MULTI-ETHNIC STUDY OF ATHEROSCLEROSIS

EXAM 6

Field Center Procedures

Manual of Operations

November 2, 2016

Multi-Ethnic Study of Atherosclerosis

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1 OVERVIEW AND CLINIC EQUIPMENT

1.1 MESA Exam 6 Overview

Welcome to Exam 6 of the Multi-Ethnic Study of Atherosclerosis (MESA)! This is a continuation of a vitally important national research project that will influence diagnosis and treatment of cardiovascular diseases over the next several decades. The study enrolled 6814 participants at six field centers and has so far consisted of five examinations, periodic surveillance phone calls, and collection of data from Events (new diagnosis of a clinical cardiovascular disease)

As we continue on, keep the above in mind when you perform the procedures on those gracious and willing participants. The ultimate value of this study depends on *you* and on the quality of the data that you collect.

1.1.1 Purpose and Objectives

The purpose of MESA is to study subclinical cardiovascular disease (CVD). Subclinical diseases are those detected by non-invasive procedures, such as MRI, CT, ECG and ultrasound, before they have produced any clinical signs or symptoms.

The primary objectives of MESA are to determine:

- What factors influence the progression of mild subclinical disease to more severe subclinical disease?
- What factors influence the progression of subclinical disease to clinical disease?

The secondary objectives of MESA are to:

- Assess ethnic, age, and gender differences in subclinical CVD prevalence and risk of progression
- Describe the interrelationships of established risk factors for subclinical CVD with new risk factors that are identified by the MESA study
- Develop population-based methods, suitable for application in future screening and intervention studies, to identify asymptomatic individuals who are at high risk for subclinical CVD.

1.1.2 Brief Description of MESA

MESA is a large and complex long-term study. Of the 6814 men and women ages 45–85, approximately 38% of the cohort are Caucasian, 28% African-American, 23% Hispanic, and 11% Asian, predominantly of Chinese descent.

The cohort was recruited from the following six field centers (site ID number in parentheses):

- Wake Forest University, Winston-Salem, NC (3)
- Columbia University, New York, NY (4)
- Johns Hopkins University, Baltimore, MD (5)
- University of Minnesota, Minneapolis-St. Paul, MN (6)

- Northwestern University, Chicago, IL (7)
- UCLA, Los Angeles, CA (8)

For this exam, there are 6 Reading Centers and Labs. These centers are located at:

- University of Minnesota (Lipid Lab)
- University of Vermont (Central Blood Lab)
- University of Vermont (Lab Repository)
- University of Iowa (Lung CT Reading Center)
- EPICARE ECG Reading Center (Heart Monitor Reading Center)
- University of Pennsylvania (Brain MRI Reading Center)
- University of Wisconsin (Ultrasound Reading Center)

The Coordinating Center at the University of Washington (Seattle) continues to coordinate all aspects of the study, including development of the Manual of Operations, development of data entry and management software, quality control, and statistical analysis of the data for publication in academic journals.

Funding for MESA is provided by the National Heart, Lung, and Blood Institute (NHLBI), a division of the National Institutes of Health. The Project Office from NHLBI also provides scientific leadership to the study.

MESA began more than 16 years ago. The first 18 months of the study were devoted to protocol development, staff training, and pilot testing. MESA Exam 1 (i.e. the "Baseline Exam") took place over a two-year period, beginning in late July 2000. The second and third exams started in late 2002 and early 2004 and each required about 18 months to complete. The fourth exam required just under two years to complete, starting in late 2005. The fifth exam was completed in early 2012 and ran for just under two years. Since the first exam, participants have also been contacted by telephone every 9-12 months to determine whether any medical events have occurred.

1.1.3 Events

In MESA, an "event" is the development of a medical condition requiring participant hospitalization or other specified types of treatment, or the death of a participant. In MESA, we are particularly interested in collecting data about myocardial infarction (MI or "heart attack"), stroke, transient ischemic attack (TIA or "mini-stroke"), angina, congestive heart failure (CHF), peripheral vascular disease (PVD), and death. When an event occurs, we will collect a separate set of data based on hospital and physician records and on interviews with participants or their proxies.

1.1.4 How to use this manual

This manual contains step-by-step instructions for completing all of the components in MESA Exam 6. Many of the steps and clinic procedures are the same as in previous exams; thus where appropriate the previous manuals of operation may also be consulted.

You should carefully study all sections that relate to procedures that you will be performing, and you should keep this manual handy as a reference. If you have questions about anything in the manual, please direct them to your Study Coordinator.

1.1.5 Supplies and Equipment

Most supplies and equipment needed for Exam 6 are similar to that of previous exams. Each clinic should be equipped with the following supplies and equipment:

Exam equipment & supplies on hand at Field Centers

Item	Procedure
Clean sheets, pillow cases, blankets	General
Consent forms (and participant folders/files)	General
Examining table disposable paper	General
Gowns or scrubs & slippers	General
Paper (PDF) copies of forms (backup)	General
Reading glasses or magnifying glass	General
Snacks	General
Surge Protectors	General
Desks/tables and chairs	Consent
Field Center specific consent forms	Consent
1 Detecto Platform Balance Scale in lbs/kg	Anthropometry
Printer	Anthropometry
Stadiometer (Accu-Hite Measure Device with level bubble)	Anthropometry
Full length mirrors	Anthropometry
Gulick II 150 cm anthropometric tapes	Anthropometry
Four 50-pound weights (certified prior to first MESA visit) to calibrate scale	Anthropometry
Germicidal cleanser and wipes	Anthropometry
Current version of PDR	Medications
Medication bags	Medications
tables/desks	Medications
Chairs and two foot rests (2 stations)	Seated Blood Pressure
Copies of Critikon chart for choosing correct BP cuff size	Seated Blood Pressure
DinamapÒ automated blood pressure devices (Dinamap Monitor Pro 100Ò, which includes printer paper, power cable, and power converter).	Seated Blood Pressure
Measuring tapes (for arm circumference).	Seated Blood Pressure
Watch or stop watches (to time five-minute rest and resting heart rate)	Seated Blood Pressure
Blood pressure cuffs in a variety of sizes (Dura-cuf Adult Assortment PackÒ [#2699]).	Seated Blood Pressure
Echo bed with stool or chair for sonographer	Echo
Regular pillows (at least 2 if head of bed cannot be raised)	Echo
Sheets	Echo
Large hand towels	Echo
Gowns (1 per participant)	Echo
Electrodes (3 per participant)	Echo
Ultrasound gel	Echo

Transducer cleaner	Echo
Wedge pillow	Echo
Blank DVD (1 per participant)	Echo
Electrodes (3 per participant)	Arterial Stiffness
USB drive for exporting data	Arterial Stiffness
Countdown timer (or stopwatch) (as back up) OR Notebook Computer with timer tool	6MWT
Mechanical lap counter	6MWT
Two small cones to mark the turnaround points	6MWT
A chair that can be easily moved along the walking course	6MWT
Worksheets on a clipboard	6MWT
A source of oxygen	6MWT
Sphygmomanometer	6MWT
Telephone	6MWT
Automated electronic defibrillator (on site)	6MWT
Pulse oximeter	6MWT
Paper copies of the three cognitive instruments for each participant (language specific)	Cognitive tests
CASI Kits	Cognitive tests
Felt tip non-toxic washable markers	ECG patch application
ZioPatch Information Packet (includes razor, cleaning supplies, return postage pack)	ECG patch application
Devon Medical Handheld Pulse Oximeter PC-66	Oximetry
SensorMedics model 1022 dry-rolling seal volume spirometer is fitted by OMI with a digital volume encoder, temperature sensor, and RS232 serial computer interface	Spirometry
OMI spirometry software (version 5.05.11) is installed on a notebook computer with Windows XP	Spirometry
Calibration syringe, 3.00 liters, Han Rudolph model # 5530	Spirometry
Spirometer hoses, 3 feet long	Spirometry
Disposable mouthpieces, nose clips	Spirometry
Albuterol metered-dose inhalers (MDIs) and spacers	Spirometry

Examination equipment provided by the Coordinating Center

Item	Procedure
Tablet PC computers	General
3 digital audio recorders	General
MESA medication bags	General

Core exam phlebotomy and laboratory supplies and equipment

Item	Procedure
Lab coats and gloves	Blood Collection
Phlebotomy chair	Blood Collection

Washcloths/Towels	Blood Collection
Smelling salts	Blood Collection
Lab mats and wipes	Blood Collection
10% bleach solution or approved biohazard disinfectant	Blood Collection
Plastic cart with wheels for phlebotomy supplies (or plastic tray with compartments)	Blood Collection
Butterfly needles (21 G) with luer adapter (BD# 367281)	Blood Collection
Vacutainer barrels	Blood Collection
Tourniquets	Blood Collection
Alcohol prep pads	Blood Collection
Gauze (2x2)	Blood Collection
Surgical tape - paper tape (easier on participants)	Blood Collection
Band-Aids	Blood Collection
Blood collection tubes:	Blood Collection
10 mL Serum tubes (BD# 367820)	Blood Collection
10 mL EDTA tubes (BD# 366643)	Blood Collection
Draw tube rocker	Blood Collection
Draw tube racks	Blood Collection
Ice bucket and crushed ice - filled 10 min before draw	Blood Collection
Stopwatches or timers	Blood Collection
Scissors	Blood Collection
Pens and Sharpie pens	Blood Collection
Participant barcode labels (from Coordinating Center)	Blood Collection
MESA Phlebotomy and Processing Forms (from Coordinating Center)	Blood Collection
Blood Spill Kit	Blood Collection
Biohazardous waste container	Blood Collection
Needle/sharps container	Blood Collection
Covidien Sterile Midstream Urine Collection Systems (Covidien2090SA), 14-375-143 (Fisher Scientific)	Urine Collection
Lab coats	Sample Processing
nitrile or latex gloves	Sample Processing
splash shield and/or safety glasses	Sample Processing
Lab mats and wipes	Sample Processing
10% bleach solution or approved biohazard disinfectant	Sample Processing
Emergency eye wash station	Sample Processing
Biohazards waste container	Sample Processing

Ice bucket with crushed ice, filled before start of processing	Sample Processing
Draw tube racks	Sample Processing
Cryovial/tube racks (Fisher 96 slot rack # 05-541-37 with Fisher cover # 05-541-28 OR Fisher 50 slot rack # 05-669-45 no cover)	Sample Processing
Pooling tubes (Fisher #05-539-1 15 mL)	Sample Processing
Fixed-volume pipettes with tips (MLA). (Volumes to be pipetted: 0.5 mL, 1.0 mL, and 1.5 mL) Note: calibrated adjustable pipets may be used.	Sample Processing
Cryovial freezer boxes (Revco boxes 2" with 9 x 9 grids Fisher #110678-24A [Mfr.No. Thermo Scientific #5954] with 9 x 9 grid Catalog# 13-989-218, Mfr.No. Thermo Scientific 6212 ordered separately)	Sample Processing
Pens and Sharpie pens	Sample Processing
Clock	Sample Processing
Stop watch or timer	Sample Processing
Test tube holders (adapters) for centrifuge	Sample Processing
Water bottles for balance	Sample Processing
Rubber bands for freezer boxes	Sample Shipping
Ziplock plastic bags for freezer boxes	Sample Shipping
Absorbent material (e.g., paper towels, absorbent pads)	Sample Shipping
Packaging tape	Sample Shipping
Dry ice (~10 - 15 pounds per shipping container)	Sample Shipping
Shipping labels (FedEx address labels)	Sample Shipping
Category B labels (UN3373 "BIOLOGICAL SUBSTANCE, CATEGORY B")	Sample Shipping
Dry Ice labels (Dry Ice UN 1845, Class 9 - Miscellaneous	Sample Shipping
Styrofoam Shipping Containers (Polyfoam Packers or Thermosafe)	Sample Shipping
-80°C Freezer	Equipment
4°C Refrigerator	Equipment
Refrigerated Centrifuge with a Horizontal (swing-out head) rotor – minimum 2000 g-force	Equipment

Epigenetics phlebotomy and laboratory supplies and equipment

AutoMACS (Miltenyi Biotech)
Countess Automated Cell Counter (Invitrogen)
Mr. Frosty freezing containers (Sigma) – store at room temperature

Cryovial Ice Bin
Refrigerated Centrifuge with a Horizontal (swing-out head) rotor
8 mL cell preparation tubes (CPT) – store protected from light at room temperature
(18-25°C)
15 mL sterile conical centrifuge tubes
50 mL sterile conical centrifuge tubes
2.0 mL sterile cryovials
Countess Chamber Slides
Replacement Columns for AutoMACS (change every 2 weeks)
Replacement Air Filters for AutoMACS (change every 12 months)
Sample Storage Boxes (5x5x2 – 100 samples)
Styrofoam Mailers with outer Cardboard sleeves for shipping
Shipping labels
10x PBS and Molecular Grade water for dilution
0.4% Trypan Blue Stain
70% Ethanol for AutoMACS
7.5% BSA to make Running Buffer for the AutoMACS
0.5mM EDTA to make Running and Rinsing Buffers for the AutoMACS
CD14 Microbeads for the AutoMACS
CD4 Microbeads for the AutoMACS
FBS to make Freezing Media A and B
DMSO to make Freezing Media B
Isopropanol (2-propanol) for the Mr. Frostys
RLT Lysis Buffer for sample storage
-70°C or - 80°C Freezer
4°C Refrigerator
-20°C *non-defrosting* freezer
Microcentrifuge for 2 mL cryovials (at 4°C if possible)
Dedicated 2-3 feet Bench Space
Lab coat and gloves
Ice bucket with crushed ice, filled before start of processing
Blood tube racks
Participant ID Labels (provided by coordinating center)
Conical tube racks for 15 mL and 50 mL tubes – 2 each
4 Cryovial racks for 2mL tubes
MESA Epi Brief Protocol and data collection forms
Pens
10% bleach and Ethanol for cleaning benchtop and pipettes
Bleach for treating AutoMACS waste before disposal
Clock
Biohazards waste container

5 mL sterile transfer pipettes
1000 uL, 200 uL and 10 uL Micropipettes and DNAse/RNAse free pipette tips

