QC reports. These reports consist of tabulated data and summary statistics, and identify protocol deviations, recurrent problems, or temporal trends. Each field center and reading center is asked to respond to the reports and to implement corrective action. The distribution of periodic QC reports is as follows:

1) QC reports on technician-specific performance are sent to the respective field center principal investigators, to study coordinators and to the QCC.

2) QC reports on laboratories/reading centers' performance are sent to the respective principal investigators and to the QCC.

3) Summary QC reports are posted to the study website.

The following individuals should respond to the reports as follows:

1) Field center PIs, study coordinators: Review each QC report including technician-specific performance measures for their field center; identify a solution to each problem; implement corrective action; report corrective action to Coordinating Center QC Committee representative.

2) Laboratories and reading center directors: Review each QC report for their laboratory/center; identify a solution to each problem; implement corrective action; report corrective action to QCC.

3) Quality Control Committee: Review each QC report with attention to deviation from protocol, recurrent technician or field center problems, and temporal trends; contact field center, reading center, or laboratory investigators to review data quality problems and ensure solutions are proposed; monitor the implementation of corrective action.

4) Steering Committee: Review QC summary reports; monitor data quality trends; direct the QCC in areas needing special attention; propose changes to protocol when necessary.

1.3. Organization of the Quality Control Manual

What follows is a detailed list of quality assurance or quality control measures addressing each data transfer point or possible source of error. Section 2 describes certification procedures for field center staff. Section 3 describes the procedures for the Repeatability Study in which 120 participants repeat the entire clinic examination. The ARIC study's system of making (blinded) repeated measurements for quality control purposes is used in so many areas of the study that a separate section is devoted to description of this topic (Section 4). Section 5 discusses the types and schedules of quality control reports and describes the analysis of study data for quality control purposes. Subsequent sections describe the quality control procedures for the various components of the data collection protocol.

2. CERTIFICATION PROCEDURES

Certification of study personnel is an essential aspect of effective quality assurance as well as quality control in clinical research. In order to maintain proper collection of data despite potential for personnel changes over the study period, the CC is responsible for establishing and providing the requisite minimum criteria and training and ensuring continued adherence to standards.

Although all ARIC staff members are expected to be familiar with the entire study protocol, the complexity of the design requires that study coordinators and staff designated to participate in certain areas of data collection for the study each be instructed and certified on specific data collection instruments and tasks.

Study coordinators are responsible for providing continuity from participant recruitment through exiting the study. Coordinators should be routinely involved in all aspects of the study with regard to participant and staff involvement as well as data collection. This includes recruitment and scheduling of participant visits as well as the performance (or supervision) of many segments of the clinic examination. Coordinators also serve as the liaison between their clinical site, laboratories, reading centers, and the CC. They communicate with participants' physicians when necessary with regard to study procedures and examination results. The study coordinator is responsible for accurate collection of data and oversight of the shipment of blood and urine samples to the Laboratories, and pertinent materials to the reading centers.

The responsibilities of study technicians can vary between field centers and with staff qualifications. The study coordinator is responsible for periodically monitoring the accuracy of the work done by auxiliary personnel. However, it should be noted that the Principal Investigator is ultimately responsible for the clinical behavior and ethical standards of all staff at his/her study center.

All study coordinators must attend the Central Training. This weeklong training covers all aspects of the study protocol and is led by individuals with specific expertise in the given exam component. Attendance at the centralized training is strongly encouraged for all study personnel.

In addition, staff must be certified in the following areas in order to collect such data. Specific criteria and requirements for training in these areas are described in detail in the following sections of Manual 2 (unless otherwise specified):

A. Informed Consent

B. Anthropometry

C. Seated Blood Pressure

D. Ankle Brachial Index/Pulse Wave Velocity

E. ECG – Manual 5

F. Biospecimen Collection & Processing – Manual 7

G. Pulmonary Function testing – Manual 4

H. Echocardiography – Manual 6

I. Interviewing techniques

J. Cognitive Function

K. Neurologic examination – Manual 17

L. MRI scanning – Manual 13

M. Retinal examination – Manual 14

Additional specialized trainings and certifications are held for technicians/examiners responsible for MRI scanning (Manual 8), and echocardiography (Manual 6) examinations.

Study technicians may train and be certified in any of the areas they have been assigned to by their Principal Investigator (PI) or Study Coordinator. Certified Study Coordinators or lead personnel may train and certify new personnel on site after initiation of the study by following the guidelines specified in Manual 2 and certification procedures described below. It should be noted that the Study Coordinator remains responsible for all data collection, data entry, and other procedures that may be delegated to staff. Study Coordinators should frequently monitor staff members to ensure the high quality performance of all procedures.

Study Coordinators will submit a Certification Request Form (Appendix 14) to the CC to document that a staff member has completed the necessary requirements for certification. The Certification Request Form documents how, when and which procedures/interviews were certified. The CC will assign a staff code number upon receipt of this form. Should staff learn more procedures and interviews for certification since the initial certification request, a re-submission of the form is needed to update those new areas of certification.

The CC will continually update records of all certifications at each study site, and staff code numbers will be compared against the data collection forms to ensure that only certified staff performs data collection on the specific procedures/interviews to which they have been assigned. Additional training and supervision will be carried out as individually needed at the field centers. Continued supervision will be the responsibility of the Study Coordinator. If at any time a center is found to be lacking in certification requirements, or the quality of data collection is found to be less than optimal by the Quality Control Committee, the center will be notified. If the center does not institute corrective action in the time allotted, further follow-up will take place by staff charged with study administration in an attempt to resolve the issues.

3. REPEATABILITY STUDY

3.1. Participant Selection

A subset of components from the Stage I clinic visit will be repeated on 80 volunteers (20 per field center) to determine reliability of measurement procedures. Biospecimen collection will be repeated on a total of 200 volunteers (50 per field center), which may include those on whom other procedures are repeated. No stage II elements will be repeated; however the neurocognitive test battery administered during Stage I will be repeated on 20 participants during a Stage II visit. Those selected to repeat Stage I and the neurocognitive test battery during Stage II may be different participants in order to keep the burden on participants low.

The assessments listed in section 3.3 will be re-administered and new samples of blood, and urine collected. Field center staff will process these samples according to protocol. Each site will recruit 20 volunteers for Stage I, 20 for the neurocognitive test battery during Stage II, and a total of 50 for biospecimen collection over the study period to participate in the Repeatability Study.

For the repeat of Stage I, only participants undergoing the full clinic visit for Stage I will be considered. That is, those undergoing the abbreviated clinic visit or the home/LTCF visit will not be considered. Additional eligibility requirements for the repeat of the neurocognitive test battery are that participants should: 1) have completed the full neurocognitive test battery (Stage I) in the clinic; 2) have participated in Stage II; and 3) be eligible for Stage III. For Stage II, at each field center, 10 of the volunteers should be cognitively "Typical" (controls) and 10 cognitively "Not typical". Because Stage III (MRI exam) will typically be scheduled at a different time from Stage II, a Stage II repeat visit may be scheduled to coincide with the regular Stage III visit.

With less than 20 months of the 24-month measurement period remaining at the time the Repeatability Study is implemented, an average of just over 1 volunteer is needed for each stage per field center per month and 2.5 per month for biospecimen collection. Initially each center should enroll one Stage I and one Stage II repeat participant per month.

Field centers should aim for representation from all subgroups (e.g., gender, age) and the representativeness will be monitored by the Coordinating Center**.** One way to achieve approximate representativeness is described in item #2 of section 3.2.

3.2. Data Collection Procedures

Field centers will use repeat visit ID numbers for data collected as part of the Repeatability Study. The repeat visit ID numbers are indistinguishable from other ID numbers, and forms belonging to Repeatability Study participants are entered just as regular study data. However, repeat visit IDs have not been pre-populated in the DMS and need to be added – see item #4 below. The Repeat Visit Form (RVF) is used to match the repeat visit ID to the original ARIC ID of those participating in the Repeatability Study. This process is described in more detail as follows:

1) Eligibility conditions for the Repeatability Study are described in section 3.1.
2) Field center staff should ask the first eligible participant seen each month if he/she is willing to be in the repeatability study. A sample invitation might be: "We are seeking volunteers who might be willing to come back in 1-2 months to check the quality and repeatability of our measures. This would entail another visit here for a few hours to have some of the tests redone. Would you be interested in volunteering for this. Your decision to volunteer or not will have no bearing on your future participation in ARIC in other ways." If not, ask the next eligible participant and continue asking participants until one agrees. This needs to be done for the Stage I and the Stage II repeat participants, with additional participants recruited to average 2.5 repeat biospecimen collections per month.
3) The repeat visit should be done no sooner than 4 weeks, and no later than 8 weeks (52 weeks for neurocognitive test[1]) after the original clinic visit.
4) The day before a participant is scheduled to have a repeat visit, one of the field center staff completes the required fields on the Repeat Visit Form (affix the ARIC participant ID label, the repeat visit ID, staff ID, and the date of the repeat visit). Also, the repeat visit

[1] Starting from May. 10, 2013

ID needs to be added to the list of IDs in the DMS. Data managers at each field center have appropriate user privileges for adding IDs.

5) Obtaining new consent for the repeat visit is optional as long as the repeat visit is covered by the initial visit 5 consent. The consent form for the repeat visit is the same as for the original visit, but with the procedures not being done crossed-off. All other consent procedures to ensure the participant is truly volunteering and not coerced will apply.

6) Data collected on the repeat visit is entered into the DMS using the repeat visit ID. The Repeat Visit Form (RVF) is used to document the link between the original and repeat visit ID.

7) The same or different technician may be used to collect the data, but he/she should refrain from accessing data from the participant's original visit (i.e., the technician should be blinded to the original measurement values).

Data from the original and repeat visit will be analyzed to estimate the reliability of all data collection procedures. Methods for computing reliability coefficients, within-person standard deviations, coefficients of variation, and systematic differences are similar to those outlined in section 5.2 of this manual.

3.3. Components to be Repeated

Stage I Components to be Repeated:

Collection of Urine Specimen
Blood Draw, Biospecimen Processing
Echocardiogram (2D only, not 3D)
Seated Blood Pressure
Pulse Wave Velocity and Ankle Brachial Index
Physical Function and Timed Gait

Stage I component to be repeated during Stage II visit

Neurocognitive test battery

4. QUALITY CONTROL SYSTEM FOR REPEATED MEASUREMENTS

To estimate the reliability of laboratory and body composition measures, some participants will provide an additional sample of blood or urine, or will have anthropometric measurements repeated by a second technician on the same visit. The repeated anthropometric measurements are recorded on a new or second "occurrence" of the Anthropometry (ANT) form in the DMS for the participant that is having the measurement repeated. QC laboratory specimens are labeled with a *phantom* participant ID that is indistinguishable from other ID numbers, so that the laboratory is blinded to the QC process. The Phantom Form (PHT) is used to match the phantom ID to the ARIC participant IDs contributing repeat measurements. The Phantom Form belonging to the phantom participant is entered into the DMS just as regular study data. The QC phantom participant folders are created as follows:

1) Affix a phantom ID label to the Phantom Form; place these in a folder.

2) Every time a participant contributes replicate data, his/her ARIC participant ID is affixed to the Phantom Form next to the type of data that was contributed. Multiple individuals will contribute the QC specimens under a single phantom ID.

3) After completing the Phantom Form for the phantom, the folder is processed along with the regular stream of participant folders as if the Exit Interview had just finished.

5. ANALYSIS OF STUDY DATA FOR QUALITY CONTROL PURPOSES

The methods to monitor the quality of the ARIC data collection process include analyses of the study data itself, overall, by center, and by technician. There will be periodic reporting by field center on:

1) status of variables in the database (no problem, skipped due to skip rule, problem with the entry), to assess the prevalence of data entry problems,

2) distribution of categorical (frequencies) and continuous variables (means, standard deviations, percentiles),

3) distribution of variables that give information on protocol adherence and the validity of data (e.g., fasting time before blood drawing).