2 OVERVIEW OF EXAM 6 COMPONENTS

2.1 Summary of Exam 6 components

2.1.1 Exam 6 Components by Day:

Day 1 Components

	Purpose	**Main or Ancillary**
Reception and Consent	Greet the participant. Review eligibility. Explain the schedule. Determine adherence to the fasting requirement. Obtain informed consent.	Main
Change Clothes	Standardize and facilitate anthropometric and other measurements.	Main
Blood Pressures	Obtain measure of sitting blood pressure of the brachial artery, at rest.	Main
Pulse Oximetry	Measure resting oxygen saturation.	Main
Anthropometry	Measure weight, height, waist and hip circumferences.	Main
Phlebotomy	Obtain blood samples for lipids, chemistry, hemostasis, and other laboratory tests and for storage.	Main/Ancillary
Urine Collection	Obtain specimen for measurement of microalbuminuria.	Ancillary (HF, N=All)
Snack	Provide the participant with a snack.	Main
Echocardiography	Assess the structure and function of the heart.	Ancillary (HF, N=All)
Arterial Stiffness Measures	Measurement of arterial pulse waves and pulse wave velocity	Ancillary (HF, N=All)
Medications	Obtain information on types and dosages of all prescribed and over the counter medications.	Main
Medical History	Obtain relevant medical history.	Main
Personal History/Demographics	Obtain standard measures of education, income, wealth, occupation, smoking, and alcohol intake.	Main
Physical Function	Obtain measures of physical functioning.	Main
Urinary Symptoms	Obtain information on urinary tract symptoms.	Ancillary (UKNOW, N=All)
Physical Activity	Obtain information on usual low, medium, and high-level activities during past month.	Ancillary (HF, N=All)
Heart Failure Symptoms/Risk Factors	Obtain information on heart failure symptoms and risk factors.	Ancillary (HF, N=All)
Cognitive Function Test	Obtain measures of cognition function (CASI, Digit Symbol Coding, Digit Span Test). Will be repeated at 15-18 months after Exam 6 visit for participants in	Ancillary (AF, N=1500) and Memory, N=540)

	the Memory Study, at the time of their first brain MRI.	
Additional Cognitive Function Testing	UDS v. 3 and PACC: expanded cognitive testing to permit adjudication of mild cognitive impairment (MCI) and dementia (includes standard outcomes collected by all Alzheimer's Disease Centers to distinguish cognitive impairment from normal aging). Will be conducted 15-18 months after initial Exam 6 visit for participants also in the Atrial Fibrillation Study.	Ancillary (Memory, N=540) and Epigenetics of Cognitive Function (N=1000)
Lung Questionnaire	Respiratory symptoms and diagnosis	Ancillary (Lung and Lung Non-Smokers, N=2650)
Spirometry	Measure lung function (including post-bronchodilator spirometry in a subset)	Ancillary (Lung and Lung Non-Smokers, N=2650)
Contrast-Enhanced Lung CT	Obtain lung CT scan to measure the pulmonary blood volume. Creatinine will be checked prior to this test.	Ancillary (Lung, N=1000)
Non-contrast Lung CT	Obtain lung CT scan to study the structure of the lungs.	Ancillary (Lung, and Lung Non-Smokers, N=1650)
ECG Patch Application	Application of ECG patch monitor.	Ancillary (AF, N=1500)
6 Minute Walk Test	Measure walking distance as a measure of functional status.	Ancillary (HF, N=All)
Vitamin D Randomization	Dispense Vitamin D supplements or placebo.	Ancillary (Vit D, N=1600)
Exit Interview	Explain next steps and answer questions and solicit comments about the exam. Discuss referrals. Obtain tracking information. Schedule second visit if needed. Thank participant.	Main

Second Visit Components

	Purpose	**Main or Ancillary**
PET MRI	Provides a non-invasive measure of inflammatory activity in plaque in the carotid vessel wall	Ancillary (MESA PET, N=350)
Cardiopulmonary Exercise Testing	Provides an assessment of activity limitation and dyspnea	Ancillary (MESA HF, N=300)
Brain MRI	In Atrial Fibrillation study, obtain MRI of the brain 18 months after Exam 6 to evaluate atrial fibrillation burden in relation to brain structure and function. Provides gray and white matter volumes, perfusion, and microvascular injury. In Memory study, brain MRI occurs within 2 weeks of first Exam 6 visit and is repeated 3 years later. First MRI will be conducted 15-18 months after Exam 6 visit for participants also in the Atrial Fibrillation Study, and will be repeated 3 years later.	Ancillary (MESA Memory, N=540; MESA AF, N=1350)
Brain Amyloid PET Imaging	An optional test that quantifies β-amyloid deposition in the brain. Occurs within 2 weeks of first Exam 6 visit Will be conducted 18 months after the Exam 6 visit for participants also in the Atrial Fibrillation Study.	Ancillary (MESA Memory subset, N=216)
MRI of the lower extremities	Imaging is performed on a 3.0T MRI scanner equipped with a knee coil to allow imaging of the lower extremities. Sodium and water content is imaged from serial sequences with calibration against "standard" tubes.	Ancillary (Tissue Sodium, N=753)
Vit D Ancillary Study Exam 6a	Seated Blood Pressure Anthropometry Phlebotomy Medications Pill Count Adverse Events	Ancillary (Vit D, N=1600)

Third Visit Components

	Purpose	**Main or Ancillary**
Lumbar CSF draw	An optional test that collects cerebrospinal fluid (CSF) for assay of AD biomarkers. Occurs within 2 weeks of first Exam 6 visit Will be conducted 18 months after Exam 6 visit for participants also in the Atrial Fibrillation Study.	Ancillary (MESA Memory subset, N=216)

Note: Ancillary study components above are set; additional components may be added for other ancillary studies.

2.1.2 Exam 6 Components by Ancillary Study:

All participants will undergo the following:

Blood Pressure: Resting blood pressure will be measured in the right arm after five minutes in the seated position. An automated oscillometric method (Dinamap) and appropriate cuff size will be used. Three readings will be taken; the second and third readings will be averaged to obtain the blood pressure levels used in analyses.

Anthropometry: Height and weight will be measured to the nearest 0.1 cm and 0.5 kg respectively. Body mass index (kg/m2) will be used a measure of overall obesity. Girths (waist at the umbilicus and hips at the maximal circumference of buttocks) will be measured to the nearest 0.1 cm using a steel measuring tape (standard 4 oz. tension).

Pulse Oximetry: Resting oxygen saturation will be measured in the seated position. A pulse oximeter with a finger probe will be used. Nail-polish will be removed, if necessary. Oximetry will be measured off supplement oxygen, if used. For participants who use supplement oxygen, supplement oxygen will be restarted immediately if they are short of breath or their oxygen saturation drops below 82%.

Laboratory Measurements: These may include a lipid profile, glucose, creatinine, insulin, and HgA1C. White cells may also be cryo-preserved for future generation of cell-lines and isolation of DNA needed for genetic studies.

Questionnaires: Standard questionnaires will be used to collect information about demographics, socioeconomic and psychosocial status, physical function medical and family history, medication use, dietary and alcohol intakes, and smoking.

Six Minute Walk Test: The Six Minute Walk Test consists of walk for 6 minutes on a level surface to see how far the participant can go. If the participant uses supplemental oxygen, it will be used during the test.

Echocardiography: All study participants will undergo comprehensive 2-dimensional echocardiography with Doppler and tissue Doppler imaging (TDI) using a commercially available ultrasound system with harmonic imaging to study the structure and function of the heart. Blood pressure will be recorded at the time of echocardiography.

Arterial Stiffness Measures: Assessment of arterial pulse waves and pulse wave velocity will be performed using a brachial and leg cuff-based approach (with simultaneous, automated recording of the cuff blood pressure) using a Fukuda VaSera and/or SphygmoCor XCEL device. Arterial stiffness measures will occur at the same time as echocardiography.

Physical Activity Questionnaire: The MESA Typical Week Physical Activity Survey is designed to identify the time and frequency spent in various physical activities during a typical week in the past month. The rationale for the selected time frame of a typical week in the past month is the intention to capture typical activity patterns in one's daily life.

Heart Failure Symptoms/Risk Factors Questionnaire: A heart failure symptoms questionnaire will be completed by all participants to determine the presence of symptoms and risk factors such as dyspnea and edema.

Urinary incontinence questionnaires: Urinary symptoms will be assessed using the International Consultation on Incontinence Modular Questionnaire (ICIQ) is a tool to identify female and male lower urinary tract symptoms.

Participants who are enrolled in the MESA Heart Failure Ancillary Study at Wake Forest may add the following:

Cardiopulmonary Exercise Testing (CPET; Wake Forest participants only): CPET will be performed at the Wake Forest exercise lab. Electrically-braked bicycle ergometry with metabolic measurement systems will be utilized. During the CPET, a 12-lead ECG will be continuously monitored and will be printed at the end of each 2-minute stage. Blood pressure will be taken during the last minute of each stage and entered into the computer. Oxygen uptake and respiratory exchange ratio (RER) will be monitored continuously throughout exercise.

Participants who are enrolled in the MESA Atrial Fibrillation Ancillary Study will undergo the following:

Cognitive Function Tests: The Cognitive Abilities Screening Instrument (CASI), Digit Span Test, and Digit Symbol Substitution Test will be administered to all participants to better understand the relationship of subclinical vascular markers with cognitive function.

ECG patch monitor application to the upper left chest – 2 monitoring episodes of up to 14 days each, for a total of up to 28 days of monitoring: The ECG patch monitor detects the presence of atrial fibrillation and other arrhythmias and quantifies the atrial fibrillation burden (the proportion of the monitored time that the heart rhythm is atrial fibrillation). Each patch monitor records heart rhythm continuously for up to 14 days. At the end of the first 14-day monitoring session, the participant mails the patch to the manufacturer for rhythm interpretation. A second patch monitor will be mailed to the participant, who will apply it to the chest, and return it by mail at the end of the second 14-day monitoring period.

Brain MRI: 1350 participants will undergo brain MRI on designated 3T MR scanners 18 months after the Exam 6 clinic exam. The protocol includes 1.0 mm, isotropic 3D FLAIR, proton density and T1 weighted images, a 2D axial resting arterial spin labeling (ASL) blood flow sequence, susceptibility-weighted imaging, and a resting/breath-hold blood oxygenation level-dependent (BOLD) sequence to evaluate vascular reactivity. The image analysis methodology classifies all brain tissue into either normal or ischemic gray or white matter and assigns the tissue type to all voxels, each of which is assigned to one of 92 anatomic regions of interest of the cerebrum. Ischemic tissue is further classified into necrotic (traditional infarct) vs. non-necrotic (leukoaraiosis) tissue. In addition, cerebral blood flow is calculated from the ASL sequence for each voxel as well as vascular reactivity by resting and breath-hold BOLD imaging. Variables of interest include ventricular volume, cerebral blood flow, ischemic lesion volume, infarction, and white matter disease (leukoaraiosis).

Participants who are enrolled in the MESA Lung Ancillary Study will undergo the following:

Spirometry: Spirometry consists of participants inhaling and exhaling as hard and as fast as they can through the mouth. Participants will also be asked to breathe in and out slowly through the mouth. These actions will be repeated at least three times to ensure valid readings. A SensorMedics model 1022 rolling-barrel spirometer will be used for all readings, and the procedure will follow American Thoracic Society guidelines. A new mouthpiece will be used for each volunteer. Participants with airflow limitation (prebronchodilator FEV1/FVC ratio<0.70 or <LLN) will receive two inhalations of 90 mcg albuterol via MDI and spacer, and will then repeat the spirometry test ("post-bronchodilator spirometry").

Lung function measured by spirometry is a specific, quantifiable marker of obstructive lung disease. It strongly predicts both pulmonary and cardiac events, including incident heart failure. Post-bronchodilator spirometry is necessary to define chronic obstructive pulmonary disease (COPD), the third leading cause of death. Repeat measures over time, as we are doing in MESA Lung, define of progression of lung disease.

Pulmonary Blood Volume on Contrast-Enhanced CT Scan: Pulmonary blood volume be will be measured on contrast enhanced full-lung CT scan. Experienced and trained technologists will scan the lungs of each consenting subject in order to obtain an accurate and reproducible assessment of pulmonary emphysema. The technologist will transmit the scans to the CT Reading Center. Serum creatinine will be checked prior to the administration of contrast in order to confirm normal renal function (eGFR>60).

Airway Anatomy on CT Scan: Airway anatomy will be measured on non-contrast full-lung CT scan. Experienced and trained technologists will scan the lungs of each consenting subject in order to obtain an accurate and reproducible assessment of airway anatomy. The technologist will transmit the scans to the CT Reading Center.

Pulmonary emphysema on CT scan is a specific, quantifiable marker for the presence of anatomical pulmonary emphysema. Its presence on CT scan is the contemporary measure of emphysema. Quantitative measures of emphysema on CT scan predict pulmonary and possibly cardiac events, and are strongly correlated with left ventricular filling in a pattern that resembles subclinical heart failure with preserved ejection fraction. Repeat measures over time provide a measure of progression of emphysema.

Lung Questionnaire and Safety Forms Participants will be asked to complete a respiratory questionnaire in addition to items to ensure safety of spirometry and, if selected, administration of albuterol and iodinated contrast.

Participants who are enrolled in the MESA Lung Non-Smokers Ancillary Study will undergo the following:

Spirometry: Pre-bronchodilator spirometry will be performed as described above, as will post-bronchodilator spirometry for participants with airflow limitation.

Pulmonary Emphysema on CT Scan: Pulmonary emphysema will be measured on non-contrast full-lung CT scan. Experienced and trained technologists will scan the lungs of each consenting subject in order to obtain an accurate and reproducible assessment of pulmonary emphysema. The technologist will transmit the scans to the CT Reading Center.

Lung Questionnaire and Safety Forms Participants will be asked to complete a respiratory questionnaire in addition to items to ensure safety of spirometry and, if selected, administration of albuterol.

Participants who are enrolled in the MESA PET ancillary study will undergo the following (Columbia only):

PET MRI of Carotid Arteries: FDG PET imaging provides a non-invasive measure of inflammatory activity in plaque in the carotid vessel wall. Several studies have found strong correlations of carotid FDG uptake with macrophage infiltration and inflammatory gene expression. Thus, FDG PET will provide a unique measure of metabolic activity in macrophages in carotid plaque that we propose to relate to the

HDL assays, over and above the information available from MRI regarding plaque burden, which represents a phenotypic manifestation of atherosclerosis accrued over a long period of time.

Additional blood collection: 14ml blood will be collected in all participants for lipids panel, plus an additional 14ml in 40 participants for monocytes assay.

Participants who are enrolled in the MESA Epigenetics of Obesity Ancillary Study will undergo the following (Wake, Columbia, Hopkins, and Minnesota only):

Additional blood collection: 32mL blood will be collected to assess fasting glucose and insulin measures and to assess monocyte and T lymphocyte phenotypes. Note: participants selected for both Epigenetics Studies will complete a single 32mL blood draw.

Participants who are enrolled in the MESA Epigenetics of Cognitive Function Ancillary Study will undergo the following (Wake and Hopkins only):

Additional blood collection: 32mL blood will be collected to assess fasting glucose and insulin measures and to assess monocyte and T lymphocyte phenotypes. Note: participants selected for both Epigenetics Studies will complete a single 32mL blood draw.