5.1. Quality Control Reports

For a report to be of use in correcting problems, it must appear frequently and reflect as much of the collected data as possible. The frequency of reports is determined by balancing the study's need for prompt and frequent monitoring with the available resources to generate such reports and the need to accumulate enough data to have an adequate sample size. For example, analysis of adjusted means by technician is not feasible on a monthly basis, but can usefully be done each quarter. The standard monthly QC reports will contain the following information:

1) Repeated measures
   a) Anthropometry
   b) Biospecimens
2) Descriptive statistics
3) Timeliness and completeness of data entry

5.2. Replicate Data Analysis

The following modeling process will be used to analyze replicate QC data. The total variance of the study data (σ_T^2) can be partitioned into two components: the measurement error component (σ_e^2) and the true variation between and within individuals in the study population (σ_b^2), so that $\sigma_T^2 = \sigma_b^2 + \sigma_e^2$. One quantity of interest for assessing data quality is the reliability coefficient, $R = \sigma_b^2 / \left(\sigma_b^2 + \sigma_e^2 \right)$, which is one minus the proportion of total variance due to error variation. The components of variance will be estimated from the replicate data using maximum likelihood (ML) or restricted maximum likelihood (REML) methods.

The estimates of reliability and error variance will be closely watched. In monitoring biospecimen data, $\hat{\sigma}_e$ for each assay is compared with the target standard deviation (SD) which the laboratory has set based on analyses of internal quality control pools. Blind replicate estimates which are more than twice the target SD are considered cause for concern. In addition, if the coefficient of variation (CV) is greater than 10% corrective action should be requested from the laboratory.

To monitor for systematic differences between original and replicate measurements, the proportion of non-zero differences which are positive is monitored. With no systematic trend, this proportion should be one-half. A sign test is done to test for significant differences, and significant differences which persist over several months are pointed out to the laboratory. Means and percentiles of these differences are also presented.

Before any analysis is done on the QC replicate pairs, the data are screened for possible mismatches or "strange" observations. For each biospecimen, the mean and standard deviation of the difference between repeat and original pairs are used to determine acceptable intervals.

6. ANTHROPOMETRY

6.1. Anthropometry Procedures

Anthropometry is performed with the participants wearing underwear under a scrub suit or examination gown. The measurements include standing height (not done at home or long-term care facility examinations), body weight, and waist and hip girth. Weight and height are measured without shoes. Important quality assurance/control measures include clear and detailed protocols for each measure, training and certification, instrument checks, replicate measurements, observation of technicians by a supervisor, and a periodic quality review of study data by the QCC.

6.2. Training and Certification

All data collectors taking anthropometric measurements must be certified by successfully completing training requirements. Training and practice sessions will be conducted prior to certification. An examiner who attends the central training and passes certification criteria can be train and certify other examiners at the field center. Certification testing requires a minimum of 5 practice subjects be measured by both the expert trainer and the trainee. Agreement between the expert and the trainer must be within 0.5 cm for height, 0.5 kg for weight, and 2 cm for hip and waist measurements among 4 of the 5 subjects.

6.3. Observation of Anthropometry Measurement

Technicians are observed by the clinic coordinator twice monthly for the first month and then quarterly to ensure standardization. The Checklist for Observation of Anthropometry Measurements (Appendix 3) is used to document these observations and deviations from the protocol are reviewed with the technicians. The observations are also summarized quarterly on the Summary of Observation and Equipment Checklists (Appendix 1). A minimum of 6 procedures every month is required in order to maintain certification. Local re-training sessions are scheduled when a lack of standardization (e.g., technicians who fail to meet the certification criteria described above) is observed among the technicians.

6.4. Maintenance of Equipment

Anthropometry equipment is calibrated frequently and results are recorded on an Anthropometry Equipment Calibration Log (Appendix 9). Scales are zero balanced daily and calibrated weekly, or when moved. Place the 10 kg calibrated weights on the scale and read the result when the digital display has stabilized. The values should be within 1.5 kg of the expected weight. If it weighs outside this range, notify the clinic coordinator to have the scale recalibrated by the manufacturer or by the appropriate institution personnel. These equipment checks may be done by any certified anthropometry technician. Quarterly, the equipment logs are summarized onto the Summary of Observation and Equipment Checklist (Appendix 1), which is then sent to the Coordinating Center. Copies of the equipment logs may be requested by the Coordinating Center.

6.5. Random Replicate Measurements

Five percent of participants will be randomly selected to have anthropometry measurements repeated by a different technician. The steps in the random selection and repeat measurement process are:

1) Field center supervisors will select one participant per week to have repeat anthropometry measurements. The Coordinating Center will provide each supervisor a

random number for each week[1] of the month which will correspond to the participant for that week that should have the repeat anthropometry measurements. For example:

	Week 1	Week 2	Week 3	Week 4	Week 5
July	5	2	8	12	1
August	4	5	9	1	9
September	5	3	1	14	3
October	12	10	8	3	7
November	7	12	8	1	7
December	5	15	5	1	6
January	7	11	8	9	14
February	3	2	10	6	6
March	7	1	11	9	14
April	1	2	4	5	12
May	4	5	9	6	3
June	6	3	5	7	2

Using the random participant table above (this is just an example table each field center will be sent their own table), for the week beginning July 18 (week 3 of July) the supervisor would select the eighth participant scheduled for that week to have the repeat measurements.

When using the random participant table consider each week to begin on a Monday. If the month changes during the middle of a week, that entire week is considered to be part of the month that Monday fell on. If there is no week 5 in a month ignore that column.

In the event that your center will not measure enough participants in a week to reach the selected participant (e.g. selected participant is #15, but you only have 14 participants scheduled for the week), select the first participant on the last day of the week for the repeat measurement.

2) The technician performing the initial measurements should not be made aware that a repeat is to be done until after the initial measurement is complete.

3) The repeat measurements should be done as soon as they can be fit in to the participant's and technician's schedules. When more than one trained technician is available, the repeat measurements should be assignment randomly to one of the certified technicians, say, by coin toss.

4) The technician who repeats the measurements completes a new or second occurrence of the Anthropometry form, without looking at the measurement determined by the first technician. Instructions on how to key a second occurrence of a form are available on the ARIC website under TRAINING --- DMS. If you have questions please call the Help Desk.

[1] Starting from 2/1/2013, Anthropometry QC repeats that are currently done weekly have been converted to monthly

Inter-technician agreement is analyzed by the QCC and serves as a criterion for recertification. Retraining sessions are scheduled at the request of the Quality Control Committee when a lack of standardization is observed among the technicians.

7. SITTING BLOOD PRESSURE

The OMRON HEM-907XL sphygmomanometer is used to measure seated blood pressure. The technician explains the procedure to the participant, measures arm circumference, wraps the arm with the correct cuff, the participant sits quietly for 5 minutes, and then records the average of the three readings. Important elements in quality assurance are training and certification programs, observation of data collection by the study coordinator, quarterly simultaneous blood pressure measurements by the technician and the study coordinator, and standard equipment maintenance procedures performed and summarized quarterly onto the Summary of Observation and Equipment Checklist (Appendix 1) and sent to the Coordinating Center. We will also monitor the distribution of readings from the OMRON to look for any irregularities.

7.1. Training and Certification

Blood pressure technicians are trained and certified at a central training session or at local field centers by a certified technician prior to participant recruitment. Certification results from training of new staff at the field centers are submitted using a Certification Request Form (Appendix 14) to the CC to document certification status.

Certification for sitting blood pressure requires the trainer to observe the trainee performing blood pressure measurements on 3 volunteers to look for adherence to protocol procedures. Results are summarized onto the Checklist for Observation of Blood Pressure and ABI/PWV Measurement (Appendix 4).

7.2. Observation of Blood Pressure Measurement

Quarterly, the blood pressure supervisor observes each technician responsible for taking blood pressure and ABI/PWV measurements using the Checklist for Observation of Blood Pressure and ABI/PWV Measurement (Appendix 4).

7.3. Maintenance of Equipment

1) Availability of all sizes of cuffs: The blood pressure supervisor makes certain that the field center always has the full range of blood pressure cuffs available at each blood pressure station. Field center staff report immediately to the supervisor if they cannot find all cuff sizes at the station.

2) OMRON sphygmomanometer: Each OMRON unit is checked every 3 months as described in Manual 2. The results of the calibration checks are recorded on the OMRON calibration log (together with the unit number, the date and the technician ID) and sent to the Coordinating Center for inclusion in the quality control reports. A sample copy of the maintenance and calibration log is found in Appendix 13.

8. ANKLE-BRACHIAL INDEX (ABI)/PULSE WAVE VELOCITY (PWV)

The OMRON VP-1000plus monitor is used to measure ABI and pulse wave velocity (an index of arterial stiffness). The participant is asked to lie supine, with arms and legs (to mid-calf) bared, on a comfortable horizontal examination table. The appropriate cuff size is selected for collection of the arm and ankle pressures. These may be different sizes. The participant lies supine for 5 minutes as the technician attaches the arm and ankle blood pressure cuffs, ECG clips, and PCG, femoral and carotid sensors. Then the technician begins the automated process of measuring systolic arterial pressures and pulse wave velocity.

Important elements in quality assurance are training and certification, observation of data collection by the study coordinator, and quarterly replicate measurements by the technician and the study coordinator.

8.1. Training and Certification

Technicians responsible for obtaining ABI and PWV measurements are trained and certified at a central training session or at local field centers by a certified technician. Certification results from training of new staff at the field centers are submitted using a Certification Request Form (Appendix 14) to the CC to document certification status.

"Stage I certification" for ABI/PWV requires submission of data and documentation (CSV and PDF files) on 10 volunteers to the lead trainer (Dr. Tanaka) via email. This level of certification is sufficient to perform pilot study measurements. Final certification requires the field center ABI/PWV supervisor to observe the trainee performing ABI/PWV measurements on 2 volunteers to look for adherence to protocol procedures.

8.2. Observation of ABI/PWV Measurements

Quarterly, the ABI/PWV supervisor observes each technician responsible for taking ABI/PWV measurements using the checklist given in Appendix 4. In addition, measurements on 2 volunteers are taken by both the supervisor and the technician and recorded. Only a single measurement is taken by the supervisor and the technician on each volunteer. Systolic blood pressures between the supervisor and technician should agree within 8 mmHg at each site and the carotid-femoral PWV should agree within 150 cm/sec. At the end of the observation the measurements should be documented on the checklist given in QC Replicate ABI and PWV Measurements (Appendix 8).

8.3. Maintenance of Equipment

1) Availability of all sizes of cuffs: The ABI/PWV supervisor(s) makes certain that the field center always has the full range of blood pressure cuffs available at the ABI/PWV station. Field center staff report immediately to the supervisor if they cannot find all cuff sizes at the station.

2) OMROM unit: Each OMRON unit is checked every month as described in Manual 2. The results of the calibration checks are recorded in Appendix 1.

9. ECG DETERMINATION

9.1. Training and Certification

All ECG technicians must go through the certification process before they are allowed to acquire study ECGs. Each technician must acquire 3 good quality grade ECGs and successfully transmit them to the ECG Reading Center. The 3 ECGs should be performed on 3 different volunteers or on one volunteer provided that there is at least 30 minutes between each ECG**.** Recertification process (required annually) is the same as the certification process. Once quality has been checked at the ECG Reading Center a certificate will be issued to successful technicians.

9.2. Monitoring Quality Grades

The ECG Reading Centre will evaluate and rank the ECG quality through an automated system with visual confirmation of the results if needed. There are 5 grades from 1 to 5. The best grade is 1 and the worst is 5. Generally, grades 1 and 2 are difficult to separate visually and they are considered good. Grades 3 and 4 are given to ECGs that have correctable problems (i.e., the ECG problems could be adjusted for on reading them). Grade 5 ECGs are given for ECGs that have major problems which make it impossible to read them. Monthly, the ECG Reading Center will compile a QC report for the QC Committee summarizing the distribution of quality grades, by technician.