Cognitive Function Testing: Cognitive testing (CASI, Digit Span, Digit Symbol, UDS v. 3 and PACC) will be performed at Exam 6 and repeated 3 years later to facilitate the cross-sectional adjudication of cognition (AD, vascular dementia, mild cognitive impairment and normal) and decline in cognitive performance over time. Wake Forest participants also enrolled in the Atrial Fibrillation Study will undergo the CASI, Digit Span and Digit Symbol portion of the tests at Exam 6, then repeat these tests along with the UDS v. 3 and PACC tests 15-18 months after the initial Exam 6 visit, at the time of the Atrial Fibrillation MRI. These participants will also receive the full battery (CASI, Digit Span, Digit Symbol, UDS v. 3 and PACC) 3 years later. All Wake Forest participants will receive an interim cognitive test (1.5 years) administered by telephone in between the two detailed cognitive assessments to assess interim changes in thinking and memory.

Participants who are enrolled in the MESA Memory Ancillary Study will undergo the following (Wake only):

Additional Blood Collection: an additional 15 mL will be collected in ancillary study participants for future assay of established and evolving AD biomarkers.

Cognitive Function Testing: Cognitive testing (CASI, Digit Span, Digit Symbol, UDS v. 3 and PACC) will be performed at Exam 6 and repeated 3 years later to facilitate the cross-sectional adjudication of cognition (AD, vascular dementia, mild cognitive impairment and normal) and decline in cognitive performance over time. Wake Forest participants also enrolled in the Atrial Fibrillation Study will undergo the CASI, Digit Span and Digit Symbol portion of the tests at Exam 6, then repeat these tests along with the UDS v. 3 and PACC tests 15-18 months after the initial Exam 6 visit, at the time of the Atrial Fibrillation MRI. These participants will also receive the full battery (CASI, Digit Span, Digit Symbol, UDS v. 3 and PACC) 3 years later. All Wake Forest participants will receive an interim cognitive test (1.5 years) administered by telephone in between the two detailed cognitive assessments to assess interim changes in thinking and memory.

Brain MRI: MRI data will be acquired in accordance with multisite protocols including ADNI2, and the NINDS Common Data Elements recommendations. All images will be acquired on a 3T Siemens Skyra

MRI scanner with a high resolution 20-channel head/neck coil. Sequences include: T1 (for morphology), T2 FLAIR (to quantify white matter hyperintensities), DTI (to assess microstructural integrity of the white matter), BOLD/fMRI (for resting state brain connectivity) and pseudo-continuous arterial spin labeling (pcASL, for quantification of cerebral blood flow). Plus the addition of specialized MRI sequences to assess neurite integrity using neurite orientation dispersion and density imaging (NODDI) and cerebral microbleeds and microinfarcts in vivo using susceptibility-weighted Images (SWI). The brain MRI protocol will be the same as in the Atrial Fibrillation Study, with a couple of extra sequences. For Wake Forest participants also enrolled in the Atrial Fibrillation Study, the initial brain MRI will be completed 15-18 months after the Exam 6 visit, concurrently with the Atrial Fibrillation MRI.

Amyloid PET Imaging: The subset of study participants who agree to participate in the optional Brain Biomarker Sub study (40%, n=216) will receive amyloid imaging. Amyloid PET brain imaging procedure is similar to those used in Alzheimer's Disease Neuroimaging Initiative (ADNI) and several large multicenter clinical trials and observational studies. Participants will be injected with an intravenous bolus of up to 5-15mCi (370 MBq) (+/- 10%) of Pittsburgh compound B (PiB, over 5-10 seconds), followed by an uptake period of 40 minutes (+/- 10%) as it crosses the blood brain barrier and binds to fibrillar amyloid in the brain. Once the participant is positioned in the PET research scanner (GE 16-slice PET/CT Discovery ST Scanner), brain emission images will be acquired continuously for 30 minutes to quantify amyloid uptake analyzed in over 700 MRI-defined regions. The extent of Aβ deposition in the brain will be quantified by PiB uptake visualized by PET using standardized uptake volume ratio (SUVR) of 6 primary cortical areas (i.e., anterior cingulate, prefrontal cortex, lateral temporal cortex, posterior parietal cortex, precuneus cortex and anteroventral striatum) relative to the uptake in the cerebellum. The total radiation exposure of the PET scan is 0.347 rems, which includes exposure associated with the head CT completed prior to the PET. Participants will be monitored from the time of tracer injection until after the imaging session is complete for signs of rare adverse events. Participants will also be contacted 24-72 hours after the procedure by telephone to inquire about adverse events.

Lumbar CSF draw: In a subset of ancillary study participants who agree to participate in the optional Brain Biomarker Sub study (40%, n=216), a lumbar CSF draw will be performed to collect cerebrospinal fluid (CSF) for assay of AD biomarkers using the standardized and well-established ADNI protocol established in 2004. Within two weeks of the first Exam 6 visit, participants will undergo LP at our Kulynych Center Clinic at WFSoM (proximal to the MESA examination site). After an overnight fast, 25cc of CSF will be collected into polypropylene tubes using a small gauge (22-24g) atraumatic Sprotte needle, immediately frozen and then stored for future assay of levels of β-amyloid, phosphorylated tau protein, isoprostanes and other neuroinflammatory markers, and markers of metabolic dysregulation (Mayo Clinic panel).

Optional brain donation: Participants will be invited to participate in an optional brain donation program (separate from the Brain Biomarker Sub study) that will collaborate with the National Alzheimer's Coordinating Center (NACC) database. Donated brains will be added to our existing brain bank for future analyses of existing and evolving neuropathological markers that may provide additional important information regarding the role of early cardiometabolic risk that leads to AD pathological features. These donated brains will receive standard AD neuropathological evaluation to quantify burden of amyloid plaque, neurofibrillary tangles and other protein aggregates that lead to dementia as well as evidence of infarction and atherosclerotic plaque burden in the Circle of Willis.

Participants who are enrolled in the Tissue Sodium Ancillary Study will undergo the following (Northwestern only):

> **MRI of the Lower Extremities:** Imaging is performed on a 3.0T MRI scanner equipped with a knee coil to allow imaging of the lower extremities. Sodium and water content is imaged from

serial sequences with calibration against "standard" tubes. This is a well-tolerated procedure that takes approximately 30 minutes of scanner time to acquire images.

Participants who are enrolled in the Vitamin D Ancillary Study will undergo the following (Wake, Columbia, Hopkins, and Northwestern only):

Vitamin D/Placebo Randomization: Participants will receive either 2000 IU vitamin D3 or placebo daily for 16 weeks. Because it is considered a dietary supplement rather than a drug, vitamin D3 is not regulated by the FDA.

2.1.3 Exam 6 Screens/Forms

All forms will be administered using the Electronic Data Capture system using tablet PC, unless otherwise noted below.

2.1.2.1 Clinic Examination Data Forms and Questionnaire

1. Clinic Reception
2. Clinic Check-off Sheet
3. Seated Blood Pressure and Oximetry
4. Anthropometry
5. Medications (Interviewer-administered)
6. Medical History (Interviewer-administered)
7. Personal History (Self-administered)
8. Physical Function (Self-administered)
9. Urinary Symptoms (Self-administered)
10. Physical Activity (Self-administered)
11. KC Cardiomyopathy (Interviewer-administered)
12. Cognitive Function – CASI (Interviewer-administered)
13. Cognitive Function – Digit Span (Interviewer-administered)
14. Cognitive Function – DSST (computer screen and paper, Interviewer-administered)
15. Lung Questionnaire (Interviewer-administered)
16. MRI Exclusion Form (Interviewer-administered)

2.1.2.2 Reading Center Completion Forms

1. Phlebotomy and Urine Completion
2. Lab Processing (paper form)
3. Echo and Arterial Stiffness Completion
4. Spirometry Completion Form
5. Lung CT Exam Completion
6. AFib Study Completion Form
7. Six Minute Walk Test Completion Form
8. CPET Completion Form (Wake Forest-only)
9. Brain MRI Completion Form
10. PET MRI Completion Form (Columbia-only)
11. PET and CSF Completion Form (Wake Forest-only)

2.1.4 Surveillance Phone Call Forms and Questionnaires:

All forms are interviewer administered.

1. Participant tracking
2. Contact Log (paper form)
3. Contact Cover Sheet
4. General Health
5. General Health – Death
6. Death Information
7. Specific Medical Conditions
8. Specific Medical Procedures
9. Other Admissions

2.2 Exam 6 component Prioritization

Participants will be scheduled and received in the clinic with the expectation that they will undergo ALL procedures and complete ALL questionnaires for which they are selected. However, for those few participants who are unable to participate fully, the following guidelines should be followed.

Core Exam procedures (blood pressure, anthropometry, medications, phlebotomy) are to be prioritized above all ancillary study procedures.

Among Heart Failure components: echo is top priority, but participants can complete any of the other procedures if they refuse the echo (Six Minute walk, KCCQ-12, Physical Activity Questionnaire).

Among Atrial Fibrillation components: Participants who do not consent or are ineligible for either the heart patch monitor or the brain MRI should not complete any of the Atrial Fibrillation study components (heart patch monitor, brain MRI, CASI, Digit Span, Digit Symbol). Participant who consent to and perform the heart patch monitor and brain MRI can refuse the CASI, Digit Span and Digit Symbol.

Among MESA Lung/Lung Non-smoker components: Participants can complete either spirometry or Lung CT without agreeing to the other. Everyone should complete the Lung Questionnaire regardless of the spirometry and Lung CT.

Among MESA Memory components: All Wake Forest participants who consent to MESA Memory should complete the full cognitive battery regardless of MRI eligibility. All cognitive function testing will be completed at AD center (even those who do not consent to MESA Memory i.e. in AFib with CASI, Digit Span, Digit Symbol only).

3 CLINIC QUESTIONNAIRES & EXAMINATION

3.1 Pre-Exam Activities

3.1.1 Preparatory Activities Prior to Participant Arrival

Participants due to have an Exam 6 visit should be contacted at minimum one week prior to the planned appointment date. During this contact, the Eighteenth Follow-up Phone interview will be completed (see section 7), an Exam 6 appointment scheduled, and if applicable, appointments for additional exam components such as Lung CT. In some cases, the exam appointment may be scheduled by a different person during a separate call.

The purpose of completing the Follow-up 18 Phone Call prior to Exam 6 is to obtain the most recent information on the participants' health status as well as new events, and to schedule the exam.

Preparatory steps prior to clinic visits are the same as for MESA Exam 1–5. Print and/or review the **Contact History Sheet** (a summary of data from the participant's Exam 1–5 visits), as well as the Follow-up 18 Phone Call forms for completeness prior to the participant's arrival. The Contact History Sheet is available at https://www.uwchscc.org/MESAE5Reports/ under "Follow-up Reports 18." Any information missing should be noted and obtained.

3.1.2 Calendars, Reports, and Forms

3.1.2.1 The clinic manager should review the clinic visits scheduled for the following day and check that the necessary materials and equipment are in place.

3.1.2.2 For each participant scheduled for the following day, print the **Contact History Sheet** and have his/her most recent Surveillance Phone Call forms available.

3.1.2.3 There is no need to print a full set of Exam 6 forms that will be used for the Exam 6 visit. With the exception of a few forms, data should be entered directly into the data collection tablet. There is no need to record answers on paper. Any patient-specific forms that are printed should not be printed more than three days in advance, in order to capture changes in eligibility for study components. For each participant, gather all the forms required for a visit, including the informed consent and medical release, and place into the participant's binder. Make sure his/her ID matches the binder.

Paper copies of Exam 6 forms are available at https://www.mesa-nhlbi.org/MesaInternal/ClinicForms.aspx.

3.1.3 Supplies and Equipment

3.1.3.1 Set up vacutainer and aliquoting tubes for the basic Exam 6on the racks and attach the pre-printed labels to the tubes. Place any additional pre-printed labels near the

racks to be affixed the next day once consent for the related procedures has been obtained. Place all phlebotomy supplies on the blood drawing table (21 g, luer adaptor, vacutainer barrel, tourniquet, alcohol pad, gauze 2x2, surgical tape, Band-Aid).

3.1.3.2 Make sure that the examination rooms are clean and have clean linen.

3.1.3.3 Prepare the participants' gowns or (scrubs) and slippers.

3.1.3.4 Prepare the examination room for seated BP, anthropometry measurement, etc. Check all instruments that will be used for the examination.

3.1.3.5 Make sure a snack will be available for the participants.

3.1.4 Staffing

3.1.4.1 Prepare staff assignment sheet and make sure everyone knows his/her responsibilities. This is particularly important if you schedule a large number of participants on a given day.

3.1.4.2 If participants have been scheduled for CT, ultrasound, or MRI, make sure that the respective technicians have the participant schedule and forms, and that the scanning centers are ready to receive the participants.

3.1.5 Instruction to Participants before the Clinic Visit

Mail instructions to the participant 7–10 days before the clinic visit and explain them over the telephone when you schedule the visit. If possible, make a reminder call to the participant the day before the clinic visit and reiterate the instructions. (If the participant is acutely ill—e.g. "flu" or bronchitis—when you make this reminder call, *tell him/her not to come to the clinic*. Arrange to contact him/her again to reschedule when he/she has recovered.) Before the examination, make sure the participants understand the following instructions.

1. Participants must fast (except water) for at least 8 hours before the examination. Instruct them to consume dinner at least 8 hours before their scheduled appointment at the clinic. Only water and prescription medications are permitted from dinner until the start of the examination the next morning.

2. Participants should avoid heavy exercise during the 12 hours before the visit.

3. Participants should not smoke on the morning of the visit.

4. Participants should bring all current medications, both prescription and over-the-counter, including vitamin preparations, dietary supplements, injectable medicines such as insulin, inhalers, patches, and herbal remedies to the clinic. If the participant forgets to bring the medications, schedule another clinic visit to obtain this information or collect the information when the participant returns for imaging procedures.

5. Participants should bring the name and complete address of their personal physician or health plan, particularly if they wish to have examination results sent to that provider. They should also bring the current contact information for proxies and contact people.

3.2 MESA Exam 6 Guidelines

3.2.1 Examination Guidelines

The MESA Exam 6 will be scheduled over an 18-month period, beginning September 6, 2016. The examination will include several questionnaires and procedures (i.e., anthropometry, blood pressure measurement, fasting blood collections, etc.). Selected participants will be asked to wear a heart monitor patch for up to 4 weeks after the exam. We estimate that the complete examination including CT and/or MRI will require between 5 and 9 hours. The examination may be performed in one day or over several days. However, every effort should be made to perform all the components of the examination within a *four-week period*. Clinics may vary the exam sequence if needed.