10. BIOSPECIMEN COLLECTION AND PROCESSING

10.1. Blood Collection and Processing

At the time of the telephone contact, participants are requested to fast for 8 hours before field center visit unless they are diabetics taking insulin or have other medical reasons that make fasting inadvisable. The specific steps to be taken in blood drawing and processing are described in Manual 2. Blood samples are either shipped refrigerated on the same day as collection or frozen at -70^{o}C for weekly shipment to the Laboratories. All shipments to the Laboratories are made by courier or overnight delivery services. These steps are performed by technicians trained in the ARIC protocol and certified to have adequately mastered its details.

The first step in quality assurance for blood drawing consists in the training and certification process. Other steps include maintaining logs of equipment checks, observation of technicians (by other technicians and by CC staff on monitoring visits) as they go through the sequence of steps in blood drawing and processing; review of the condition of samples received at central laboratories for problems in shipment; and periodic analysis of the study data for participant compliance with fasting and for signs of problems in drawing or processing, such as hemolysis or delays in completing processing.

Quarterly, the field center supervisor observes each technician responsible for collection, processing, and shipping of the bio-specimens using the checklist given in Appendix 5. These observations are summarized quarterly on the Summary of Observation and Equipment Checklists (Appendix 1).

10.2. Training and Certification

To be certified, technicians complete a central training taught by certified laboratory staff which includes bio-specimen (blood, urine) collection, processing, packaging and shipping as well as quality control measures such as phantom specimens and blind replicate matching. Each technician must complete the training and pass both written and practical exams before becoming certified for the ARIC study. Certification requirements for personnel who do not attend the centralized training are:

- Collection, processing, and shipping specimens for 3 volunteers under the supervision of the certified lead technician at the field center, and
- Completion and submission to the CC of the written exam (Appendix 11)

Those learning phlebotomy must also conform to their own institution's requirements for certification in this area. Once certified, each technician should draw and process at least once per week to maintain their certification status.

10.3. Maintenance of Equipment

Each field center performs daily temperature checks on the refrigerators, freezers and the refrigerated centrifuge as well as the rooms in which these are located. The actual speed of the centrifuge is checked and recorded annually with a tachometer. The results of these checks are recorded on the Daily Centrifuge, Freezer, Refrigerator and Room Temperature Log (Appendix 10) kept at the blood processing station, and are summarized onto the Summary of Observation and Equipment Checklist (Appendix 1) quarterly and sent to the Coordinating Center.

In addition, each technician is responsible for maintaining his/her pipettes for blood processing. Certificates should be purchased with each pipette and filed. Pipettes should be calibrated and cleaned professionally on an annual basis. Monthly calibrations can also be done professionally.

10.4. Monitoring by the Central Laboratory

The Laboratories reviews the drawing and processing time, as recorded on the Biospecimen Collection Form. If there are extreme values that raise questions about the validity of laboratory

results, the field center is alerted to the problem. If a value is considered suspicious or an "outlier", the Biospecimen Collection Form is reviewed for any collection/processing discrepancies, and if there are concerns related to the collection/processing time the field center is notified by the lab. Monitoring is described in more details in the laboratory manual.

10.5. Packing Samples for Shipment to the Laboratories

All vials of blood samples as well as the plastic bags in which the samples for a given participant are packed for shipment to the laboratories are labeled with the laboratory ID. To avoid delays in transit to the laboratories which might cause samples to be warmed or thawed in shipping, all samples are shipped by an overnight delivery service. One tube is shipped to the Laboratories the same day as it is collected. All frozen plasma, sera, packed cells, urine, and Paxgene tubes collected and stored within the last work week are shipped to the Laboratories on Monday with the exception of Quality Control aliquots, as discussed in the Quality Control section below. Samples can be shipped on Tuesday if the Field Center is closed on Monday, but the contact person at the Laboratories must be notified that the shipment will arrive one day later than usual.

A shipping list is enclosed with each shipment to the Laboratories giving the IDs for all sets of samples that are enclosed (see Manual 7). The person unpacking these samples at the Laboratories verifies that the IDs on the vials match the ID on the plastic bag and checks both against the shipping list. If any discrepancies are detected, the Laboratories contact the field center to resolve the problem.

For samples that are shipped weekly to the Laboratories, the staff receiving the shipment will monitor that the shipment was delivered overnight. If delays are found, the Laboratory notifies the field center to alert them. If the problem persists, and fault lies with the delivery service, the field center will change to an alternate delivery service. If delays are due to protocol violations at the field center, the CC is contacted in addition to the field center.

Blood vials shipped to the Laboratories must be packed securely to avoid both breakage and warming. Full instructions for packing samples are specified in Manual 7. The laboratories monitor the arrival condition of the samples sent from each field center on the Shipping Form. If problems are encountered, the laboratories notify the Field Centers involved. If a pattern of sample damage becomes apparent that suggests a need to modify the materials used to ship samples (e.g., excessive leakage of a certain type of vial) or how samples are packed, the QCC should be alerted to ensure appropriate action is taken.

10.6. Urine Collection and Processing

After a participant is greeted at the clinic, he/she is asked to provide a urine specimen at the participant's convenience. When the participant is ready to void, a specimen cup (labeled with the laboratory ID) is provided, and the participant is instructed to fill the cup if possible. If the sample is insufficient for processing, the participant is requested to void again in a clean container prior to leaving the field center. Prior to processing, the technician records on the Biospecimen Collection Form whether a urine sample was obtained, the collection time of the initial (if more than one) urine sample, and adequacy of volume.

10.7. Replicate Blood and Urine Specimens

Repeat samples are collected for 10 blood specimens and a urine sample. A replicate sample is obtained by either drawing 1 to 4 additional tube(s) of blood, or by dividing a urine sample into separate containers. The replicate samples are then processed using the same method as for the original samples. Over the entire study, replicate samples will be obtained on 5% of all specimens (n = 433 if the target of 8660 participants are examined). 5 participants will be needed to provide a complete set of QC replicate specimens (10 tubes of blood and 1 urine specimen) for a phantom ID. Thus, 25% of participants (n=2165, or 5×433) will contribute to the pool of replicate specimens. During the first year of the study all participants will contribute one or more QC

replicate samples. After this initial period, replicate sample(s) will be collected from the first participant seen in the clinic each day. Ongoing monitoring of the quality of replicate biospecimen data will be conducted by the Coordinating Center and adjustments to the number of participants needing to provide replicate data will be made as needed. The extra specimen(s) will be labeled with a laboratory ID corresponding to a phantom participant ID. Eventually, a single phantom ID will have a complete collection of blood, and urine, contributed by several participants. Each month, the Coordinating Center reviews the number of QC phantom forms completed to ensure the procedures for obtaining replicate samples is being followed.

A replicate urine sample requires that the participant provide at least 15 mL of urine. A total of 12 mL are divided among eight 2.0 mL vials for determination of creatinine and albumin levels by the Laboratories and storage of 6 aliquots are reserved for future testing (see Manual 7 for details). To reduce the chance of error in linking the real participant ID with the phantom ID, as soon as replicate sample is obtained the real participant ID label is affixed to the appropriate space on the Phantom Form.

11. BIOSPECIMEN PROCESSING AT THE LABORATORIES

11.1. Procedures for Laboratories Analyte Determinations

Blood samples are collected and processed at the field centers for shipment to a single laboratory for analysis of several analytical tests. In the present section, the emphasis is on quality assurance in the central laboratories, beginning with the receipt of samples. This section differs from other chapters of this manual in being more of a general overview and summary of quality assurance measures. These matters receive careful and detailed discussion in the laboratories manual, which covers procedures for: receiving samples and storing them at a proper temperature until analysis; schedules of equipment maintenance; storage and handling of reagents, calibration standards, and quality control materials; internal and external quality control programs; and transcription and reporting of measurement results. This section of the manual supplements the laboratory manual by its discussion of reporting on the effectiveness of laboratory quality assurance procedures and of the utilization for quality control of (1) analyses of study data and (2) blind replicate samples from participants sent to the laboratory.

11.2. Receiving Samples at Laboratory

At the Laboratories, a record in the local data base is created using the laboratory ID number for each specimen when it arrives. It is important in handling ARIC frozen blood samples to avoid any unnecessary exposure to room temperature. Clear procedures for unpacking specimens upon arrival are set out in the Laboratories' protocol to minimize such exposure. While awaiting analysis, specimens are to be kept in storage at -70^0C. The laboratory has provisions for (1) prompt detection of power failure or of failure of freezer to maintain the proper temperature, including both local alarms and alarm signals to a central security office that will notify appropriate laboratory personnel if a problem develops after hours; (2) back-up power supplies in the event of power failure; (3) plans for the use of dry ice to maintain the sample temperature until any problems with the freezer can be repaired.

The probable stability of different analytes in frozen storage has been assessed and standards set for how soon analyses will be performed after the arrival of specimens at the laboratory.

11.3. Maintenance Procedures at the Laboratories

Maintenance procedures for laboratory equipment are fully specified in the laboratory protocols or in manufacturers' manuals referenced in the protocols. Technicians are fully instructed in these procedures.

A regular schedule is set up for routine maintenance procedures, with logbooks kept on their performance. The laboratory supervisors review these logs on a regular basis to verify that proper

maintenance procedures are being carried out according to the schedule set and that any special maintenance procedures needed are carried out.

The laboratory protocol fully specifies the reagents used, the sources from which they are procured, and the procedures used to prepare and store reagents to guarantee the stability of the reagent and the accuracy of the assay. The laboratory protocol also fully specifies the sources of calibration standards and quality control materials, the procedures used to prepare and store calibration standards and quality control materials, to guarantee the stability of the material and the accuracy of the assay. To maintain the comparability of measurements using new and old calibration standards and controls, an overlap period is carried out, during which concentration values for the new standard are determined using the standard which is being replaced.

11.4. Internal Quality Control Pools

The Laboratories maintains an internal quality control program involving the analysis of multiple samples from quality control pools in each analysis run in which ARIC study samples are analyzed. Results on these samples are used to decide whether the measurement process is in control and whether the results on the study samples will be accepted or whether the measurements should be repeated after taking corrective action. Quarterly, the Laboratories provides a summary of the internal quality control results to the Coordinating Center, including the following information for each assay: (1) monthly summary statistics (n, mean, and standard deviation) on all quality control pools, including new pools being overlapped to replace established QC pools; (2) summaries of any unusual problems or conditions noted. The Coordinating Center reviews these reports for evidence of trends with time in results on these pools.

Results on analyses of quality control pools are analyzed by the Coordinating Center for trends over time that may represent either (1) shifts in measurement or (2) changes over time in the concentration of the analyte in a given pool. To determine which of these is the case, trends in a given pool can be compared with (1) trends in other pools (if any) used to control analyses of a given analyte; (2) trends in differences on measurements of samples from quality control phantom participant duplicates which are repeated several months apart; (3) trends in the study data. If there is evidence of changes in the concentration of a control pool over time, it should be replaced.

11.5. External Quality Control

For many of the assays performed in the ARIC study, the Laboratories participates in various standardization or certification programs run by outside agencies, such as the College of American Pathologists or the CDC Lipid Standardization Program. The Laboratories should continue to maintain acceptable results in these programs and promptly provide the Coordinating Center with copies of any reports on their performance generated by these programs. Should any of the results achieved in these programs appear problematic, they are reviewed by the Coordinating Center and the Laboratory Committee together with other quality control information on the assay in question to determine what action is appropriate.

12. Removed, no longer applicable

13. SPIROMETRY

13.1. Training and Certification

Certification following the central training for pulmonary function testing includes a written examination (50 multiple choice questions), calculation of spirometry results from a spirogram (25 points), and a practical demonstration of skills including leak and calibration checks, cleaning, and testing of a volunteer (25 points). A passing score of at least 75 points is necessary for certification.