1. A pregnancy test should be performed within 48 hours before the CT exam in all women of child-bearing potential who are scheduled to have a CT exam. This could be done in the clinic or in the Radiology Department.
2. Questionnaires and clinic procedures should be performed before the CT and/or MRI exams. Heart Monitor patches cannot be worn during CT or MRI.
3. Anthropometry and blood collection should be performed while the participant is fasting. (If participant is not fasting, record date and time he/she last ate or drank.) Blood pressure measurement should be done before venipuncture. CT, MRI, spirometry, and questionnaires do not require fasting.
4. Blood drawing should be done after an 8-hour fast and before 12:00 noon.

3.2.2 Examination Order

Guidelines for clinic order are listed below. Many elements are left to the discretion of the individual field center.

1. Anthropometry, blood pressure, and urine collection should be done immediately following the greeting and informed consent, and before venipuncture.
2. Resting blood pressures should be obtained after the subject has been in the seated position for at least five minutes.
3. Venipuncture should be performed in the fasting state after blood pressure measurement. If a participant comes to the clinic non-fasting, perform exam components that do not require fasting, and schedule the participant for another clinic visit for fasting blood collection.
4. Questionnaires and other exam procedures may be administered at any time during the examination. During the interviews, make every effort to avoid distractions, ensure privacy, and maintain confidentiality for the participant. Do not conduct interviews during the snack or in the waiting area in the clinic.

3.2.3 Guidelines for Examination of Diabetic Participants

1. Diet-controlled diabetics must fast overnight and are treated the same as non-diabetics.
2. Diabetics taking oral hypoglycemic medications or insulin must fast overnight (unless a bedtime snack was prescribed by their physician) and to come to the clinic without taking their hypoglycemic medication. They should bring their morning medication dose with

them to the clinic. Schedule all known diabetics taking oral hypoglycemic medications or insulin for examination as early as possible (before 9 a.m.). Draw fasting blood samples promptly on arrival at the clinic (after measuring blood pressure). Immediately following venipuncture, serve breakfast and instruct participants to take hypoglycemic medication as prescribed.

3.3 Participant Selection, Clinic Reception, & Clinic Check Off Screens

3.3.1 Participant Selection Screen

I. PURPOSE

The C*heck In and Reception p*rocess is the first thing the participant experiences upon arrival and sets the tone for the entire visit. It is the means by which the computer is prepared for entry of all subsequent information.

II. METHODS

1 General Instructions

1.1 Participants are selected from the Master List and added to the Checked In List as they arrive.

1.2 No forms or screens will be available for a given participant until he or she is checked in on the computer.

2 Specific Instructions for Completing the Participant Selection Screen

2.1 Print the face sheet for the participant in advance. It will include Participant ID, Name, Acrostic, Birth Date, QC ID, and Language spoken, and any procedures for which the participant has been selected.

2.2 The clinic reception process is very important in setting the participant's frame of mind for the rest of the exam day. Greet each participant warmly as soon as he/she arrives at the clinic. (If a participant arrives at the clinic acutely ill—e.g., "flu" or bronchitis—do not continue with the clinic examination. Make arrangements to contact him/her to reschedule the appointment after he/she has recovered.)

2.3 Enter the participant ID number and acrostic in the fields provided in the upper left part of the screen. (Typing of this information in full will avoid ID number errors and accidental selection of forms for the wrong participant). The language that the participant used at previous exams will be indicated in the "Select a Language" section. The language can be updated by selecting another language that the participant prefers to use.

2.4 Once the correct identifying information has been entered, click the Continue button and the participant will be added to the Checked In List, which is the large white area on the lower half of the screen.

2.5 The computer will go to the Check-off screen, which at this point will provide only the Check-in/Consent

3.3.2 Check-in/Consent (Clinic Reception)

I. PURPOSE

The *Check-in/Consent* process is the means by which important information is collected as soon as the participant arrives. The participant's consent status is recorded on this screen, so it must be completed before any procedures can be performed. In addition, it serves the purpose of informing clinic staff of specific procedures the participant has been selected to undergo.

II. DEFINITIONS

- Exclusion criteria: A list of medical conditions, procedures, events, and medications that exclude participation in the study. These are first applied to the respondent during the recruitment/screening process, and respondents who respond affirmatively to any of them are excluded from the study.

- Daily calendar: The list of participants scheduled for a given day. It lists the name, acrostic, recruitment/household ID, preferred language, and time of appointment. There is also a field to record participant status.

- Acrostic: A code used instead of the name for confidentiality reasons. It is composed of the first four letters of the last name, the first two letters of the first name, and gender indicator (F/M).

III. METHODS

1 General Instructions

1.1 Instruct the participant to read the informed consent documents carefully, answer the questions at the end, and sign it (see section on informed consent). Once the participant has completed and signed the informed consent, the specific permissions must be entered in the Clinic Reception screen (can be done while participant changes clothes). Following this, the procedures to be performed will be displayed on the computer and the clinic visit will begin.

1.2 Ask the participant if he/she has any questions. After you have answered any questions, give the participant a gown (or robe) and slippers and take him/her to a dressing room to change. Provide a locker or other safe place for the participant's clothing and any other items that need to be stored. This concludes the Clinic Reception phase of the clinic visit.

2 Specific Instructions for Completing the Check-in/Consent Screen The consent screen will first ask if the consent for the main Exam 6 has been signed. Once the participant has signed the consent, Click "Yes" and additional items will be displayed on the screen.

2.2 Ask the participant when he/she last ate or drank. Record the information in military (24:00 hours) time. Record the time, again in military time, when this form is being completed. The computer will calculate and display the amount of time elapsed since the participant last ate or drank.

2.3 Ask if the participant has been ill in the last seven days (e.g., cold, flu, fever, vomiting.) If the participant responds "Yes," inform the participant that the clinic exam cannot be completed at this time, thank him/her and reschedule another visit.

2.4 The Visit Date and check in time will automatically be filled with the current date and time; in the event that the actual visit took place on a different date, this field may be changed. Whenever possible, the second appointment date for Exam 6, if any, should be entered in the screen. If the second appointment cannot be scheduled at this time, a clinic staff person should go back and enter the second appointment date as soon as the information is available.

2.5 Associated permissions (HIPAA consent, medical records release, etc.) should be completed on this screen. Click Next Page to continue with the consent options.

Note about the HIPAA Release Form: HIPAA forms are needed for making medical records requests (during clinical events surveillance and ascertainment). Hospital records departments require a copy of the form (the more recent the better) before they will provide the requested medical records. Because a recent HIPAA form is best when requesting medical records, Field Centers often request a new one each time the participant comes into clinic.

HIPAA consent applies only to medical records release (as a requirement of the hospital providing the medical records) and does not limit or otherwise inform concerning participation in any other aspect of MESA. Participants sign the consent form (specific to a study exam) prior to each clinic exam. When they sign that consent form, they are agreeing to participate in the study as defined in that document. That document is necessary and sufficient for participation in the activities it describes and no other document (or failure to sign some other document) would be allowed to supersede the consent (including the HIPAA consent form).

2.6 Indicate participant consent for any ancillary study components for which he or she has been selected. On this screen, also indicate other permissions related to sharing of data and samples.

2.7 In the Local Medial/Hospital Identification Number field, record the participant's local hospital or medical record number (if any). This number is not required, however.

2.8 Once all consent responses have been entered, the remaining forms for the visit will be available.

3.3.3 Clinic Check Off Screen

I. PURPOSE

The *Clinic Check off Screen* is the means to ensure that all parts of Exam 6 are completed or scheduled. All Exam 6 forms, along with any ancillary study procedures for which the participant was selected and gave consent, will be displayed on this screen to allow for the tracking of the

participant's progress through Exam 6. Activities for checking out the participant at the end of the visit are also included on this screen.

II. METHODS

1 General Instructions

1.1 The screen is used to access all the data entry screens and is not accessible until the consent process has been completed.

1.2 Make sure to schedule dates for the participant's CT, and/or MRI, examinations, if appropriate.

1.3 Provide the participant with appointment reminders for the CT, and/or MRI exams, if appropriate.

1.4 Produce the Exit Report and give to participant.

1.5 Ask the participant if he/she has any questions at exam exit time. After you have answered any questions, thank the participant. This concludes the Clinic check off screen and the clinic visit day for the participant.

2 Specific Instructions

2.1 Print the Phlebotomy sheet and give/send to phlebotomist immediately.

2.2 To enter the data for a given procedure, click on that procedure on the Check-off screen; the selected computer form will open and will be ready for data entry.

2.3 Visit day progress order should be as shown on the screen for the first five steps/procedures. The remainder of the procedures could be performed in any order, but the heart monitor patch must be applied after the Lung CT scan.

2.4 For participants selected to have CT, and/or MRI in Exam 6, schedule CT and/or MRI examinations if you have not done so and prepare appointment reminders to give to the participant on exit. Record the date and time for the appointment/s in the appropriate field on the screen.

2.5 When the participant has finished the exam, check the list of forms to be sure all are Complete. If there are forms or procedures remaining, schedule a second visit to complete the exam.

2.6 Click Check Out/Exit. This screen will allow you to print an exit report for the participant.

3.4 Interviews - Questionnaires

3.4.1 Interviewing Guidelines and Techniques

I. GENERAL INTERVIEW INFORMATION

1. Interviewer bias is any preference or inclination that creates a systematic difference between responses obtained by different interviewers. It can be affected by:
   - Respondent's perception of the interviewer and his/her reaction to that
   - Interviewer's perception of the respondent and his/her reaction to that

2. Characteristics of a good interview

   2.1 The interviewer creates a friendly, but businesslike atmosphere.

   2.2 The respondent is at ease. Keep these factors in mind:
   - the respondent may view a female interviewer as less threatening.
   - the respondent may view a much older interviewer as judgmental.
   - the respondent may view a much younger interviewer as inexperienced

   2.3 The interviewer obtains the answer to the question that is asked by:
   - proper use of probes and repeating a question rather than interpreting it.

   2.4 The interviewer obtains clarification of confusing answers.

   2.5 The interviewer gives only neutral responses to the respondent's answers.

   2.6 The interviewer accurately records responses.

3. Specific skills required for interviewers

   3.1 The ability to ask questions at the correct pace and in a conversational tone.

   3.2 A thorough knowledge of the questions and response categories (this will keep the interview flowing smoothly).

   3.3 Knowledge of how and when to use probes.

   3.4 The ability to think as an interviewer and to temporarily put aside other roles (e.g., researcher, health care provider).

   3.5 The ability to maintain a positive attitude about the interview (this lets the respondent know that the interview is important).

   3.6 The ability to keep some level of control over the interview process (e.g., by rewarding the respondent for answering questions but not for other behavior).

II. INTERVIEWING TECHNIQUES

1 Standardized Interviewing Technique

1.1 MESA is a collaborative study being conducted through six field centers located throughout the United States. In order to produce data that can be considered collaborative, MESA study designers must develop and use standardized approaches to train interviewers and collect information about participants. Standardization is achieved by using scripts in training, training supervisors centrally, establishing qualifications for supervisors, reviewing collected data, taping and reviewing interviews, and, finally, observing interviewers in the field.

1.2 It is critically important that interviewers read the sections in this manual that are applicable to the questionnaires they will be administering.

III. THE INTERVIEW

All interviews should be recorded for quality control purposes if the participant is willing to allow it.

The following procedures are recommended for a successful interview:

1. Prior to the visit prepare all materials (e.g. appropriate report, identification, stamped self-addressed envelopes) that will be necessary for the interview.

2. Find an area where both you and the participant can talk and use the computer comfortably with minimal distractions.

3. Make sure that the participant understands the questions and that you are interpreting the responses accurately. Do this by restating what you think the participant is telling you. At the same time, be careful not to impose your interpretations on the interview questions or the participant's comments.

4. Convey your interest in the participant's thoughts and feelings, but do your best to keep him/her focused on the interview questions. When the participant strays from a question, try to use what he/she is saying to redirect the conversation back to the interview questions. Give positive reinforcement for direct answers. If necessary, set time limits at the outset of the interview to encourage the participant to stay on track.

5. Participants may try to convince you to answer certain questions for them. Let the participants know that you are interested in their answers.

6. Be aware of any hearing and vision impairments and their effects on the participant's understanding of the interview questions. If necessary, read the interview questions to participants who have visual impairments or limited reading ability.

7. Encourage, but do not force, participants to answer to all questions.

8. If non-participants are present during the visit, address the participant directly and do not encourage conversation with other parties. If necessary, ask that you and the participant be left alone for a brief time to complete the questionnaire.

9. Be able to adapt to interruptions. Let the participant know that you are willing to continue the

interview after the interruptions are completed.

10. Make the interview a positive experience for the participant. React favorably to answers and give compliments, when appropriate.

11. Give the participant clear information about when the next clinic visit will be conducted and follow through with the plans that you make.

3.4.2 Participant Tracking

I. PURPOSE

The Tracking Form is an update of information collected during previous surveillance interviews. It allows us to collect information (name, address, telephone number, and email address) on the participant, his/her health care provider(s), and any proxies or contacts he/she may designate. We will use this information to contact and communicate with the participant and his/her physician(s), proxies, or other contacts. In Exam 6, this information needs to be reviewed and updated with any changes since form completion during the most recent follow-up contact.

Participant tracking is typically administered as part of the follow-up interview process. If this has not occurred, it should be administered during the clinic exam.

II. MATERIALS/EQUIPMENT

The participant's personal address book or contact list, a phone book, and a computer will all be useful in helping participants find and record the information asked for during this process.

III. DEFINITIONS

Proxy. A person designated by the participant to knowledgeably answer questions about the participant, in the event that he/she is unable to answer. A proxy may, but does not have to, live with the participant and should be familiar with the status of the participant's health.

Contact. A person designated by the participant who may be relied upon to know the participant's whereabouts. A contact does not live with the participant, but always knows how to get in touch with him/her.

Second surname. Another last name used by the participant. Some participants (e.g., some members of the Hispanic population) use two last names. Also, some married participant use both their maiden name and their spouse's last name.

IV. METHODS

General instructions

1.1 The most recent data for this questionnaire is pre-printed on the Follow-up Call tracking form and was probably collected within the past month. If this is the case, tracking does not need to be repeated. The following instructions should be followed for participants whose 18th Follow-up Call interview has not yet been done.

1.2 Current information is essential for maintaining contact with participants and for communicating with their contacts and health care providers. You should emphasize to the participants that the tracking form needs to be updated as completely and accurately as possible. Also encourage participants to designate as proxies ***only*** those people who are familiar with the status of their health, because it is the proxies who will answer health-related questions if the participant is unable to.