Certification of new technicians after the initial central training sessions may be performed by a technician who was centrally trained. The written exam will be administered locally, and the first 20 pulmonary function tests performed will be observed by a certified pulmonary function technician and found to be satisfactory before the new technician is certified. To retain certification, technicians must test at least ten participants each month.

13.2. Maintenance of Equipment

Each field center must check the spirometer for leak and perform calibration checks on a daily basis. The results of these checks are recorded on the Daily Spirometer Leak and Volume Check Log (Appendix 11) kept at the pulmonary function station, and are summarized onto the Summary of Observation and Equipment Checklist (Appendix 1) quarterly and sent to the Coordinating Center.

13.3. QC Reports from Reading Center

Monthly, the Reading Center will compile a QC report for the QC Committee summarizing the following:

- average number of acceptable maneuvers, by technician
- percentage of subjects with non-repeatable tests results, by technician
- percentage of subjects with less than 3 acceptable maneuvers, by technician
- percentage of subject with less than 2-acceptable maneuvers, by technician
- average FVC quality score, by technician
- average FEV1 quality score, by technician.

The report will be identify technicians by ID and not be technician name.

14. Removed, no longer applicable

15. Removed, no longer applicable

16. PARTICIPANT INTERVIEW

Establishing quality control for interviews is critical in ascertaining whether interviews are conducted according to protocol. If all interviews are not conducted according to protocol, then the information that one interviewer obtains from a participant may be different from the information another interviewer might have obtained from the same participant. Audio recording and observation are used to monitor the quality of the data that interviewers collected as described below.

16.1. Certification on Interviewing Techniques

Requirements for certification or re-certification on general interviewing techniques include:

- Attending central training, or reviewing a presentation on General Interviewing Techniques (on study website).
- Successfully completing a short written exam on material, for initial certification. Completed written exams are sent to the CC for evaluation.

16.2. Observation of Interviewing Technique

Quarterly, the field center supervisor will observe each interviewer twice while the interview is in progress. Interviewers will not know in advance which interviews will be monitored for quality control purposes. The supervisor will rate the interviewer's performance using standard criteria from the Checklist for Observation Interviewing Techniques (Appendix 2) and give the interviewer immediate feedback. These interviews should be summarized on the Summary of Observation and Equipment Checklists (Appendix 1). Complete the Checklist for Observation Interviewing Techniques (OIT).

16.3. Recording of Interview

For a one week period every month, all interviews (**Table 16.3.1**) are audio recorded with a handheld digital recorder and recordings tracked on an inventory list. Prior to recording, participants should be reminded that interviews are used for quality control purposes and the information on the audiotape would be kept confidential and destroyed after review. Interview components to be recorded separately are the General Interview, and the Neurocognitive test battery (see Chapter 17).

Table 16.3.1. Interview components to be recorded

Component	Form Acronym	Interview component
General interview	1. AQC	Access and Quality of Care
	2. MHX	Medical History
	3. MSR	Medication Survey
	4. PAC	Physical Activity
	5. PHX	Personal History
	6. PRO	PROMIS – anxiety
	7. SFE	SF-12 Health Survey
	8. RSE	Respiratory Symptoms
Neurocognitive	9. MME	Mini-Mental State Exam
	10. NCS	Neurocognitive test battery
Neurologic	11. CDI	CDR-Informant Interview
	12. CDP	CDR-Subject Interview

Instruction for recording on OLYMPUS DM-520 Digital Voice Recorder

The Olympus DM-520 recorder uses rechargeable batteries that allow at least 24 hours of use in recording mode. The batteries can be charged by connecting the device into a computer USB port using the cable provided. By default, the DM-520 records at 100% volume level to prevent accidentally recording with the volume set too low. Microphone sensitivity can be adjusted via the MIC SENSE option in the recorder's menu (see next paragraph for instructions on changing device settings).

Record using MP3 (MPEG Audio Layer-3) format at a bit rate of 192 kbps. Approximately 46 hours of audio can be recorded at this setting. A microSD card (up to 16 GB) can be purchased and installed into side slot to increase this capacity. The devices should be preset with these settings, but if you need to modify: press the **MENU** button for 1 second or longer, then press **–** button to get to the Rec Menu, and then press the **OK** button. At the Rec Menu, press the **–** button to get to Rec Mode and then press the **OK** button. Choose MP3 and 192 kbps.

Step 1: Turn the recorder on. If you are not at the Home Screen, Press the **Home** button and select **Recorder**.

There are 5 possible recording folders that each hold up to 999 files. For ease of finding files, each interviewer should be assigned specific folder for use throughout the study. Note, however, that more than one interviewer can be assigned to the same folder.

Step 2: Select the staff-assigned recording folder using **+** or **–** button.

Step 3: Press the **REC** ● button on side of recorder to start recording. The recording indicator light glows and [●] appears on the display.

Step 4: The interviewer dictates 4 items before beginning the interview:

- Name and Staff Code number
- Interview component (General Interview, Neurocognitive, Neurologic)
- Participant ID number
- Date

Step 5: If recording the General Interview component, Press the **SCENE** button at the end of each questionnaire to create and index marks, or digital tags, to allow the user to easily skip forward or backwards in a single file to listen to a particular questionnaire.

Step 6: Press **STOP** button on side of recorder to stop recording.

Separate digital files are used to record each interview component listed in **Table 16.3.1** for a given participant. The exception may be for the General Interview if multiple interviewers administer the set of questionnaires to a participant.

Instruction for download digital recordings to your computer.

Step 1: Turn the recorder on. If you are not at the Home Screen, Press the **Home** button and select **Recorder**.

Step 2: Connect the USB connection cable to the USB port of your computer, then connect the USB cable to the bottom of the recorder.

Once connected, Windows Autoplay feature will give you the option to Open Folder to View Files using Windows Explorer. Once you select this option, you will be taken to the device drive name, usually DM_520 (D:). If you do not get this option, simply open My Computer to see the device drive.

Step 3: Select the **Recorder** folder. Copy folders A-E the file to a known location on your computer. Rename the files using naming convention that identifies the staff ID of the interviewer,

the date of the interview and the content. The date is specified in YYYY-MM-DD format so that it is easy to find fill when sorted alphabetically. The label/name of the recorded file(s) should look like:

File name	Center+Staff ID	Date (YYYY/MM/DD)
F123_2011-08-20_General Interview	F123_	2011-08-20
M313_2011-08-20_Neurocognitive	M313_	2011-08-20
W429_2011-08-20_Neurologic	W429_	2011-08-20

Step 4: Delete folders A-E in the Windows Explorer window. Note these folders will get recreated on the recorder.

Step 5: Leave your recorder connected until fully charged. When you want to disconnect the device, click on the "Safely Remove Hardware" icon of your task bar. From this dialog you can click on the device you want to remove, and press **Stop**. Once Windows is done with it, you can then remove the device.

One recorded participant interview file **per technician** should be randomly selected and reviewed by the interview supervisor each month, checking for adherence to protocol, using the Observation of Interview Technique form (OIT form; Appendix 2) and entered into the DMS. These reviews should be summarized on the Summary of Observation and Equipment Checks (Appendix 1).

Round-robin review: Quarterly, the coordinating center will randomly select two participant interview recordings from each field center for review by another field center. The selected interview recordings will be available for download from the Clinic Audio portion of the ARIC website. Notes about any inconsistencies in implementing the interview protocol should be documented on the OIT form. Once the OIT forms are complete for the 2 round-robin recordings, create a PDF document of your OIT forms and email the forms to the interview supervisor at the field center you evaluated. Please copy the coordinating center on the email, so that the coordinating center also has a record of this. The interview supervisors can then provide appropriate feedback to the technicians who were evaluated.

The CC will run periodic reports to see if there are staff who have not been part of the monthly recording and quarterly reviews. In this case, the CC and the Field Center will work together in order to insure that all staff are recorded during the next quarterly review.

Table 16.3.2 -Schedule for exchange of audio tapes between field centers:

Exchange	Originating Field Center	Reviewing Field Center
#1	Jackson	Forsyth
	Forsyth	Jackson
	Minnesota	Washington
	Washington	Minnesota
#2	Jackson	Minnesota
	Forsyth	Washington
	Minnesota	Jackson
	Washington	Forsyth
#3	Jackson	Washington
	Forsyth	Minnesota
	Minnesota	Forsyth
	Washington	Jackson
#4	Jackson	Washington
	Forsyth	Jackson
	Minnesota	Forsyth
	Washington	Minnesota

16.4. Instructions for Uploading Audio Files for Review

Digital audio recordings are shared between sites by uploading them to the "Secure" portion of the study website under Exam5 → Clinic Audio. Each field center receives a username and password to access the "Clinic Audio" link.

TO UPLOAD AUDIO FILES

The digital recordings are named following a standard naming convention: field center letter, staff ID, date (in YYYY-MM-DD format) and the interview component as described in the previous section and shown here: ***W406_2010-10-23_Neurocognitive***

Step 1: Go to Study website (http://www.cscc.unc.edu/aric/) and enter the "Secure" area. Select Exam5 → Clinic Audio. You will be asked for your username and password.

Step 2: Select the "Manage Files" link in the top right of the screen.

Step 3: In Clinic Audio line, Select "Upload"

Step 4: Enter information required by fields as follows:

a. *Committee or Working Group*: Select the appropriate committee association among the following options:
"QC - General Interview"
"QC - Neurologic"
"QC - Neurocognitive"

b. *Date*: Put the date included in the file-name.

c. *Title*: Type the name of the file (or copy the filename after loading)

d. Leave the questions about whether these are *"draft"* or *"archival Clinic Audio files"* blank.

e. *Send this file*: Browse for the audio file you want to upload.

f. *Type of first file:* Select **MP3** from the list.

g. *Send this file*: Browse for the file that contains forms that you want to upload.

h. *Type of second file:* Select **PDF** from the list.

i. Select "Upload Clinic Audio" to finalize the upload.

Step 5: Verify that your files have been uploaded by going back to the Exam5 → Clinic Audio

TO LISTEN TO AUDIO FILES

Each reviewer is provided with a common username/password with "read" access only to be able to listen to the audio recordings.

1. Login to the Exam5 → Clinic Audio area
2. Click on the music icon for the digital recording you wish to listen to. Windows Media player should open.
3. Enter your login information / password and listen to the audio file.
4. Click on the PDF icon to view the documentation associated with the audio file.

16.5. Analysis of Study Data

Study data will be analyzed periodically to assess frequency of interviews for each interviewer, for each questionnaire. Minimum levels will be set to allow for continued certification. Levels of missing data will also be assessed by interviewer, and maximum acceptable levels set.

17. COGNITIVE FUNCTION

A battery of neurocognitive tests that tap global mental status (MMSE) and five cognitive domains will be administered: memory, executive function, language, visuospatial, and attention.

17.1. Training and Certification

Prior to the examination, examiners will be trained centrally to a common level of proficiency in the administration and scoring of the neurocognitive measures. Following central training, examiners will submit 3 audio-taped neurocognitive assessments (Mini-mental State Exam [MME], and the Neurocognitive Test Battery) and associated paper forms to a designated investigator on the Neurocognitive Committee for review. Certification assessments should not be performed on ARIC participants. Examiner certification for the neurocognitive exam is achieved by review and approval of performance by the neurocognitive expert.

The field center lead examiner or study coordinator is responsible for the basic training of all new field center examiners. Following basic training and approval by the field center study coordinator, new examiners will submit 3 audio-taped neurocognitive assessments for review and approval.

Maintaining proficiency in the administration of the neurocognitive measures requires regular exposure to the protocol. In order to maintain certification, examiners will administer the neurocognitive measures at least once per month.

17.2. Audio-recording of Neurocognitive Component of Interview

During the first 6 months of the study, 2 audiotaped sessions and associated documentation for each interviewer will be reviewed by a neurocognitive expert to ensure appropriate pacing, adherence to protocol, and accuracy of recorded responses. Notes about any inconsistencies will be relayed to the study coordinator. After the initial 6 month period, the neurocognitive expert will review one neurocognitive session per interviewer, noting deviations from the standardized protocol. For new hires, continue with 2 tapes per month for the first 3 months after certification (then reduce to 1/month). General feedback that pertains to all examiners will be provided on QCC conference calls. These calls will also provide an opportunity to discuss and problem-solve various exam issues that may arise.