1.3 The interviewer should verify all changes in the appropriate text fields in the tracking form. The participant should not use a nickname in place of a full, legal name. He/she should provide an area code with each phone number, even if within the local calling area. Boxes/spaces for items of information that are not applicable should be left blank. You should verify health care provider information using a local telephone directory. Obtain missing information over the phone.

Specific Instructions:

If the eighteenth follow-up surveillance interview was not done prior to the Exam 6 visit, ask the participant as outlined below to obtain participant information:

Section A. Participant Information:

Begin with, "***Please VERIFY your name, address, telephone number(s), and email address (if you have one).***" Note any changes in the text fields in the electronic form. Then ask the participant the following questions:

A1. *"Do you plan to change your name within the next year?"* (Note that this is question as well as questions A2 & A3 are not written in the form)
If "**no**", continue to question A2.
If "**yes**", ask, "***what will your new last name be?"***
Record the information in section "A", "Changes" column. Then, continue to the next question, A2.

A2. "*Do you plan to be out of this area for an extended period of time (a month or longer) within the next year?"*
If "**no**", continue to question A3.
If "**yes**", ask, "***approximately when will you leave and when will you return?"***
Record the month/year for both in section "A", "Changes" column. Then, continue to the next question, A3.

A3. *"Will there be a change in your local address within the next three months?"*
If "**no**", continue to section B, Contacts.
If "**yes**", ask, "***what will your new address be?"***
Record the street address, city, state, and ZIP code in section "A", "changes" column. Then, continue with section B.

Section B. Contacts Information:

"*Please update the following information on people who are familiar with the status of your health AND who could help us contact you, if necessary. If possible, please include one person who lives with you and one who does not."*

The participant should provide as much information as possible. Assist him/her, if necessary, in obtaining information. Record any changes regarding 'contacts' in the lines to the right of that particular 'contact'.

If a 'contact' was used to obtain the information on this form, the interviewer should check the

appropriate box under the name of the 'contact' person.

If the 'contact' used to obtain the information on this form is not listed among the current contacts, ask the 'contact' for his/her name, relationship to the participant, complete address, and telephone number. Fill the information in the spaces provided at the end of section B.

Encourage the participant to list contacts that do not all live at one address to obtain at least one contact that might be available if an entire family/household moves away.

For each Contact, ask the participant: **"May we send [Contact Name] a brochure or newsletter to tell him/her about MESA and his/her role as your contact person for MESA?"** Answer "Yes" or "No."

After each contact is reviewed, ask **"Which of your contacts is the best person to provide information about your health status or any hospitalizations that you may have had if we cannot reach you?"** Select the named contact from the drop down list, or choose "Any" or "None."

Section C. Health Care Providers Information:

"Please update the following information about your health care providers i.e. a clinic, doctor, nurse, or physician's assistant who provides your usual medical care?"

If the participant does not have a health care provider then the form is complete. Thank the participant.

If the participant has a health care provider, record any changes in the "Changes" column. The form is now complete. Thank the participant.

3.4.3 Personal History

I. PURPOSE

The Personal History questionnaire is used to collect information on socio-economic status (SES) and smoking and drinking habits, all of which are related to an individual's risk of cardiovascular disease.

II. METHODS

General instructions:

This is a **self-administered questionnaire**. Open the questionnaire on the data collection tablet for the participant and give brief instructions for completion. If the participant is unable to self-administer the questionnaire, then a MESA staff member will administer the questionnaire.

Ask the participant to try to answer all questions, unless instructed to skip the question. Remind him/her to request assistance from a staff member if anything is unclear. Most participants should be able to complete the questionnaire on their own. However, if the participant expresses or appears to have difficulty reading or comprehending the questions, offer to help and make arrangements for an interviewer administered version in the appropriate language.

Specific instructions:

- Instruct the participant to read the questions and their instructions carefully then fill out all questions, except those he/she is instructed to skip as a result of his/her response to a specific question.
- If he/she is unsure about an exact answer (e.g., for "average number of drinks per week"), tell him/her to give a best estimate.
- In questions where the participant is asked about number of times used, instruct him/her to fill in "00," if use is less than one.

Participant Information (questions 1–3)

The participant will begin the questionnaire with the introduction below:

This form is intended to collect information about your background and lifestyle which may impact your risk of cardiovascular disease. Please complete all items except those which you are specifically instructed to skip. If you are unsure about the answer to a specific question, please estimate the answer to the best of your ability. If you have a question about a particular item, ask a staff member for clarification.

1. ***A. At your last MESA exam, you described your current occupation as [current occupation]. Has your employment status changed?*** Choose Yes or No.
   If no, skip to question #2.
   If **yes**, continue with 1b.

1. **B.** ***Choose one of the following that best describes your current occupation.*** **Select a choice and fill in** the appropriate bubble.

2. Where do you usually go for medical care?
Participant should select (or write in) the place he/she goes most often for medical care. Participant should mark "other" only if the response clearly does not fit one of the given responses.

3. *To help pay for your medical care, do you now have:*
Participant should select (or write in) all applicable items.

Alcohol usage and smoking (questions 4–15)

All participants should answer questions 4, 9, 13, 14, and 15. People who drink should complete questions 5–8; former and current tobacco smokers should complete question 10 and 11; and current tobacco smokers should complete question 12. Marijuana or hashish user should complete questions 15a – e. If the participant feels uncomfortable with these questions, please reassure him/her that all collected information is strictly confidential. This section begins with the following introductory script:

The following questions are about smoking and alcohol use... They will help us better understand the role of smoking and alcohol use in the risk of cardiovascular disease.

4. *Do you presently drink alcoholic beverages?*
Choices are "yes" or "no". **If no, skip to question 9.**

5. *How many glasses of red wine do you usually have per week?*
(1 serving = 3.5 oz glass, 1 bottle = 750ml = 8 glasses)
Provide the average number of drinks per week. Record "00" if less than one glass of red wine per week.

6. *How many glasses of white wine do you usually have per week?*
(1 serving = 3.5 oz glass, 1 bottle = 750ml = 8 glasses)
Provide the average number of drinks per week. Record "00" if less than one glass of white wine per week.

7. *How many cans, bottles, or glasses of beer do you usually have per week?*
(1 serving = 12 oz glass, 1 bottle = 355ml = 1 glass)
Provide the average number of 12-ounce drinks per week. Record "00" if less than one serving of beer per week.

8. *How many drinks of liquor or mixed drinks do you usually have per week?*
(1 serving of liquor = 1.5-ounce shot-glass, or one mixed drink)
Provide the average number of drinks per week. Record "00" if less than one drink of liquor per week.

***9.* Which of the following best describes your current smoking status?**
Choose the appropriate response and fill in the bubble.
If never smoked, skip to question 13 and continue with the questionnaire.
These questions refer to cigarette smoking only. Vaping or e-cigarettes should not be included.

10. On the average of the entire time you smoked…

10a. How many cigarettes did you smoke per day?
Provide the number of cigarettes smoked per day.

10b. Did you inhale the cigarette smoke? Select a choice and fill in the appropriate bubble.

10c. In the morning, how much time usually goes by before you smoke your first cigarette? Enter the number of minutes.

11. Have you smoked cigarettes during the last 30 days?
Choose "yes" or "no" and fill in the bubble.
If no, skip to question 13. If yes, continue with question 11

12. On average, about how many cigarettes a day do you smoke?
Provide the number of cigarettes smoked per day and then skip to question 13.
The participant should record 00 if the average number of cigarettes per day is less than one. Make sure participants record the number of *cigarettes* per day. If a participant answers in number of packs per day, recalculate into number of cigarettes per day (1 pack = 20 cigarettes).

13. **Current non-smokers only:** ***During the past year about how many hours per week were you in close contact with people when they were smoking? (e.g., in your home, in a car, at work, other close quarters, etc.)***
Provide number of hours per week.
This question applies *only to current non-smokers and former users of any kind of tobacco product.* The goal of the question is to obtain information on passive exposure to *cigarette* smoke (excluding cigars, pipes, etc.) in any type of close quarters during the past 12 months. Record the number of hours in a *typical* week; do not include isolated or atypical situations, such as holiday gatherings or short-term house guests who smoke. If participants do not remember the exact amount of time, ask them to give their best estimate. Record 00 if participant was exposed to less than 1 hour of cigarette smoke per week.

14. Did anyone smoke in your residence in the past 12 months? (This includes you)
Choices are "yes" or "no". **If no, skip to question 15.**

14a. ***On average, how often did someone smoke in your residence in the past 12 months?*** Click on the most appropriate choice.

14b. ***On average, how many cigarettes per day were smoked in the residence by each smoker in the past 12 months?***
Enter the number of cigarettes per day smoked by each of up to three smokers. If participant is a smoker, smoker 1 should be the participant.

14c. ***On average, how many cigars per day were smoked in the residence by each smoker in the past 12 months?***
Enter the number of cigarettes per day smoked by each of up to two smokers.

If participant is a smoker, smoker 1 should be the participant.

The following questions ask about the use of marijuana or hashish. Please remember that your answers to these questions are strictly confidential. Marijuana is also called pot or grass. Marijuana is sometimes smoked either in cigarettes, called joints, or in a pipe. It is also sometimes cooked in food. Hashish is a form of marijuana that is also called hash. It is usually smoked in a pipe.

15. Have you smoked more than 100 marijuana or hashish joints/pipes in your life?
Choices are "yes" or "no". **If no, skip to question 16.**

15a. ***Have you ever smoked marijuana or hashish regularly (at least once per month)?*** Choices are "yes" or "no". If no, skip to question 16.

15b. ***For how many years did you smoke marijuana or hashish regularly?***
Enter the number of years.

15c. ***During the time that you smoked marijuana or hashish regularly, how often would you usually smoke it?***
Click on the most appropriate choice.

15d. ***On the days that you smoked marijuana or hashish, how many joints or pipes would you usually smoke?***
Enter the number of joints or pipes.

15c. ***How long has it been since you smoked marijuana or hashish?***
Click on the most appropriate choice.

16. ***For how many years has an indoor open fire with wood, crop residues, dung, coal, or coke been used in your home as a primary means of heating or cooking?***
Enter the number of years. An indoor **open** fire refers to an indoor fire that is visible, and is *not* completely enclosed by a solid material (e.g., glass, steel, cast iron)."

17. ***For how many years has an indoor enclosed fire with wood, crop residues, dung, coal, or coke been used in your home as a primary means of heating or cooking?***
Enter the number of years. An indoor **enclosed** fire refers to an indoor fire that is completely enclosed in a solid material (i.e. in a wood-burning stove or 'insert' make out of glass, steel, cast iron).
If 0, skip to question 18.

The following questions have to do with family finances. We know from other research that financial strain is common and very important to consider in understanding people's health. The following questions will be used to help give us a picture of the various financial situations experienced by persons participating in the MESA study. Any information you provide is strictly confidential and will be used for research purposes only.

18. Below is a list of income groups. Please tell me which group best represents your total combined family income for the past 12 months. This includes the total income, before taxes, earned in the past year by all family members living with you. Please include

money from jobs; net income from business, farm, or rent; pensions, dividends, welfare, social security payments, and any other money received by you or any other family member living with you.
Click on the most appropriate choice.

18a. ***Including yourself, how many people are supported by the income listed in the previous question?*** Write a number in the box provided.

18.b ***How many of these are:***
- ***Children under 18?***
- ***Adults 65 and over?***

Write a number in each box. Enter 00 if no one in that age category is supported by the given income.

At this point, the participant has completed the questionnaire. MESA staff will review the questionnaire for completeness, clarify any question that were not answered, and complete the questionnaire by filling out the box "For MESA Field Center Use Only:"

- If the form was self-administered, check for completeness.
- Mark if form was self-administered or interviewer-administered.
- Record Interviewer or Reviewer ID.
- Record Data Entry ID.

3.4.4 Medical History

I. PURPOSE

The Medical History identifies the participant's medical conditions and provides other information that may:

- be used to adjust for co-morbidity;
- characterize the participant's access to medical care

II. METHODS

General instructions:

This is an **interviewer-administered** questionnaire. Questions should be read to the participant verbatim as they appear on the form to ensure standardization. In addition, any introductory and transitional wording should be read verbatim.

For most questions, possible responses are "Yes", "No," "Don't Know," and/or "Not Applicable" or "N/A" (not applicable). A few other questions have choices as indicated. The interviewer should read all choices to the participant and have the participant choose the appropriate response/s for each question.

Do not probe to make interpretations about a participant's specific symptoms. Ask questions as written and record answers as given by the participant.

Specific instructions:

Begin the questionnaire by reading to the participant the following introduction:
The following are some questions about your medical history. Questions refer to things that happened since your last MESA visit on _____. Please answer to the best of your knowledge.

1. ***In general, would you say your health is:***
   Choose the appropriate response to the best estimate.

2. ***How would you say your health currently compares with other persons of your age?***
   Select "better," "same," or "worse." Choose the appropriate response to best estimate.

The following two questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

3. ***MODERATE ACTIVITIES, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf***
   Choose the appropriate response to best estimate.

4. ***Climbing SEVERAL flights of stairs***
   Choose the appropriate response to best estimate.

During the PAST 4 WEEKS, have you had any of the following problems with your work or other regular activities AS A RESULT OF YOUR PHYSICAL HEALTH?

5. ***ACCOMPLISHED LESS than you would like***
   Choose YES or NO.

6. ***Were limited in the KIND of work or other activities***
   Choose YES or NO.

During the PAST 4 WEEKS, were you limited in the kind of work you do or other regular activities AS A RESULT OF ANY EMOTIONAL PROBLEMS (such as feeling depressed or anxious)?

7. ***ACCOMPLISHED LESS than you would like***
   Choose YES or NO.

8. ***Didn't do work or other activities as CAREFULLY as usual***
   Choose YES or NO.

9. ***During the PAST 4 WEEKS, how much did PAIN interfere with your normal work (including both work outside the home and housework)?***
   Choose the appropriate response to best estimate.

The next three questions are about how you feel and how things have been DURING THE PAST 4 WEEKS. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the PAST 4 WEEKS

10. ***Have you felt calm and peaceful?***
    Choose the appropriate response to best estimate.

11. ***Did you have a lot of energy?***
    Choose the appropriate response to best estimate.

12. ***Have you felt downhearted and blue?***
    Choose the appropriate response to best estimate.

13. ***During the PAST 4 WEEKS, how much of the time has your PHYSICAL HEALTH OR EMOTIONAL PROBLEMS interfered with your social activities (like visiting with friends, relatives, etc.)?***
    Choose the appropriate response to best estimate.

14. ***Are you unable to walk due to a condition other than shortness of breath?***
    If Yes, indicate the nature of the condition and skip to question 19.

15. ***Do you get short of breath when hurrying on the level or walking up a slight hill?***
    Choose YES, NO or DON'T KNOW.

16. ***Do you walk slower than people of the same age on the level because of breathlessness or have to stop for breath when walking at my own pace on the level?***

Choose YES, NO or DON'T KNOW.

17. ***Do you stop for breath after walking about 100 yards or after a few minutes on the level?*** Choose YES, NO or DON'T KNOW.

18. ***Are you too breathless to leave the house or breathless when dressing?*** Choose YES, NO or DON'T KNOW.

19. ***Are you taking aspirin on a regular basis?*** Examples of "regular" are daily, every other day, and weekly. If the participant says less than once a week, record "no." Select YES, NO or DON'T KNOW. If yes, ask the following: *"**how many days a week?"*** Record number of days/week.

20. ***Do you usually bring up phlegm from your chest on most days for 3 or more months during the year?*** Select YES or NO. If Yes, answer ***For how many years have you had this cough?*** Enter number of years.

21. ***Do you usually have a cough on most days for 3 or more months during the year?*** Select YES or NO. If Yes, answer ***For how many years have you brought up phlegm from your chest like this?*** Enter number of years.

22. ***In the last 12 months, have you had wheezing or whistling in your chest?*** Select YES or NO. If NO, skip to question 23.

    22a. ***In the last 12 months, how often have you had this wheezing or whistling? (Read the options)?*** Choose the most appropriate response.

    22b. ***In the last 12 months, have you had an attack of wheezing or whistling in the chest that has made you feel short of breath?*** Select YES or NO.

Questions 23 and 30 pertain to conditions the participant has been told he or she has by a doctor. The participant should choose "Yes" or "No" if he/she is fairly sure about the diagnosis and "Don't Know" if he/she believes he/she might have been told about the diagnosis but is not sure. If the person is cared for primarily by a health care provider other than a physician, such as a nurse practitioner, try to determine that the diagnosis was made in a medical setting and, if so, include the response. Any conditions that have been previously reported will be skipped.

Has a doctor ever told you that you have any of the following conditions?

23. ***Diabetes*****?**
    Choose YES, NO or DON'T KNOW.
    If YES to Diabetes, ask ***Are you currently taking medication for your diabetes?***
    If YES to medications, ask ***What kind of medicine are you taking for your diabetes?***
    Choose the appropriate response.

24. ***High blood pressure*****?**

Choose YES, NO or DON'T KNOW.

25. ***High cholesterol*?**
Choose YES, NO or DON'T KNOW.

26. ***Emphysema or Chronic Obstructive Pulmonary Disease (COPD)*?**
Choose YES, NO or DON'T KNOW.

27. ***Asthma*?**
Choose YES, NO or DON'T KNOW.
If YES, answer question 27a:

27a. ***For some people, asthma symptoms completely go away as they grow older. Later in life, however, asthma may recur. At approximately what ages did you experience each of the following events? (Read the options)*** Enter approximate age for each event, or indicate ***As a child (age not know) or Don't know*** as appropriate.

28. ***Atrial Fibrillation*?**
Choose YES, NO or DON'T KNOW.

29. ***Kidney Disease*?**
Choose YES, NO or DON'T KNOW.
If YES, answer question 29a:

29a. ***Did you have kidney failure, require dialysis or transplantation?*** Select YES or NO.

30. ***Has your doctor or health care provider ever told you that you had a kidney stone?***
Choose YES, NO or DON'T KNOW.
If YES, answer question 29a and 29b.

30a. ***How old were you during your first stone episode?*** Enter age in years.
30b. ***How many kidney stones have you had in the past?*** Choose the appropriate response.

If NO, go to question 31:

31. ***Did you pass a kidney stone since your last MESA visit?***
Choose YES, NO or DON'T KNOW.
If YES, answer question 31b.

31a. ***How many kidney stones have you had in the past?*** Choose the appropriate response.

32. ***Have any first degree relatives (i.e. mother, father, siblings, children) ever had a kidney stone?***
Choose YES, NO or DON'T KNOW.

33. ***Has a dentist ever told you that you had periodontitis, or that you had bone loss around your teeth?*** Choose YES, NO or DON'T KNOW.

34. ***Has a dentist ever told you that you had periodontitis, or that you had gum disease?***
Choose YES, NO or DON'T KNOW.

Question 35a will only be answered if the participant has previously reported using a pacemaker or implanted cardioverter defibrillator:

35a. ***Based on your prior MESA interviews, I see that you have had a [pacemaker or other device type from investigation] implanted on Month/Day/Year [CC inserts date of insertion based on event investigation]. Is that right? Do you still have an implanted device?***
Choose YES, NO or DON'T KNOW.
If YES, answer questions 35c and 35d.
If NO or DON'T KNOW, go to question 36 for women. Men are finished with the questionnaire.

Question 35b will only be answered if the participant has NOT previously reported using a pacemaker or implanted cardioverter defibrillator:

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35b. ***Do you have an implanted cardiac pacemaker or an implanted cardioverter-defibrillator (ICD)?***
Choose YES, NO or DON'T KNOW.
If YES, answer questions 35c and 35d.
If NO or DON'T KNOW, go to question 36 for women. Men are finished with the questionnaire.

35c. ***Is it a cardiac pacemaker or a cardioverter-defibrillator?***
Choose the appropriate response.

35d. ***What doctor do you see for regular evaluation of that device?***
Enter the name and location (City and State) of the health care provider.

<u>At this point, men are done with the questionnaire.</u>

<u>Reproductive History</u>
—for women only—

36. ***Between the ages of 16 and 40, about how long was your average menstrual cycle (time from first day of one period to the first day of the next period)?***
Choose the appropriate response.

37. ***Have you ever had hot flashes or night sweats related to menopause?***
Choose YES, NO or DON'T KNOW.
If YES, answer questions 37a-c.

37a. ***At what age did the hot flashes or night sweats start?*** Enter age in years.

37b. ***At what age did the hot flashes or night sweats stop?*** Enter age in years.
37c. ***Were the symptoms:*** Choose the appropriate response.

38. ***At what age did you go through menopause (change of life)?***
Enter age in years. This question will be skipped if the information was previously reported.

39. ***Did you go through menopause naturally, or as a result of surgery (hysterectomy or removal of both ovaries)?***
Choose the appropriate response.

Determine if participant has previously reported removal of both ovaries. If yes, skip to question 40c. If this has not been previously reported, begin with question 40.

40. ***Have you had surgery to remove your ovaries?***
Removal of the ovaries might have been in conjunction with a hysterectomy.
If NO or DON'T KNOW record and skip to question 41.
If YES ask the following:

40a. At what age?" Record the response in the boxes.
40b. How many ovaries were removed?" Select 1 or 2.
40c. What was the reason for removing your ovaries? Select all that apply.
40d. Were you still having menstrual periods at the time of the surgery?
If NO or DON'T KNOW go to question 41.
If YES ask the following: ***How long before surgery did your periods stop?*** Enter number and select months or years.

Determine if participant has previously reported hysterectomy. If yes, mark box and skip to question 41b. If this has not been previously reported, proceed with question 41.

41. ***Have you have a hysterectomy (surgery to remove your uterus/womb)?*** Hysterectomy might have been done in conjunction with removal of the ovaries.
If NO or DON'T KNOW record and skip to question 42.
If YES ask the following:

41a. At what age?" Record the response in the boxes.
41b. What was the reason for removing your uterus? Select all that apply.
41d. Were you still having menstrual periods at the time of the surgery?
If NO or DON'TKNOW go to question 42.
If YES ask the following: ***How long before surgery did your periods stop?*** Enter number and select months or years.

42. ***Have you ever used birth control pills?***
If NO or DON'T KNOW record and proceed to question 43.
If YES ask the participant at what age she stopped taking birth control pills. Keep in mind that she may have started and stopped several times.

43***. Since your last MESA visit, have you taken hormone replacement therapy?***
If NO **questionnaire completed.**
If YES, ask the following:

a. ***Are you currently using hormone replacement therapy?"***
If YES ***at what age did you begin?*** Record age and proceed to question b.
If NO, ***at what ages did you take hormones?*** Provide age started and age stopped and proceed to question b.

b. ***Which type of therapy were you on?***
Select "estrogen alone," or "estrogen with progestin," or "other types of hormone replacement"
(Common estrogen-only preparations are Premarin or Estratab; common estrogen+progestin regimens are Premarin plus Provera, Estratab plus Provera, Prempro, or Premphase.)

After completing the form, a technician should check to make sure all questions were answered and attempt to complete by asking the participant about any skipped questions.

3.4.5 PROMIS Physical Function

I. PURPOSE

PROMIS® (Patient-Reported Outcomes Measurement Information System) is a set of person-centered measures that evaluates and monitors physical, social, and emotional health in adults and children. It can be used with the general population and with individuals living with chronic conditions.

Physical Function measures self-reported capability rather than actual performance of physical activities. This includes the functioning of one's upper extremities (dexterity), lower extremities (walking or mobility), and central regions (neck, back), as well as instrumental activities of daily living, such as running errands.

II. METHODS

General instructions:

This is a **self-administered questionnaire**. Open the questionnaire on the data collection tablet for the participant and give brief instructions for completion. If the participant is unable to self-administer the questionnaire, then a MESA staff member will administer the questionnaire.

- PROMIS self-report measures are intended to be completed by the respondent without help from anyone else.
- If respondents are unable to answer on their own, have someone else (a "proxy") report on their behalf. Respondents requiring a proxy may include: people in the early stages of dementia who may not recognize the extent of their impairment, people with cognitive or communication deficits, and people with severe disease burden.
- Keep respondents' privacy in mind, but have staff readily available to help with any technology issues that may arise.
- It is acceptable for staff to define a term (e.g., "nausea"), but not to define a concept where the respondent's subjective interpretation is the goal of the question (e.g., "quality of life").

Specific instructions:
Begin the questionnaire by opening the PROMIS Physical Function Questionnaire on the data collection tablet and handing the tablet to the participants. Explain that the questionnaire is designed to be completed without the help of study staff, but that you will be available if questions arise.

Please respond to each item by marking one box per row.

The responses for the first 5 questions are: Not al all, Very little, Somewhat, Quite a lot, Cannot do.

1. ***Does your health now limit you in doing vigorous activities, such as running, lifting heavy objects, participating in strenuous sports?***
   Choose the appropriate response.

2. ***Does your health now limit you in walking more than a mile?***
   Choose the appropriate response.

3. ***Does your health now limit you in climbing one flight of stairs?***
   Choose the appropriate response.

4. ***Does your health now limit you in lifting or carrying groceries?***
   Choose the appropriate response.

5. ***Does your health now limit you in bending, kneeling, or stooping?***
   Choose the appropriate response.

The responses for the last 5 questions are: Without an difficulty, With a little difficulty, With some difficulty, With some difficulty, With much difficulty, or Unable to do.

6. ***Are you able to do chores such as vacuuming or yard work?***
   Choose the appropriate response.

7. ***Are you able to dress yourself, including tying shoelaces and doing buttons?***
   Choose the appropriate response.

8. ***Are you able to shampoo your hair?***
   Choose the appropriate response.

9. ***Are you able to wash and dry your body?***
   Choose the appropriate response.

10. ***Are you able to get on and off the toilet?***
    Choose the appropriate response.

3.4.6 Medications

I. BACKGROUND AND RATIONALE

The Medications Form is designed to enable collection of data on participants' use of all types of medications, both prescription and non-prescription, including supplements. Information about participants' use of medications is collected at the initial (baseline) clinic visit and at follow-up visits. The participant is asked to bring to the clinic containers for all medications used during the two weeks prior to the visit. The interviewer then transcribes the name of each medication, its strength, and for prescription medications, frequency of administration from the containers onto the data collection form. As the information is transcribed, the interviewer queries the participant about actual usage of each medication.

Collecting this information will allow us to describe medication use and any changing patterns of use over time, and may help us ascertain the effect of medications on the progression of atherosclerosis in this study population. It will be important to know what medications each participant is taking, in order to assess and perhaps attempt to explain subsequent participant events and any change in the degree of disease detected at follow-up visits.

II. MATERIALS AND EQUIPMENT

Current version of the Physician's Desk Reference (PDR)
Printed list of participant's previous medications, collected at most recent prior visit.

III. DEFINITIONS

Time frame: All prescription and over-the-counter medications and supplements used during the *two weeks prior* to the clinic visit should be included.

Prescription medication: Medication for which a prescription was written by a physician or physician assistant and dispensed by a pharmacist or a physician.

Non-prescription or over-the-counter medication: Medication or supplements purchased without a prescription.

It should be noted that occasionally a physician would write a prescription for a non-prescription medication. In that case, the medication should be recorded as prescription. If, however, the physician *recommends* a medication, rather than actually writing a prescription for it, it should be recorded as non-prescription.

IV. METHODS

This is an **interviewer-administered questionnaire**. Questions should be read to the participant verbatim as they appear on the form to ensure standardization. In addition, any introductory and transitional wording should be read verbatim.

Obtaining medication containers. A letter is sent to the participant before the clinic visit that includes instructions regarding medication containers. The participant is asked to bring to the

clinic containers for all supplements, prescription, non-prescription medications and herbal medicines taken during the two weeks prior to the clinic visit.

Medication use interview. Prior to beginning the interview, place all medications in front of the participant. You will have a list of medications the participant reported at the previous exam. Check each medication brought in by the participant against this list. For each one that appears on the list, check the "Keep?" box at the left of that particular medication. *IMPORTANT NOTE: You can only mark a medication to keep if the name and strength are identical to what appears on the list.* Any other medications must be recorded as new medications, either in the spaces provided at the bottom of the list or on the standard Medications form.

When asking the participant about a particular medication, show the container to the participant, keeping the other medications in view. Always conclude the interview by asking the participant if any other medications have been taken during the previous two weeks. If the participant remembers other medications, record the name, strength and frequency administered for each one in as much detail as possible. *If you are unsure about the accuracy of the participant's responses, schedule a telephone interview to verify the prescription label information.* At the end of the visit, make sure to return all medications and other personal belongings to the participant. Guidelines for completing the Medications Form follow:

Section A. Medication Reception

As you know, the Multi-Ethnic Study of Atherosclerosis will be describing all medication its participants are using, both prescription and over-the-counter. These include pills, liquid medications, skin patches, eye drops, creams, salves, inhalers (puffers), and injections, as well as cold or allergy medications, vitamins, herbal remedies, and other supplements. The letter you received about this appointment included a plastic medications bag for all your current medications and asked you to bring them to the clinic. Have you brought this bag with you? Are these all the medications that you have taken in the past two weeks?