18. STAGE II EXAM (NEUROLOGIC EXAM AND CDR)

18.1. Training and Certification

Study nurses are trained and certified at a central training session or at a local field centers by certified technicians prior to administering the neurologic exam on a participant. Training involves instruction on general interviewing techniques, review of each exam component (forms and QxQ instructions, the Neurologic Exam manual, and discussion of challenges to data fidelity.

Trainees must complete the online training and certification for the NIH Stroke Scale (http://learn.heart.org/ihtml/application/student/interface.heart2/nihss.html), even though the entire test is not being used (the neurologic exam includes most components of the NIHSS, however). During the central training, practice exams will be conducted in the presence of the lead neurologist trainer who will provide feedback to reach criterion performance. Following central training, 3 video-taped recordings of the Physical and Neurological Exam (PNE) and Unified Parkinson's Disease Rating Scale (UPR) per trainee will be reviewed by a study neurologist.

Online training and certification for the CDR is required (www.adrc.wustl.edu). After selecting "Begin CDR Training", the user will be asked to register after which they will have access to 9 videos, each approximately 30 minutes in duration. The trainee should plan to review these videos over several days. Two audio-taped recordings of the CDR interviews (Informant and Subject interviews) and associated documentation (CRD-informant, CDR-subject, and CDR-Summary forms) per trainee, will be reviewed by a study neurologist for certification.

18.2. Audio-recording of Neurologic Exam Interviews

During the first 6 months of the study, each certified examiner should provide 2 audio taped sessions and associated documentation per month. These recordings will be reviewed by a neurocognitive expert to ensure appropriate pacing, adherence to protocol, and accuracy of recorded responses. Notes about any inconsistencies will be relayed to the study coordinator. After the initial 6 month period, the neurocognitive expert will review one neurocognitive session per interviewer, noting deviations from the standardized protocol. For new hires, continue with 2 tapes per month for the first 3 months after certification (then reduce to 1/month). General feedback that pertains to all examiners will be provided on the Study Coordinators or Quality Control Committee conference calls. These calls will also provide an opportunity to discuss and problem-solve various exam issues that may arise.

18.3. Uploading Audio-recordings

Examiners should provide audio recordings and corresponding PDFs of the following testing items:

- Testing packet
- Neurocognitive scoring summary form
- Trails A & B
- Digit Symbol Substitution form
- Incidental Learning form

- Intersecting Pentagons (from the MME)

All of these items may uploaded to the ARIC website under Exam5 – Clinic Audio – Manage Files – Upload.

20. MEDICATION TRANSCRIPTION

20.1. Training and Certification

The Medication Survey (MSR) records all prescription and over-the-counter medications, including cold and allergy medications, vitamins, herbals or supplements used by participants in the four weeks preceding their interviews. The survey ascertains usage of up to 25 medications. Ascertainment includes scanning of twelve-digit Universal Product Code (UPC) bar code symbols when available. Medical Therapeutic Classification (coding) is automated where possible. Otherwise, manual coding is centralized (performed only in the Coordinating Center).

Interviewers are centrally trained and when certified, assume responsibility for providing local staff training in medication scanning / transcription.

Interviewers are certified to administer the MSR by attending the central training, completing the scanning / transcription exercise designed by the central trainer, and passing with a score of ≥ 80%. New staff unable to attend central training are eligible for remote certification when:

- The candidate is trained by the lead certified interviewer at the corresponding Field Center.
- The Coordinating Center has sent to the Study Coordinator a mock medication bag with detailed instructions for the candidate's certification.
- The candidate independently completes an MSR and enters it into the Data Management System.
- The Study Coordinator returns the medication bag scenario (identifying its contents) and a printout of the completed MSR for to the Coordinating Center for evaluation.

The candidate passes with a score of ≥ 80%.

21. Heart Failure Oriented Physical Examination

21.1. Training and Certification

Certification requires familiarity with the protocol and equipment, and successful performance of the two components of the physical examination on five volunteers, inclusive of data entry and transfer to the lead trainer (Dr. Loehr). After initial training and certification, continued education is based on performance indicators monitored by the ARIC Quality Control Committee. Re-training / re-certification may be required at the request of this committee.

22. Physical Function

The measures of physical function includes the Short Physical Performance Battery (SBBP) which consists of chair stands, a regular paced 4 meter walk, and balance tests, as well as grip strength.

22.1 Training and Certification

A training video for the SPPB is available online. Instructions for downloading the video ("Instructions – " as a Word document) and the demonstration video ("CD (Download and Execute – (.exe)) can be found at http://www.grc.nia.nih.gov/branches/ledb/sppb/index.htm. This video should be reviewed prior to initial training session and every 6 months. Interviewers can be trained centrally or locally. Training includes:

- Review of the manual, form and QxQ instructions

- Practice on other staff or volunteers
- Discussion of problems and questions with local expert
- Review of SPPB training video

Certification will include:

- Complete training requirements
- Administration of physical function exam on two volunteers and observed by lead supervisor to have been completed according to protocol (see QC manual for checklist)
- SBBP times agreeing within ± 0.5 second of lead supervisor for SPPB
- Kilograms agree within ± 2 kilograms of QC officer for grip strength

22.2 Equipment Checks

Weekly calibration checks of the grip strength dynamometer are made by hanging 5 kg and 20 kg (or 10 and 50 lb) weights across the handle using two Velcro straps, one strap on each side of the dynamometer handle, or one wide strap that covers the whole handle. Lift the weights slowly from the floor while they are strapped to the dynamometer handle and record the maximum kilograms registered. The lifting motion should be very slow and smooth, and the weight should remain evenly distributed between the two sides of the handle. Repeat the procedure three times and record each result.

Average the three calibration trials. The dynamometer should be accurate within ± 2 kgs for the average of the three calibration trials. It may be necessary to send the dynamometer to the manufacturer for repair and recalibration. Calibration problems can be caused by dropping the dynamometer or by leaks in the hydraulic system.

22.3 Quality Control

The data collected by each interviewer are periodically reviewed by the Quality Control Committee from quality control analyses performed by the Coordinating Center. Data patterns suggestive of deviations from protocol are brought to the attention of the field center principal investigator and project manager. Observation of the assessments then follows, with discussion of possible remedial actions with staff.

23. Retinal Examination

Digital images of each will be captured into a table mounted laptop computer, archived internally for the site's use, and will also be exported and transmitted over a secure FTP site to the OERC in Madison, Wisconsin, for analysis.

23.1 Training and Certification

Each examiner taking fundus photographs will need to become certified before taking photographs for the study. The initial group of photographers will receive didactic and hands-on training provided by the OERC team. Following the training, each photographer will return home to setup their photography system, practice taking photographs and prepare photographic sets for submission to Tiffany Jan at the OERC for certification. Certification begins with the completion of the Photographer Certification Request Form (see Attachment 3 of Manual 14a. Retinal Photography). This form will be submitted along with images of 10 eyes (5 right eyes and 5 left eyes, F1 and F2 of each) following the study protocol. A photographer is fully certified after submitting satisfactory quality images of 10 eyes taken on non-study volunteers and the Photographer Certification Form is signed by the OERC and sent back to the Coordinating Center.

23.2 Quality Control

Photographers are the first to provide an assessment of photo quality, a big advantage of digital

imaging. This “on the spot” review of images allows for the immediate assessment of image quality and the opportunity to retake the images before the patient leaves the photography area. Additionally, reading center staff will continuously monitor photographic quality throughout the study. Initially all photographs will be reviewed by reading center staff and feedback will be provided to photographers in cases that warrant critique. A telephone call, e-mail or letter will be used detailing problems and suggesting improvements. Once the study is underway and the photographers sufficiently trained, data on photo quality will be generated from the photograph readers’ evaluations of all photographs. In cases where problems with photo quality persist, additional training may be arranged at the Ophthalmic Photography Learning Center (OPLC) located in Madison, Wisconsin.

Appendix 1. Summary of Observation and Equipment Checklists

Instructions: This form should be completed quarterly and sent to the Coordinating Center.

FIELD CENTER ☐☐☐☐☐☐☐☐ DATE: ☐☐/☐☐/☐☐☐☐ (Month / Day / Year)

Quarterly reporting period: Jan-Mar 20☐☐ Apr-Jun 20☐☐ Jul-Sep 20☐☐ Oct-Dec 20☐☐

A. Observation Checklist

		Technician ID	Supervisor ID	Date (mm/dd/yy)
General interview techniques	Cross-site review (Y/N)			
Neurocognitive Interview (review by neurocognitive expert)				
Neurologic Interview (review by neurologic expert)				
Anthropometry				
Sitting blood pressure				
ABI/PWV				

Physical Function			
Biospecimen collection			

B. Equipment Checklist

	Frequency	**No. times assessed**	**No. times within calibration**
Anthropometry			
1) Scale read zero	Daily		
3) Weight scales	Weekly		
Physical Function			
1) Grip strength dynamometer	Weekly		
Biospecimen collection			
1) Refrigerators, freezers, room temp	Daily		
2) Speed of centrifuge	Annually		
3) Pipettes	Annually		
ABI/PWV			
1) Air leakage test	Quarterly		
2) Pressure accuracy test	Quarterly		
Spirometer			
1) Checked for leaks	Daily		
2) Volume checked	Daily		

Comments: _____

_____

Appendix 2. Checklist for Observation of Interviewing Techniques

ID NUMBER: | | | | | | | |

FORM CODE: | O | I | T |

DATE: 09/22/2011
Version 1.0

ADMINISTRATIVE INFORMATION

0a. Completion Date: ☐☐/☐☐/☐☐☐☐ (Month / Day / Year)

0b. Supervisor ID: ☐☐☐

0c. Tech. ID: ☐☐☐

0d. Type of Interview Observed:

AFU/Recruitment	☐
Exam 5	☐

Proficiency in Interview technique	Yes	No	Comments
1. Introduces her/himself at beginning of the interview; thanks participant at the end.	☐	☐	_____
2. Explains purpose of interview when appropriate, e.g., reads introductions or transition statements when included on form.	☐	☐	_____
3. Reads questions exactly as written, stressing time frame and key elements.	☐	☐	_____
4. Demonstrates familiarity with content, flow, definitions, and skip patterns.	☐	☐	_____
5. Uses standardized tone of voice with supportive, non-judgmental statements.	☐	☐	_____
6. Paces interview in response to participant's level of comprehension/comfort.	☐	☐	_____
7. Trains participant in response patterns when appropriate.	☐	☐	_____
8. Refrains from probing except to clarify ambiguous, unclear, untrue, or inconsistent responses.	☐	☐	_____
9. Uses standardized definitions when asked for clarification.	☐	☐	_____
10. Repeats questions stressing portions of question which were misunderstood.	☐	☐	_____
11. Selects appropriate type of probe.	☐	☐	_____
12. Accurately records participant's responses.	☐	☐	_____

Comments: _____

_____

_____

Appendix 3. Checklist for Observation of Anthropometry Measurement

Instructions: This checklist documents observation of anthropometry technicians by supervisors. Quarterly checklists and logs are summarized onto the **Summary of Observation and Equipment Checklists** (Appendix 1).