If "yes", ask to see the medications and record the information in the boxes in Section B of the form or in the appropriate area at the bottom of the list.
If NO, make arrangements to obtain medications at another time but record any available information as described above as best possible by interviewing the participant for the information.
If "refused", record reason for refusal in Comments Section
If "took no medicines", *form is complete.*

1. Medication containers may be unavailable to the interviewer for a variety of reasons. Regardless of the reason, however, the interviewer should make an attempt to obtain the information necessary to complete the medication form.

2. If the participant forgets to bring medication(s) to the clinic, the interviewer is responsible for obtaining the necessary information at a second visit or by telephone interview.

3. If the participant remembers additional medication(s) taken during the previous two weeks, the interviewer should record as much information about the medication as possible at the time of the visit and then follow up with a telephone interview to check for accuracy and completeness.

4. If the medication containers are unavailable because the participant refuses to bring them to the clinic, the interviewer should document the reason for refusal in the Comment Section. The interviewer should then attempt to obtain the participant's cooperation in obtaining the data, either by a second visit or by telephone.

5. If the participant brings a list of medications, instead of the medication containers, record all pertinent information from the list and note this in the Comments Section. If the interviewer has any doubt about the accuracy of the list, a follow-up telephone call should be scheduled to confirm what has been recorded.

6. Whenever medication information is collected by phone or from a list brought in by the participant instead of from the prescription container, try to verify the spelling of the name and the strength prescribed by referring to the PDR or some other source of accurate medicine listings.

Section B. Prescription Medications

1. The interviewer transcribes the name and dosage information from each medication container onto the Medications Form using the following guidelines:

2. Medication name. Print complete medication name using block capital letters. Record all characters and numbers referring to strength as well as the units. The name of each medication should be recorded *exactly* as it is written on the container. Medication names that are misspelled or otherwise recorded incorrectly will cause data entry and analysis problems because they will not match the drug database. Do not record flavors of products or whether the preparations are sugar-free or sodium-free. If the medication name is longer than the 20 spaces available on the form, transcribe as much as possible and then record the complete medication name in the Comments Section. If it is not possible to transcribe the medication name, insert an asterisk (*) and explain in the Comments Section.

3. Combination Medications contain two or more drugs. Some combination medicines, such as Dyazide, come in only one fixed combination (hydrochlorothiazide 25mg and triamterene 50mg). These combination medicines do not usually list strength. Record the name in the "Medication Name" space and leave the "Strength" column blank.

Other combination medications are available in more than one fixed dose combination. For example, Inderide, which is a combination of propranolol and hydrochlorothiazide, is available as propranolol 40mg and hydrochlorothiazide 25mg, or propanolol 80mg and hydrochlorothiazide 25mg. These combination medications usually list the strength as in "Inderide 40/25" or "Inderide 80/25." For these medications, record the name in the "Medication Name" space and the strength combination (e.g., 40/25) in the "Strength" space.

4. Strength.

- Record the strength of each medication in milligrams (mg) whenever possible, beginning with the first space on the left in the "Strength" column.

- When strength is in milligrams, *do not* record the abbreviation "mg;" record *only* the amount of drug (e.g., if the strength is "250 mg," record only "250").

- When strength is not recorded as milligrams, record *all* numbers, digits, and characters used to denote strength, including:

  - milliliter (ml)
  - per milliliter (/ml)
  - milliequivalent (mEq)
  - hour (hr)
  - per hour (/hr)
  - percent (%)

- When strength is separated by a "/" (e.g. 40/25, as in combination medications), record them in this section.

- When strength is given in grains (gr), convert to milligrams using the following formula: (number of grains) x 65 = number of milligrams. (1 gr = 65 mg.)

- When strength is given in micrograms (mcg or µg), convert to milligrams using the following formula: (number of micrograms) ÷ 1000 = number of milligrams. (1000 mcg = 1 mg.)

- When strength is given in milligrams per milliliter (mg/ml), as is often the case with liquid medicine, record as in the following example: Ampicillin 125 mg / 5 ml is recorded as "125/5 ml." (Note omission of "mg.")

- When strength is given as a percentage (%), record as such.

- When strength is given in units (U) or units/milliliter (U/ml), as is often the case with Insulin, record as in the following examples: "100/ml" or "100U/ml."

- When it is not possible to record the strength, such as when it is not recorded on the medication label, record an asterisk (*) and explain in the Comments Section.

- Note: Do not record in the "Strength" column the number or quantity of medication items (e.g., number of tablets or tablespoons). See "Number Prescribed," below.

5. Number Prescribed. This column is designed to capture information on the number of pills (or milliliters, drops, units, etc) *prescribed* as opposed to the number actually taken. Information on the number prescribed should be taken from the medication labels.

- Record the total number of medication items (e.g., "tablets") prescribed per the given time period (e.g., day, week, or month). Circle the appropriate letter in the "Number Prescribed" column to show whether the prescribed number is per day (D), per week (W), or per month (M).

- If the instructions include a range in the number of medication items and/or times/day (or week or month) they are to be taken, record the lowest number of each. For example, if

the label says, "take 1–2 tablets 3–4 times per day," record as "3 tablets/day" (i.e., 1 tablet 3 times/day = 3 tablets/day); or, if the label says, "take 1–2 tablets every 4 hours while awake," record as "5 tablets/day" (i.e., 1 tablet every 4 hours from 7 a.m. to 11 p.m.).

- When it is not possible to record the number of medication items prescribed per day, record an asterisk (*) and explain in the Comments Section.

- When instructions read "take as directed," record "1" as the number prescribed per day.

- When dosing instructions are complex (e.g., "take 1 pill every other day, alternating with 2 pills every other day"), record the *average* number per day (or week or month).

6. Number Prescribed: Specific Medications.

- Pill/Tablets/Capsules: Record the total number prescribed per day (or week or month).

- Solutions: Record the total number of milliliters prescribed per day (or week or month). Use the following conversions:
- 1 teaspoon = 5 ml
- 1 tablespoon = 15 ml
- 1 ounce = 30 ml

- Eye Drops: Record the total number of drops prescribed per day (or week or month). For example, "two drops in right eye, three times a day" = 6 drops, or "one drop in each eye, twice a day" = 4 drops.

- Inhalers (puffers): Record the total number of sprays or puffs prescribed per day (or week or month).

- Insulin: Record the total number of units injected per day (or week or month).

- Creams/Lotions/Ointments: Record the total number of applications prescribed per day (or week or month).

- Patches: Record the total number to be applied to the skin per day (or week or month).

- Nitroglycerin Ointment: Record the total number of inches to be applied to the skin per day (or week or month).

7. PRN ("as needed") Medication is generally used for allergy, pain, or sleep; sublingual nitroglycerin is also used PRN.

- Use the "PRN Medicine?" column to indicate whether the medication is prescribed to be taken on an "as needed" basis.

- Circle "Y" only when the prescription instructions state "as needed," "when needed," "if needed," etc.

- Circle "N" when the prescription instructions do *not* use the words "as needed," "when needed," "if needed," etc.

- The words "as directed" do *not* mean the same as "as needed."

8. Number Taken. This column is designed to capture information on the number of pills (or milliliters, drops, units, etc) *actually taken* as opposed to the number prescribed. Information on the number *actually taken* should come directly from the participant. People do not always take their medications as prescribed. It is important to record information about both the number prescribed and the number actually taken as accurately as possible.

- Ask the participant, **"On the average during the last two weeks, how many of these pills (or other medication items) did you take a day (or week or month)."**

- Record the average number of pills (or other medication items) taken per day (or week or month) during the last two weeks.

- Code "0" if none of the medication items was taken during the previous two weeks. This includes instances in which a prescription was filled but none of the medication was taken during the past 2 weeks.

- When the number taken cannot be determined, record two asterisks (**) and explain in the Comments Section.

- Circle the appropriate letter (D, W, M) to show whether the prescribed medication was taken per day, per week, or per month.

C. Over-the-Counter Medications

Complete this section following instructions for Section B, above, but disregarding the instructions pertaining to "Number Prescribed" and "PRN Medication."

D. Chinese and Other Traditional Medicines

Whenever possible, *in the comment section*, record traditional medicine use in the same fashion as with other medicine i.e. name, dosage, frequency. If this is not possible, record the *purpose* of the medicine.

3.4.7 Physical Activity

I. PURPOSE

The MESA Typical Week Physical Activity Survey (TWPAS) is designed to identify the time and frequency spent in various physical activities during a typical week in the past month. It is a Self-Administered form. The rationale for the selected time frame of a typical week in the past month is the intention to capture typical activity patterns in one's daily life.

The survey has 20 question items in categories of household chores, lawn/yard/garden/farm, care of children/adults, transportation, walking (not at work), dancing and sport activities, conditioning activities, leisure activities, occupational activities and volunteer activities.

II. METHODS

1. General Instructions

1.1 This survey is a **self-administered** questionnaire. Provide the participant with a laptop computer with the Physical Activity Survey screen already open and give brief instructions for completion. Ask the participant to try to answer all questions. Remind him/her to request assistance from a staff member if anything is unclear. Most participants should be able to complete the survey on their own.

1.2 Instruct participant to give the laptop back to the interviewer when the form is completed. (Instruction will also be displayed on screen).

1.3 If the participant expresses or appears to have difficulty reading or comprehending the questions, or if he or she has difficulty using the computer, offer to help and make arrangements for an interviewer administered version in the appropriate language. If interviewer administered, questions should be read to the participant verbatim as they appear on the form to ensure standardization. In addition, any introductory and transitional wording should be read verbatim.

1.4 For the majority of the questions, response choices are ―Yes‖ or ―No‖. Record the response given by the participant. If ―Yes, ask for the number of days per week, amount of time in hours and/or minutes per day the participant spent doing the particular activity.

2. Specific Instructions

Items to be completed by the interviewer:

The ***Date*** will be pre-filled. Please verify that the date the form was completed is correct. For example, April 1, 2010 would be entered as 04/01/2010.

ID# & **Acrostic** will be pre-filled. Please verify that the ID and acrostic are a match to the participant.

- Instruct the participant to read each question and its instructions carefully then enter his or her response.
- Show the participant how to click on choices or enter responses.
- Explain that the computer will help by automatically skipping the questions that don't need to be answered because of a prior response.

- Explain that not checking a number is interpreted the same as 0 (e.g. for 15 minutes only the hours would remain unchecked while the minutes would be recorded as 15).
- Explain that if the participant would like to change an answer to one of the questions, that the question response should first be checked ―No‖ (which will reset the days, hours, and minutes all to unchecked). Then if the participant would like to record a different amount of time indicate ―Yes‖ and then proceed with responding with the corrected number of days, hours, and minutes.
- If he/she is unsure about an exact answer (e.g., for number of days per week of an activity), tell him/her to give a best estimate.

Begin the questionnaire by reading the following instructions to the participant:

Think about the types of activities you did in a typical week in the past month. Please indicate whether you did or did not perform each of the following activities in a typical week. For each item that you respond "YES" you will be asked for the number of days in a typical week you did these activities and the average amount of time per day in hours and minutes.

Define intensity levels for the participant:
Most of the survey questions ask about light, moderate, and heavy intensity activities.
Light intensity *refers to activities that require little effort and are easy to do.*
Moderate intensity *refers to an effort that is harder than light intensity but is not an all-out effort.*
Vigorous intensity *is a very hard activity and requires all-out effort.*

Show the participant using the following example: Begin this with, ―***Let me show you an example of how we will fill out the survey."***

To orient him/her to the past month, you will identify that period for the participant. In the text box above, if we assume, for instance, that the current date is September 15, the past month would start on August 15.

Use the example below and review each step with the participant. Give him/her time to consider each step and to ask questions. Explain that, if the participant continued usual physical activities while on vacation (or during some other atypical period of time), he/she should report them as usual for a typical week. However, if usual activities were stopped during a vacation, or if the participant took up other activities *only during that period,* then he/she should not record them as typical activities.

Questions people might ask about completing the Physical Activity Questionnaire, and some sample responses:

What if every week in the past month was different?
Think about the week that was most typical of your activity patterns for that activity in other times of the year and fill in the circle for the number of days and hours per day and or minutes per day.

What if the length of time is different each day?

Think about the average in all the days that reflects your typical time for the activity in a typical week.

I was on vacation in the past month when I went on a 2-week bicycle trip. Should I include this in the estimates?
In this case, think about a typical week in the past couple of months that reflects your usual activity patterns. We are trying to identify the activity patterns you do on a usual basis, so if your vacation was not typical, do not include it. Once you have reviewed the sample question with the participant and explained the difference between typical and atypical activities, ask if he/she has any questions.

It is possible that a person will spend more time doing activities on one day or another (e.g., weekends). If this is the case, ask him/her to estimate the usual time during each event in a typical week, averaging in the longer and shorter days.

For example, if the participant engages in an activity for 30 minutes/day 5 days/week and 1.5 hours/day 1 day/week, ask him/her to add about 15 minutes extra to each day (45 minutes/day 5 days a week), to take into account a single day that has a prolonged bout of activity compared to the usual.

3. Item-by-Item Clarification

Household chores
"In a typical week in the past month, did you do… (light effort household chores)." The examples should be read to the participant for clarification.
If no, record no and you will be skipped ahead to the next question.
If yes, then ask, ***"About how many days per week?"*** *record* the number of days.
Then ask, ***"About how many hours or minutes per day?*** Record the number of hours and/or minutes e.g. the participant response 1hr and 15 mins, record 1 under hours and 15 under minutes. These series of questions should be applied to similar types of questions in the questionnaire.

1. Light effort Household Chores: These activities are light intensity, routine, usually daily activities that people do during the care and maintenance of a household. Examples include cooking and cleaning after cooking, straightening up the house, grocery and household shopping and putting things away, changing the bed, doing the laundry, ironing. Housecleaning in a structured, organized way should not be included here, as that would involve more moderate intensity chores.

2. Moderate or Heavy Effort Household Chores: These activities are more structured and might not occur on a daily basis. Examples include heavy cleaning (washing windows, moving furniture to clean), vacuuming, scrubbing the floors or walls, mopping—either standing up or on hands and knees—repairing home appliances or lawn and garden tools, washing the car.

Lawn/Yard/Garden/Farm
"In a typical week in the past month, did you do… (moderate effort lawn/yard etc.)"
3. Moderate Effort Lawn/Yard/Garden/Farm etc. activities: These activities refer to outside chores involved in caring for a house, farm, or ranch. They may involve yard

work, cleaning out the garage, raking the leaves, sweeping the porch or sidewalk, or other moderate effort chores. Encourage the participant to think of activities done in a typical week in the past month. This category may include seasonal activities; if so, the activities reported should be typical of the past month.