TECH ID NUMBER: ☐☐☐ SUPERVISOR ID NUMBER: ☐☐☐ DATE: ☐☐/☐☐/☐☐☐☐ (Month / Day / Year)

	Yes	No	Comments
1. Anthropometry is done BEFORE the snack.	____	____	_____
2. If the participant is wearing any nylon hose other than knee highs, the participant is instructed to remove hose.	____	____	_____
3. Participant is wearing light-weight, non-constricting underwear.	____	____	_____
4. Participant is wearing a light clothes or scrub suit.	____	____	_____
5. Participant has removed shoes.	____	____	_____
6. Participant has emptied bladder.	____	____	_____

Standing Height Measurement

1. Procedure is explained to participant.	____	____	_____
2. Participant's spine and heels are placed against the wall.	____	____	_____
3. Participant's eye to ear plane is horizontal [i.e., Frankfort plane].	____	____	_____
4. Measurement is taken with triangle or measuring block.	____	____	_____
5. Data recorded accurately in cm	____	____	_____
6. Technician's measurement of participant height:	_____ cm		
7. Supervisor's measurement of participant height::	_____ cm		

Weight Measurement	**Yes**	**No**	**Comments**
A. Equipment			
1. Scale firm on floor.	____	____	_____
2. 10 kg standard weight available.	____	____	_____
3. Anthropometry Equipment Calibration log up-to-date.	____	____	_____

B. Procedure

1. Participant prepared and procedure explained.	____	____	_____
2. Participant is bare-foot.	____	____	_____
3. Position of participant on center of scale.	____	____	_____
4. Balance achieved.	____	____	_____
5. Recordings completed.	____	____	_____

Technician's measurement of participant weight: _____ kg

Supervisor's measurement of participant weight: _____ kg

Waist Measurement	**Yes**	**No**	**Comments**
1. Procedure is explained to participant.	____	____	_____
2. Subject stands erect, yet relaxed, with weight equally distributed on both feet, and feet together.	____	____	_____
3. Place the tape horizontally at the level of the umbilicus (navel).	____	____	_____
4. Subject takes a normal breath and gently exhales, holding breath in a relaxed manner at the end of exhalation.	____	____	_____
5. Tape is horizontal and snug, but not tight enough to compress tissue. [Invert tape, if needed, to insure reading edge of tape is snug to skin for measurement.]	____	____	_____
6. Reading is recorded to the nearest centimeter, rounding down.	____	____	_____

Technician's measurement of participant waist: _____ cm

Supervisor's measurement of participant waist: _____ cm

Comments: _____

_____

_____

Appendix 4. Checklist for Observation of Blood Pressure and ABI/PWV Measurements

Instructions: This checklist documents observation of technicians certified to perform blood pressure and ankle brachial index (ABI)/pulse wave velocity (PWV) measurement by supervisors. Quarterly checklists and logs are summarized onto the **Summary of Observation and Equipment Checklists** (Appendix 1).

TECH ID NUMBER: ☐☐☐ SUPERVISOR ID NUMBER: ☐☐☐ DATE: ☐☐/☐☐/☐☐☐☐
Month Day Year

Blood Pressure Measurement	Yes	No	Comments
1. Checks function settings on OMRON unit (ENTER, 3 inflations, 30)	_____	_____	_____
2. Checks Mode and P-setting on OMRON unit	_____	_____	_____
3. Makes sure AC adapter for OMRON unit is securely connected (tends disconnect from unit)	_____	_____	_____
4. Checks AC adapter cord and tubing for cracks	_____	_____	_____
5. Cleans all the equipment	_____	_____	_____
6. Allows subject to rest for five full minutes	_____	_____	_____
7. Performs arm measurement and cuff selection properly	_____	_____	_____
8. Identified brachial pulse location properly	_____	_____	_____
9. Proper cuff placement	_____	_____	_____
10. Attaches cuff to monitor	_____	_____	_____
11. Uses proper settings on OMRON unit	_____	_____	_____
12. Turns monitor on with ON/OFF button	_____	_____	_____
13. Sets MODE selector to AVG	_____	_____	_____
14. Sets P-SET knob to AUTO	_____	_____	_____
15. Pushes START button	_____	_____	_____
16. Records 1st, 2nd, 3rd systolic and diastolic BP readings and average heart rate	_____	_____	_____
17. Instructions to participant are clear	_____	_____	_____
18. Holds arm vertically for 5 seconds between readings	_____	_____	_____
19. Informs participant of average readings	_____	_____	_____

Comments: _____

_____

ABI/PWV Measurement	Yes	No	Comments
1. Checks Examination Table for No Tilt			
2. Checks Examination Table for proper length			
3. Inspects arms and ankles for open lesions			
4. Measures arms and legs for correct cuff size			
5. Inspects BP cuffs for cleanliness			
6. Palpates right and left brachial arteries			
7. Wraps cuff around right and left arms			
8. Wraps cuff around right and left ankles			
9. Attaches ECG clips around both wrists			
10. Attaches PCG sensor at right places			
11. Palpates left common femoral artery			
12. Secures femoral sensor			
13. Palpates left common carotid artery			
14. Marks left common carotid artery			
15. Measures arterial path lengths			
16. Inputs arterial length on the machine			
17. Records arterial length on data form			
18. Places carotid sensor			
19. Starts measurements			
20. Removes carotid sensor upon completion			
21. Wait at least 1 minute			
22. Repeats the measurements			
23. Removes all the sensors			
24. Unwraps all 4 BP cuffs			
25. Fills out the Procedure Completion Form			

Comments: _____

_____

_____

Appendix 5. Checklist for Observation of Biospecimen Collection and Processing

Instructions: This checklist documents observation of technicians responsible for biospecimen collection processing and shipping by supervisors. Quarterly checklists and logs are summarized onto the **Summary of Observation and Equipment Checklists** (Appendix 1). Copies of this log may be requested by the CC.

TECH ID NUMBER: ☐☐☐ SUPERVISOR ID NUMBER: ☐☐☐ DATE: ☐☐/☐☐/☐☐☐☐
Month Day Year

Biospecimen Collection	**Satisfactory/ Unsatisfactory**	**Comments**
1. Labels checked	___	_____
2. Participant prepared and procedure explained	___	_____
3. Tourniquet application and release	___	_____
4. Venipuncture technique	___	_____
5. Tube collection sequence	___	_____
6. Inversion technique	___	_____
7. Tube incubation location	___	_____
8. Stasis obtained	___	_____
9. Needle disposal	___	_____
10. Laboratory Collection form completion	___	_____

Biospecimen Processing		
1. Knowledge of centrifuge operation	___	_____
2. Aliquotting supply set-up	___	_____
3. Stage 1 tube spin	___	_____
4. Stage 2 aliquotting	___	_____
5. Stage 3 tube spin and processing	___	_____
6. Stage 4 urine and processing	___	_____
7. Volume correct for each aliquot	___	_____
8. Vials sealed	___	_____
9. Biospecimen Form completed	___	_____
10. Freezer organization	___	_____
11. Time constraints	___	_____

12. Disposal of contaminated supplies ___ _____

Biospecimen packing and shipping

1. Specimens bagged ___ _____
2. Adequate dry ice used in shipping ___ _____
3. Shipping paperwork ___ _____

Miscellaneous

1. Incident(s) documented on Biospecimen Form ___ _____
2. QC Procedure ___ _____
3. Containers correctly labeled for shipping ___ _____

Comments: _____

_____

_____

Appendix 6. removed, no longer applicable.

Appendix 7. Checklist for Observation of Physical Function

Instructions: This checklist documents observation of technicians responsible for physical function by the lead supervisor. Quarterly checklists and logs are summarized onto the **Summary of Observation and Equipment Checklists** (Appendix 1). Copies of this log may be requested by the CC.

TECH ID NUMBER: ☐☐☐ SUPERVISOR ID NUMBER: ☐☐☐ DATE: ☐☐/☐☐/☐☐☐☐
Month Day Year

Chair Stands	**Satisfactory/ Unsatisfactory**	**Comments**
1. Back of chair against a wall	___	_____
2. Script correctly and clearly delivered	___	_____
3. Correctly demonstrates single stand, emphasizing keeping arms tight across chest	___	_____
4. Correctly demonstrates two stands, emphasizing full stand and return to complete sit	___	_____
5. Says “ready? Go” for each test	___	_____
6. Counts each chair stand and records final time after participant sits down on the fifth stand	___	_____
7. Records and explains unusual values	___	_____
8. If task was not performed, codes and explains reasons	___	_____
Standing Balance/Side-by-side Stand		
1. Script correctly and clearly delivered	___	_____
2. Correctly demonstrates position	___	_____
3. Timing started coincident with participant release and stopped when participant takes a step or holds on	___	_____
4. If task was not performed, codes and explains reasons	___	_____
Semi-tandem Stand		
1. Script correctly and clearly delivered	___	_____
2. Correctly demonstrates position	___	_____
3. Timing started coincident with participant release and stopped when participant takes a step or holds on	___	_____

4. If task was not performed, codes and explains reasons ___ _____

Tandem Stand

1. Script correctly and clearly delivered ___ _____
2. Correctly demonstrates position ___ _____
3. Timing started coincident with participant release and stopped when participant takes a step or holds on ___ _____
4. If task was not performed, codes and explains reasons ___ _____
5. Repeats second trial, if necessary ___ _____

Short Walks, *Usual Pace*

1. Script correctly and clearly delivered ___ _____
2. Correctly demonstrates ___ _____
3. Toes touching start line ___ _____
4. Timing started coincident with participant's first movement ___ _____
5. Time stopped when the first foot crosses imaginary plane extending vertically up from the ending line/tape ___ _____
6. Repeats second trial ___ _____

Grip Strength

1. Asked pt about recent surgery on hands ___ _____
2. Asked pt about pain and arthritis in hands ___ _____
3. Recording dial reset to zero after sub maximal practice ___ _____
4. Appropriate hand placement and grip adjustment if needed ___ _____
5. Forearm resting on table, elbow bent to approximate right angle ___ _____
6. Standard encouragement (motivation and feedback) offered to participant ___ _____
7. Recording dial (peak hold needle) reset to zero after first trial ___ _____

Comments: _____

_____

_____

Appendix 8. QC Replicate ABI and PWV Measurements

Instructions: Quarterly Ankle-brachial Index (ABI) and Pulse Wave Velocity (PWV) measurements are taken by a technician and supervisor on the same two volunteers. The technician and supervisor record their measurements onto this form and the supervisor calculates the differences between the two sets of measurements. If the systolic blood pressure measurements differ by more than 8 mmHg at any of the 4 sites, or the carotid-femoral PWV measurement differs by more than 150 cm/sec the supervisor should indicate the corrective action taken on this form.

TECH ID NUMBER: ☐☐☐ SUPERVISOR ID NUMBER: ☐☐☐ DATE: ☐☐/☐☐/☐☐☐☐
Month Day Year

Participant	Measurement	Technician ID	Supervisor ID
1	Right brachial systolic BP		
	Right ankle systolic BP		
	Left brachial systolic BP		
	Left ankle systolic BP		
	Carotid-femoral pulse wave velocity		
2	Right brachial systolic BP		
	Right ankle systolic BP		
	Left brachial systolic BP		
	Left ankle systolic BP		
	Carotid-femoral pulse wave velocity		

Comments:

_____

_____

_____

Appendix 9. Anthropometry Equipment Calibration Log

Instructions: This checklist documents the daily, weekly and monthly calibration of anthropometry measurement equipment. Quarterly checklists and logs are summarized onto the **Summary of Observation and Equipment Checklists** (Appendix 1). Copies of this log may be requested by the CC. There should be one such log done each week though the monthly portion will be filled out only in the weeks that it is needed. If there is more than one piece of equipment used for a particular function indicate the checks for each piece on the same log.

Week of:_____ Field Center:_____ Tech ID:____

[Monday's Date]

Daily Checks:

Scales read zero

___	___	___	___	___	___	___
M	T	W	Th	F	Sa	Su

Weekly Checks

A. Reading of scale with 10 kg weight (if reading outside 9.5 to 10.5 range, scale should be serviced.

Date: ___/___/___ Reading: _____

Date service REQUESTED, ____/____/____

Date RECALIBRATED by service technician. ____/____/____

B. Repeat calibration because of moving scales

Date: ____/____/____ Reading: _____

Date: ____/____/____ Reading: _____

Appendix 10. Daily Centrifuge, Freezer, Refrigerator and Room Temperature Log

Tech ID	Date	Centrifuge	Freezer	Refrigerator	Room
_____	___/___/___	☐☐☐	☐☐☐	☐☐☐	☐☐☐
_____	___/___/___	☐☐☐	☐☐☐	☐☐☐	☐☐☐
_____	___/___/___	☐☐☐	☐☐☐	☐☐☐	☐☐☐
_____	___/___/___	☐☐☐	☐☐☐	☐☐☐	☐☐☐
_____	___/___/___	☐☐☐	☐☐☐	☐☐☐	☐☐☐
_____	___/___/___	☐☐☐	☐☐☐	☐☐☐	☐☐☐
_____	___/___/___	☐☐☐	☐☐☐	☐☐☐	☐☐☐
_____	___/___/___	☐☐☐	☐☐☐	☐☐☐	☐☐☐
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_____	___/___/___	☐☐☐	☐☐☐	☐☐☐	☐☐☐
_____	___/___/___	☐☐☐	☐☐☐	☐☐☐	☐☐☐
_____	___/___/___	☐☐☐	☐☐☐	☐☐☐	☐☐☐
_____	___/___/___	☐☐☐	☐☐☐	☐☐☐	☐☐☐
_____	___/___/___	☐☐☐	☐☐☐	☐☐☐	☐☐☐
_____	___/___/___	☐☐☐	☐☐☐	☐☐☐	☐☐☐
_____	___/___/___	☐☐☐	☐☐☐	☐☐☐	☐☐☐
_____	___/___/___	☐☐☐	☐☐☐	☐☐☐	☐☐☐
_____	___/___/___	☐☐☐	☐☐☐	☐☐☐	☐☐☐
_____	___/___/___	☐☐☐	☐☐☐	☐☐☐	☐☐☐
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_____	___/___/___	☐☐☐	☐☐☐	☐☐☐	☐☐☐
_____	___/___/___	☐☐☐	☐☐☐	☐☐☐	☐☐☐
_____	___/___/___	☐☐☐	☐☐☐	☐☐☐	☐☐☐
_____	___/___/___	☐☐☐	☐☐☐	☐☐☐	☐☐☐

BLOOD DRAWING PRACTICAL EXAM

1. Place the following blood collection tubes in the correct set-up order and location for the venipuncture: 2-10 mL red top, 3-10 mL lavender top, 2-4.5 mL blue top, 1-4 mL lavender top, 1-2 mL lavender tub, 2.5 mL Paxgene tube, and 1-4mL CPT tube.
2. Specify which tube(s) remain at room temperature after collection, which are put into a cup with ice slush, which are stored in the refrigerator.
3. Remove the appropriate tubes from the tray and place them in the centrifuge in balanced positions. How long do they spin? At what speed?
4. Set up a sponge tray with the appropriate number and order of specimen storage tubes. Indicate the colors of screw caps and the types of specimen put into these tubes.
5. Place the collection tubes in front of their respective sample tubes. Describe what further processing is required of each collection tube before it is aliquotted into its respective sample tube.
6. Organize the color-capped sample tubes and prepare them for shipment.
7. Describe the quality control for each piece of equipment.
8. Describe the steps for processing the PAX tube.
9. Using a disposable plastic Pasteur pipette, add how many drops of 3 N HCl into a 1.5 mL aliquot of a urine specimen if the sample is what pH. What should you do if a drop of acid comes in contact with your skin or clothes?
10. What do you do if the collected urine is < 30 mL?

BIOSPECIMEN COLLECTION & PROCESSING TECHNICIAN WRITTEN EXAM

NAME		FIELD CENTER		DATE: ☐☐/☐☐/☐☐☐☐ Month Day Year

1. When handling biological specimens, which of the following protective apparel must ALWAYS be worn?

a) gloves

b) sterile shoe covers

c) sterile head covers

d) lab coat and gloves

2. Initially, how many ARIC participants at each field center will be asked to donate additional blood specimens collected to be used as part of the phantom duplicate?

a) One per day

b) Two per week

c) Everyone

d) Eight per week

3. From which tubes are the packed cells used?

a) #1 and #2

b) #4 and #5

c) #6, and #7

d) #3 and #8

4. How long should tubes #1and #2 sit at room temperature before centrifugation?

a) 5 minutes

b) 30 minutes

c) 2 hours

d) No waiting time required

5. Why is this step (un)necessary?_____

6. Which tube must be held below the arm during collection?

a) 10 mL lavender-stoppered

b) 4.5 mL blue-stoppered

c) 10 mL red-stoppered

d) 2.5 mL Paxgene

7. For what type of tests will the 4.5-mL blue-stoppered tubes be used?

a) Chemistry

b) Lipid

c) Coagulation

d) DNA testing

8. Which of the following labels must be affixed to the outside of a frozen shipping box?

a) biohazardous specimens

b) dry ice

c) exempt human specimens

d) dry ice and exempt human specimens

9. What is the minimum amount of dry ice that must be used for frozen shipments?

a) 2 lbs

b) 5 lbs

c) 10 lbs

d) 12 lbs

10. Labeling of aliquot vials always include which of the following?

a) Participant ID

b) Vial # of total # of vials

c) sample type

d) all of the above

11. When transferring plasma to the microvials, how much plasma is left above the cells in the tubes?

a) ¼ - ½ inch

b) ½ - ¾ inch

c) ¾ - 1 inch

d) none, all the plasma possible is removed

12. Tube #3 (4 mL CPT) is shipped when and how?

a) weekly, wrapped in paper toweling, on dry ice

b) daily, wrapped in Styrofoam sheets, on dry ice

c) weekly, wrapped in Styrofoam sheets, on frozen refrigerant gel packs

d) daily, wrapped in paper toweling, on frozen refrigerant gel packs

13. In what manner is the buffy coat from tubes #4 and #5 initially pipetted?

a) Using slow aspiration avoiding plasma and red cells.

b) Using slow aspiration and include the remaining plasma and some red cells.

c) Using quick aspiration avoiding plasma and red cells.

d) Using quick aspiration and include the remaining plasma and some red cells.

14. What paperwork is completed and sent with each weekly frozen shipment?

a) Copy of the Biospecimen Collection form

b) Original of the Biospecimen Collection form

c) Shipping Form Contents Sheet(s)

d) Shipping Form Face Sheet and Contents Sheet(s)

15. In addition to the extra labels, what paperwork is completed and sent with each daily refrigerated shipment?

a) Copy of the Biospecimen Collection form for all participants seen that day.

b) Original of the Biospecimen Collection form for all participants seen that day.

c) Copy of the Biospecimen Collection form only for participants samples in the shipment.

b) Original of the Biospecimen Collection form only for participants samples in the shipment.

Appendix 12. Daily Spirometer Leak and Volume Check Log

<u>Instructions:</u> This checklist documents the daily spirometer checks. Quarterly checklists and logs are summarized onto the **<u>Summary of Observation and Equipment Checklists</u>** (Appendix 1). Copies of this log may be requested by the CC. There should be one such log done each month. If there is more than one spirometer used indicate the checks with a separate log for each spirometer.

Month/Year: ___/______

Day of Month	Spirometer Checked for Leaks	Volume checked on Spirometer
_______	_______	_______
_______	_______	_______
_______	_______	_______
_______	_______	_______
_______	_______	_______
_______	_______	_______
_______	_______	_______
_______	_______	_______
_______	_______	_______
_______	_______	_______
_______	_______	_______
_______	_______	_______
_______	_______	_______
_______	_______	_______
_______	_______	_______
_______	_______	_______
_______	_______	_______
_______	_______	_______
_______	_______	_______
_______	_______	_______
_______	_______	_______
_______	_______	_______

Appendix 13. OMRON BP Monitor Maintenance and Calibration Log

Instructions: This checklist documents the quarterly checks for the OMRON BP machine. There should be one such log done every quarter. If there is more than one BP monitor used indicate the checks with a separate log for each monitor.

TECH ID NUMBER: ☐☐☐ FIELD CENTER ☐ DATE: ☐☐/☐☐/☐☐☐☐
Month Day Year

Blood Pressure Measurement **OMRON unit #:**_____

	Y/N	**If YES, action**
Cracking		
Holes		
Worn outer cloth of Velcro		
Leakage of cuff bladder		
Calibration Check with Pressure-Vacuum Meter		
Smooth descent of OMRON LED mm Hg from 280 to 20 mm Hg		
Observed pressure values 250 to 20 mmHg, in approximant decrements of 20 mmHg	**OMRON (mmHg)**	**Pressure-Vacuum Meter (mmHg)**
Measurement Number 1	☐☐☐☐.☐	☐☐☐☐.☐ mmHg
Measurement Number 2	☐☐☐☐.☐	☐☐☐☐.☐ mmHg
Measurement Number 3	☐☐☐☐.☐	☐☐☐☐.☐ mmHg
Measurement Number 4	☐☐☐☐.☐	☐☐☐☐.☐ mmHg
Measurement Number 5	☐☐☐☐.☐	☐☐☐☐.☐ mmHg
Measurement Number 6	☐☐☐☐.☐	☐☐☐☐.☐ mmHg
Measurement Number 7	☐☐☐☐.☐	☐☐☐☐.☐ mmHg
Measurement Number 8	☐☐☐☐.☐	☐☐☐☐.☐ mmHg
Measurement Number 9	☐☐☐☐.☐	☐☐☐☐.☐ mmHg
Measurement Number 10	☐☐☐☐.☐	☐☐☐☐.☐ mmHg
Measurement Number 11	☐☐☐☐.☐	☐☐☐☐.☐ mmHg
Measurement Number 12	☐☐☐☐.☐	☐☐☐☐.☐ mmHg

Appendix 14. Certification Request Form

Instructions: This form documents which procedures/interviews a staff member is certified for and how they received certification. It is submitted by the **Trainer** or **Study Coordinator** to Chris Baggett at the Coordinating Center (CC) for final evaluation and assignment of staff code number.

NAME OF TRAINER		FIELD CENTER		DATE: ☐☐/☐☐/☐☐☐☐ Month Day Year

Staff name _____ or code number ☐☐☐ (if already assigned)

Specify for which procedure/interviews the staff member has completed certification requirements and describe specific actions that were taken to achieve these steps (including supervisors or certified staff members who observed the process).

Procedure & Interview	Date Certified	*Certification Method (choose all that apply)	CC approval (Y/N)
Anthropometry			
Seated BP			
ABI/PWV			
ECG			
Biospecimen collection, processing			
Pulmonary function			
Neurologic exam			
Interviewing Techniques			

Procedure & Interview	Date Certified	*Certification Method (choose all that apply)	CC approval (Y/N)
Cognitive Function			
Medication and Supplements			
Recruitment			

* 1 = Attended central training presentation
2 = Certified by central trainer
3 = Direct observation by the local certified lead staff member in specified area
4 = Completed written exam
5 = Completed practice. Specify how many sets of practice were performed, and the differences of the measurements compared to the local trainer's for local certification.
6 = Other (specify)
7 = N/A (not applicable to the staff member)

Coordinating Center Use Only

Assigned staff code number: _____

Date Received: _____ **Processed by** _____

Appendix 15. Timeline for Observation and Equipment Checks

Daily	Anthropometry scales balanced to read zero (Appendix 9) Temperature check in refrigerators, freezers, etc. (Appendix 10) Check the spirometer for leaks and perform calibration checks (Appendix 12)
Weekly	Anthropometry scales calibrated or when scaled moved (Appendix 9) Grip strength dynamometer calibrated
Quarterly	Interviewers observed twice locally (Appendix 2), recorded (Appendix 1) Cross-site review of two randomly selected audio-recordings (Appendix 2), recorded (Appendix 1) Review of one cognitive interview per interviewer by neurocognitive expert, recorded (Appendix 1) Review of one neurologic exam interview per technician by neurologic expert, recorded (Appendix 1) Anthropometry technicians observed (Appendix 3), recorded (Appendix 1) Blood pressure technicians observed (Appendix 4), recorded (Appendix 1) ABI/PWV technicians observed (Appendix 4), recorded (Appendix 1) Biospecimen collection, processing observed (Appendix 5), recorded (Appendix 1) Repeat measurement of ABI/PWV (Appendix 8) OMRON BP equipment checks and calibration (Appendix 13), summarized on (Appendix 1) Anthropometry equipment checks summarized, info sent to CC (Appendix 1) Biospecimen equipment checks summarized, info sent to CC (Appendix 1) ABI/PWV equipment checks summarized, info sent to CC (Appendix 1) Spirometry equipment checks summarized, info sent to CC (Appendix 1)
Annually	Checking of the actual speed of the centrifuge (Appendix 1) Calibration and professional cleaning of pipettes (Appendix 1)

Appendix 16. Minimum Frequency of Procedures and Interviews to Maintain Data Quality[1]

TO: ARIC Executive, Quality Control, and Operations committees

FROM: Chris Baggett, Kim Ring, Gerardo Heiss

DATE: December 19, 2011

RE: Minimum Frequency of Procedures and Interviews to Maintain Data Quality – Draft

To ensure data quality the ARIC study protocol strives for an optimal frequency of data collection for specific instruments or procedures. To implement such standards the experts responsible for individual domains of the data collected by ARIC specify a minimum frequency of data collection required to maintain certification.

Implementing this process in the busy setting of the ARIC field centers is challenging. While fully committed to high standards of data quality, field center managers and supervisors have to reconcile the need for a large number of cross-trained technicians to manage a long and complex exam day, with the need to maintain their certification status. The study leadership is aware of this challenge, which has to be reconciled with the observation that data quality declines when intricate procedures are performed only occasionally.

As requested by ARIC Study Coordinators we propose the revised set of minimum frequency of data collection standards shown in the following table, for review by the ARIC Executive Committee on December 21st. It reflects the operations and staffing patterns now in place for the ARIC and NCS examinations, and the number of procedures than can be reasonably expected per month for different stations and interviews. It takes into account that certain ARIC technicians are more specialized, and it allows for designated back-up personnel. The latter are trained and certified individuals – frequently a supervisor – who perform other functions but are designated to fill in in case of staff absences or unforeseen circumstances, to avoid missing data. Importantly, it also forms the basis for a plan for the ARIC Coordinating Center to routinely report the number of procedures and interviews conducted by ARIC personnel, in a way that identifies outliers.

We have prepared a broad list of procedures and interviews (but we did not include all in place for Visit 5). Our recommended minimum frequencies are calibrated to the number of interviews and procedures to be observed and reviewed as part of the QC protocol, and to the number of exams we can expect for stages I and II. Many of the procedures and forms did not have a minimum frequency specified in the pertinent protocol manual or the QC manual. Similarly, the enclosed table does not specify a minimum frequency under the following circumstances:

a. For procedures/data that are routinely monitored by a reading center, with feed-back to the field center technicians and/or the ARIC QC committee. This applies to ECG, echocardiograms, aortic scans, spirometry and retinal photography.
b. Interviews and procedures performed by a core of specialized personnel, for whom achieving a minimum frequency of interviews/procedures per month is rarely a concern. This applies to sonographers, AFU interviewers/recruiters, and possibly others.

For a & b above, the reports by the ARIC Coordinating Center will suffice to identify and monitor situations of infrequent performance of exams and interviews.

[1] Starting from 2/1/2013, for ARIC personnel who have been certified for 6 months or more are exempt from the minimum number of procedures per month or per technician requirements.

Minimum Frequency of Procedures to Maintain ARIC Visit 5 Protocol Certification

Proposal to the ARIC Executive Committee – 12.16.11

Procedure (and associated forms)	Min. # / Month Primary Technicians	Min. # / Month Designated Back-up Techs	Experts Consulted/To be Consulted
Reception	--	--	QC, OPS Cmte.
Informed consent/ICT	--	--	
MRI Consent Addendum	--	--	
Anthropometry	6	4	
ABI	4	4	Tanaka
PWV	4	4	
ECG	--	--	Soliman
Cardiac Echo	--	--	Solomon
Aortic scan	--	--	Folsom
Blood collection & processing	4	4	Rhodes
Urine collection	--	--	
Spirometry	--	--	Hankinson
DLco	--	--	London
Seated BP	4	4	QC, OPS Cmte.
Lung sounds & Lower extremity	4	4	Loehr
Retinal photography	--	--	Klein
Physical Function	4	4	Windham
Procedures Form	--	--	--
General interviewing technique	--	--	QC, OPS Cmte.
AFU (+Recruitment)	--	--	
TICS	--	--	Coker
SAF/GEN/DEC	--	--	QC, OPS Cmte.
PSA	--	--	
MRI Exclusions	--	--	
Adverse events (SAE / MAE)	--	--	

Alert Tracking	--	--	
Medication Survey	4	4	
Procedure (and associated forms)	Min. # / Month Primary Technicians	Min. # / Month Designated Back-up Techs	Experts Consulted/To be Consulted
Physical Activity	4	4	
Physical Ability	4	4	
Personal Hx	4	4	
Respiratory Symptoms	4	4	
SF-12 Health Survey	4	4	
NSS	4	4	
CES Depression	4	4	
Mini-Mental State	4	4	
Neurocognitive + Summary	4	4	
Phys & Neurological exam	2	2	
Clin Dementia Rating (Ppt.)	2	2	Mosley
Clin Dementia Rating (Informant)	2	2	
Neurologic Hx	2	2	
Neurologic Family Hx	2	2	
Neuropsychiatric Inventory	2	2	
Unified Parkinson's Rating	2	2	

Appendix 17. Revision of the QC Schedule

TO: ARIC Study Coordinators

FROM: Hengrui Sun, Kim Ring, David Couper

DATE: February 8, 2013

RE: Revision of the QC Schedule

To reflect the decrease in the number of participants examined per week as ARIC-NCS approaches to the end of study, starting from Feb. 1, 2013, the schedules for QC are revised as follows:

- ARIC personnel who have been certified for 6 months or more are exempt from the minimum number of procedures per month or per technician requirements. The rationale is that given the remaining amount of time in the study, and the reduction in the number of participants coming in for the visits, and the level of expertise gained over a 6-month period, these ARIC personnel are qualified to continue to do the measurements without meeting the prior minimum requirements.

- For certification purposes, certifications can be performed with on-site or on-staff volunteers; not necessary for them to be participants.

- Anthropometry QC repeats: these are currently done weekly and have been converted to monthly.

Appendix 18. MRI Repeatability Study

Table of Contents

List of Abbreviations

CC	ARIC Coordinating Center
CDART	Carolina Data Acquisition and Reporting Tool
DMS	Data Management System
MEF	MRI Exclusion Form
MQS	MRI Vascular Lab Quality Scores Form
MRA	Magnetic Resonance Angiogram
MRT	MRI Repeatability Tracking Form
PRO	Procedures Completion Form
RTS	Recruitment Tracking and Scheduling Form
TOF	Time–of-Flight

1. **Overview**

The purpose of the MRI repeatability study is to assess the accuracy and precision of the items being measured in the vascular component of the NCS MRI scan. To do this, 100 participants will be recruited to undergo a repeat MRI scan. Eligibility for the repeat scan will be determined by the MRI Vascular Reading Center. Field center personnel will check the eligibility status of participants and recruit 25 participants to have a repeat MRI scan.

2. Eligibility Criteria:

Twenty-five participants from each field center (total of 100) are needed for this study. The criteria for eligibility for a repeat scan are:

a) Time since initial MRI scan is at least a week but less than six months;
b) Presence of 1 or more atherosclerotic plaques in initial MRI scan, based upon the vascular lab's assessment;
c) QC Score of MRA [TOF quality] of either "adequate" or "excellent", based upon the vascular lab's assessment;
d) QC Score of Vessel wall MRI [Space quality]of either "adequate" or "excellent", based upon the vascular lab's assessment

3. Protocol

a) MRI Vascular Lab:
After the initial MRI scan is performed the image data is transmitted to the Mayo MRI Lab, as per usual standards. The MRI Vascular Lab will receive the scan from Mayo. Analysts at the MRI Vascular Lab assess the presence of atherosclerotic plaques as well as the quality of the MRA TOF and vessel wall components of the image data and record their findings in the MQS Form in the CDART DMS.

(NOTE: The MRI Vascular Lab is entering scan results into their own RedCap database, including the plaques and quality information. The ARIC CC will download the presence of plaques and quality scores from the MRI Vascular lab RedCap database on or about March 19, 2013. The ARIC CC will then import the values one time into the CDART DMS. From that date forward, the MRI vascular lab will key the presence of plaques and the two quality scores into the MQS Form.)

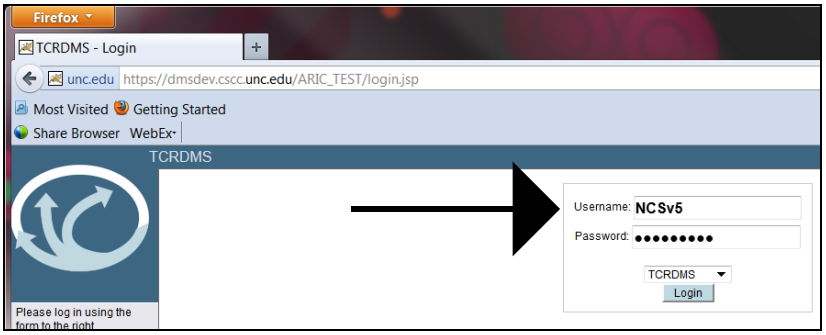
b) Field Center
   i. Determination of eligibility for repeat MRI scan:
   Each week, or with whatever frequency the study coordinator feels is appropriate, a field center staff member runs the **MRI repeat scan selection** report in the CDART DMS.

Logging in to the DMS

To log in to the DMS, do the following:

1. Go to the URL: https://cdart.cscc.unc.edu/ARIC/login.jsp. You will see a web page looking like this:

2. To log in, enter the Username and Password that was assigned to you and click 'Login':



For questions about the DMS, contact the help desk at arichelp@unc.edu or 877-967-8732.

3. Click on "Data Extraction" on the left side of the main DMS window.
4. Click on "Reports." A new screen will appear (partial image shown below).
5. A pop-up window with "Parameter" at the top will appear (image shown below).
6. Select the method by which you want to sort the list of eligible participants – by date of initial MRI scan (default) or by ID.
7. The list will appear.

ii. Recruitment

1. Field center staff will contact eligible participants to recruit them for the repeatability study.

2. Eligibility with regard to determining any existing medical conditions that may interfere with the MRI is determined for a repeat scan by the MEF form using the MRI Repeat ID.

iii. Data collection

1. The MRT form is completed as soon as a participant is contacted to determine whether s/he wants to participate in the repeat MRI study. Record the date of initial contact in MRT Q0a. Ideally, the date the form was completed will be the same date the participant was contacted. If the participant does not agree to participate, record No to MRT Q1 and record the reason given by the participant in MRT Q1a.
2. If the participant agreed to participate, record Yes for MRT Q1 and select an MRI Repeat Visit QC ID from the list distributed by the CC [see Memo "022.2013: V5 MRI Repeat ID's and Acrostics" for the list of IDs]. Record this ID in MRT Q2. This is the form that links Cohort ID to MRI Repeat Visit ID. Do NOT record the MRI repeatability study ID in the RVF.
3. Schedule the repeat MRI, working with the participant and the MRI center at your site. Do not complete an RTS for the repeat MRI.
4. Enter a MEF for the participant using the MRI Repeat Visit QC ID (from (2)).
5. Enter a PRO (Q16 – Q19a **only**) for the participant using the MRI Repeat Visit QC ID (from (2)).
6. The repeat MRI scan should be performed following the same procedures as the initial MRI scan. It is important to use the ACROSTIC that was generated for repeatability studies (specifically ECHO) for each participant who completes the MRI repeatability study. This should avoid inadvertent unblinding of the analysts at the MRI Reading Centers. See Memo "022.2013: V5 MRI Repeat ID's and Acrostics" for the list of repeatability study ACROSTICS.