4. Heavy Effort Lawn/Yard/Garden/Farm etc. activities: These activities require heavy effort and may be seasonal. Examples include digging dirt, shoveling snow or using a snow blower, chipping ice, tilling a garden, chopping and hauling wood, and removing trees.

Care of Children/Adults

"In a typical week in the past month, did you do… (light effort child/adult care)"

5. Light Effort Children/Adult Care: These activities require physical movement by the respondent and include bathing, feeding, changing diapers, playing with a child, or other similar activities. Do not count time sitting with a child (as in babysitting) without active engagement in physical activities. Include only the time spent involved in physical activities.

6. Moderate Effort Children/Adult Care: These are intentional activities that require moderate effort to complete and may include activities of lifting and carrying dependent others, pushing a wheelchair or stroller. Include only the time spent moving.

Walking (not at work)

"In a typical week in the past month, did you do… (walking to get to places, etc.)"

7. Walking to get places. In general, walking is underreported in the time estimates. This would include walking for transportation, walking to and from work, walking to the store or from the car into the store and back, walking to get the mail, etc.

8. Walking for exercise, pleasure, social reasons, walking during work breaks, or walking the dog. These are classified as intentional walking and are different in intention then those in item #7. The walking may be for exercise or part of a daily routine that is done with family members, animals, or for personal reasons. Walking for transportation should be included in item 7.

Dancing/Sport Activities

"In a typical week in the past month, did you do… (dancing in church/team sport, etc.)"

9. Dancing in church, ceremonies, or for pleasure. Remind the participant to think of a typical week in the past month to estimate usual dancing behaviors. Some may dance only occasionally—a few times a year. This would not be included as a "yes" response to this category unless it was typical of the past month. Ceremonial or religious dancing would need to be done regularly enough to represent a typical week in the past month.

10. Team sport. The purpose of including team sports activities is to group exercise activities that are done with others. These are probably seasonal activities that are done in leagues or other organized settings. Remind the participant to think of a typical week in the past month and to stay within that framework when responding.

11. Dual sports. These activities involve mostly racket sports or other one-on-one sports activities. They could include fencing, ping-pong, or other activities done with another person.

12. Individual activities that maybe classified as sports. These may be sports activities, such as golf and bowling, or more individual relaxation/meditation activities, such as yoga or Tai Chi. Remind respondents to think of days and time spent during a typical week in the past month only.

Conditioning Activities.

"In a typical week in the past month, did you do… (moderate effort conditioning, etc.)"

13. Moderate Effort Conditioning Activities. Conditioning activities are those that can be done alone or with others. They are different from sports, because the intention is to gain an element of fitness rather than have a contest or win a game. Moderate effort activities are not for competition, nor are they all-out effort. Intensity of exercise should be moderate enough that respondents should be able to talk with others while they are performing the activities. Examples are low impact aerobics, recreational (slow) bicycling, rowing on a rowing machine or in a lake, swimming in a pool or lake, or using weight lifting or conditioning machines at a health club.

14. Heavy Effort Conditioning Activities. These are very intense activities done for maximum fitness levels and include high impact aerobics (e.g., Tai-bo, kick boxing), competitive or maximum effort running, bicycling, swimming, and work on health club machines. Exercise at this intensity would be very hard and the respondent would have difficulty carrying on a conversation during the performance.

Leisure Activities.

"In a typical week in the past month, did you do…(these leisure activities, watching TV)"

15. Watching TV. This is a sedentary, leisure-time pursuit. Do not include the time watching TV while doing other things. The question is to be used as a marker of sitting or reclining and watching TV as a single pursuit.

Occupational or Volunteer Activities.

If participant indicated that they are employed or volunteering (personal History form), Questions 16-19 will be available for response.
If the participant has not indicated they are employed or volunteering, questions 16-19 will be skipped and the participant will be asked to continue with question 20.

"At work (or volunteering), did you do…."

16. Light Effort/Sitting Activities. For most respondents, this will be the most hours in the work day.

17. Light Effort/Standing Activities. These are likely intermittent activities that would be done in a clerical setting (e.g., office work related to filing, using a copy machine) or sustained activities done in a labor setting (e.g., check-out clerk in a store, assembly line worker assembling parts, medical field examining patients). Teaching in a classroom falls into this category.

18. Moderate Effort/Standing or Walking Activities: For some occupations (office work, clerical, professional), these may be more intermittent, as in walking down the hall, walking between office buildings, and delivering items. For labor settings, this could relate to jobs such as delivery person (overnight express delivery, food delivery, mail delivery) or

jobs that require mostly walking and standing (nurse, custodian, physical education teacher, coach, firefighter, police officer, physical therapist).

19. Heavy Effort/Manual Labor: These occupations require manual effort that involves substantial movement and labor. Types of activities may include digging ditches, ranch or farm labor, delivering furniture, loading and unloading trucks, seasonal farm work.

Walking Pace

20. ***When you walk outside of your home, what is your usual pace?***

Ask respondent to estimate the usual pace he/she walks most of the time. Consider all walking activities (e.g., at work, on the way to work, for exercise, in walking with children or others, or when running errands). Fill in appropriate circle.

Offer the following guidelines:

Slow or Casual strolling pace = 2 mph = 30 minutes per mile
Average or normal pace = 2-3 mph = 20-30 minutes per mile
Fairly brisk pace = 4-5 mph = 12-15 minutes per mile (very fast or almost a slow jog)
Brisk or striding pace = More than 5 mph = 10 minutes per mile (race-walking)

After completion of the interview, the interviewer should check to make sure all questions were answered then indicate whether the survey was completed as self-administered or interviewer- administered at the end of the survey.

3.4.8 KCCQ-12 Dyspnea Instrument

I. PURPOSE

The Kansas City Cardiomyopathy Questionnaire is a quality-of-life measure for patients with congestive heart failure. It is a reliable, predictive tool that tracks how patients are doing if they have weakened heart muscle due to prior heart attacks, heart valve problems, viral infections, or other causes.

II. METHODS

General instructions:

This is an **interviewer-administered** questionnaire.

Do not probe to make interpretations about a participant's specific symptoms. Ask questions as written and record answers as given by the participant.

Specific instructions:

Begin the questionnaire by reading to the participant the following introduction:

Some people have heart failure, others have symptoms such as shortness of breath or fatigue, and don't know if they have heart failure, or may have other reasons for these symptoms. In the following questions, where we ask about heart failure, you may substitute in your mind "shortness of breath or fatigue", and if you do not have such symptoms, consider your general health status when answering the questions below.

Please note that this questionnaire was designed to be administered to patients with heart failure. For MESA Exam 6, it will be administered to all participants. If after reading a question, the participant responds that they do not have heart failure, ask them to think about their "general health status" instead of heart failure and replace "heart failure" with "general health status in all future questions. The questions were originally designed to be self-administered, but in MESA, it will be interview-administered.

The following questions refer to your heart failure and how it may affect your life. Please read and complete the following questions. ***There are no right or wrong answers.*** Please mark the answer that best applies to you.

Note: do not read "Please read and complete the following questions" or "please mark the answer that best applies to you."

1. ***Heart failure[Your general health status] affects different people in different ways. Some feel shortness of breath while others feel fatigue. Please indicate how much you are limited by heart failure (shortness of breath or fatigue) [your general health status] in your ability to do the following activities over the past 2 weeks.***

   Showering/Bathing. Choose the appropriate response.

Walking 1 block on level ground. Choose the appropriate response.
Hurrying or jogging (as if to catch a bus). Choose the appropriate response.

2. ***Over the past 2 weeks, how many times did you have swelling in your feet, ankles or legs when you woke up in the morning?*** Choose the appropriate response.

3. ***Over the past 2 weeks, on average, how many times has fatigue limited your ability to do what you want?*** Choose the appropriate response.

4. ***Over the past 2 weeks, on average, how many times has shortness of breath limited your ability to do what you want?*** Choose the appropriate response.

5. ***Over the past 2 weeks, how many times have you been forced to sleep sitting up in a chair or with at least 3 pillows to prop you up because of shortness of breath? Choose the appropriate response.***

6. ***Over the past 2 weeks, how much has your heart failure [general health status] limited your enjoyment of life***? Choose the appropriate response.

7. ***If you had to spend the rest of your life with your heart failure [general health status] the way it is right now, how would you feel about this?*** Choose the appropriate response.

8. ***How much does your heart failure [general health status] affect your lifestyle? Please indicate how your heart failure may have limited your participation in the following activities over the over the past 2 weeks.***

Hobbies, recreational activities. Choose the appropriate response. Do not read the last response option (not applicable).
Working or doing household chores. Choose the appropriate response. Do not read the last response option (not applicable).
Visiting family or friends out of your home. Choose the appropriate response. Do not read the last response option (not applicable).

3.4.9 Urinary Incontinence – ICIQ-FLUTS/MLUTS

I. PURPOSE

The International Consultation on Incontinence Modular Questionnaire (ICIQ) Female Lower Urinary Tract Symptoms (FLUTS) and Male Lower Urinary Tract Symptoms (FLUTS) are patient-completed questionnaires for evaluating female and male lower urinary tract symptoms and impact on quality of life (QoL) in research and clinical practice. These questionnaires are used to screen for lower urinary tract dysfunction and to obtain a brief yet comprehensive summary of the level and impact of urinary symptoms.

II. METHODS

General instructions:

This is a **self-administered questionnaire**. Open the questionnaire on the data collection tablet for the participant and give brief instructions for completion. If the participant is unable to self-administer the questionnaire, then a MESA staff member will administer the questionnaire.

Ask the participant to try to answer all questions, unless instructed to skip the question. Remind him/her to request assistance from a staff member if anything is unclear. Most participants should be able to complete the questionnaire on their own. However, if the participant expresses or appears to have difficulty reading or comprehending the questions, offer to help and make arrangements for an interviewer administered version in the appropriate language.

Specific instructions ICIQ - FLUTS:

Instruct the participant to read the questions and their instructions carefully then fill out all questions.

Many people experience urinary symptoms some of the time. We are trying to find out how many people experience urinary symptoms, and how much they bother them. We would be grateful if you could answer the following questions, thinking about how you have been, on average, over the PAST FOUR WEEKS.

1. ***Please write in your date of birth: This question will be pre-filled for the participant.***

2. ***a. During the night, how many times do you have to get up to urinate, on the average?*** Choose the appropriate response. If none, skip to question 3.

   b. How much does this bother you? Please select a number between 0 (not at all) and 10 (a great deal). Choose the appropriate response.

3. ***a. Do you have a sudden need to rush to the toilet to urinate?*** Choose the appropriate response. If never, skip to question 4.

   b. How much does this bother you? Please select a number between 0 (not at all) and 10 (a great deal). Choose the appropriate response.

4. ***a. Do you have pain in your bladder?*** Choose the appropriate response. If never, skip to question 5.

   b. How much does this bother you? Please select a number between 0 (not at all) and 10 (a great deal). Choose the appropriate response.

5. ***a. How often do you pass urine during the day?*** Choose the appropriate response.

   b. How much does this bother you? Please select a number between 0 (not at all) and 10 (a great deal). Choose the appropriate response.

6. ***a. Is there a delay before you can start to urinate?*** Choose the appropriate response. If never, skip to question 7.

   b. How much does this bother you? Please select a number between 0 (not at all) and 10 (a great deal). Choose the appropriate response.

7. ***a. Do you have to strain to urinate?*** Choose the appropriate response. If never, skip to question 8.

   b. How much does this bother you? Please select a number between 0 (not at all) and 10 (a great deal). Choose the appropriate response.

8. ***a. Do you stop and start more than once while you urinate?*** Choose the appropriate response. If never, skip to question 9.

   b. How much does this bother you? Please select a number between 0 (not at all) and 10 (a great deal). Choose the appropriate response.

9. ***a. Does urine leak before you can get to the toilet?*** Choose the appropriate response. If never, skip to question 10.

   b. How much does this bother you? Please select a number between 0 (not at all) and 10 (a great deal). Choose the appropriate response.

10. ***a. How often do you leak urine?*** Choose the appropriate response. If never, skip to question 11.

    b. How much does this bother you? Please select a number between 0 (not at all) and 10 (a great deal). Choose the appropriate response.

11. ***a. Does urine leak when you are physically active, exert yourself, cough or sneeze?*** Choose the appropriate response. If never, skip to question 12.

    b. How much does this bother you? Please select a number between 0 (not at all) and 10 (a great deal). Choose the appropriate response.

12. ***a. Do you ever leak urine for no obvious reason and without feeling that you want to go?*** Choose the appropriate response. If never, skip to question 13.

b. How much does this bother you? Please select a number between 0 (not at all) and 10 (a great deal). Choose the appropriate response.

13. ***a. Do you leak urine when you are asleep?*** Choose the appropriate response. If never, go to END.

    b. How much does this bother you? Please select a number between 0 (not at all) and 10 (a great deal). Choose the appropriate response.

    Thank you very much for answering these questions.

Specific instructions ICIQ - MLUTS:

Instruct the participant to read the questions and their instructions carefully then fill out all questions.

Many people experience urinary symptoms some of the time. We are trying to find out how many people experience urinary symptoms, and how much they bother them. We would be grateful if you could answer the following questions, thinking about how you have been, on average, over the PAST FOUR WEEKS.

1. ***Please write in your date of birth: This question will be pre-filled for the participant.***

2. ***a. Is there a delay before you can start to urinate?*** Choose the appropriate response. If never, skip to question 3.

   b. How much does this bother you? Please select a number between 0 (not at all) and 10 (a great deal). Choose the appropriate response.

3. ***a. Do you have to strain to continue urinating?*** Choose the appropriate response. If never, skip to question 4.

   b. How much does this bother you? Please select a number between 0 (not at all) and 10 (a great deal). Choose the appropriate response.

4. ***a. Would you say that the strength of your urinary stream is...*** Choose the appropriate response.

   b. How much does this bother you? Please select a number between 0 (not at all) and 10 (a great deal). Choose the appropriate response.

5. ***a. Do you stop and start more than once while you urinate?*** Choose the appropriate response. If never, skip to question 6.

   b. How much does this bother you? Please select a number between 0 (not at all) and 10 (a great deal). Choose the appropriate response.

6. ***a. How often do you feel that your bladder has not emptied properly after you have urinated?*** Choose the appropriate response. If never, skip to question 7.

b. How much does this bother you? Please select a number between 0 (not at all) and 10 (a great deal). Choose the appropriate response.

7. ***a. Do you have a sudden need to rush to the toilet to urinate?*** Choose the appropriate response. If never, skip to question 8.

   b. How much does this bother you? Please select a number between 0 (not at all) and 10 (a great deal). Choose the appropriate response.

8. ***a. Does urine leak before you can get to the toilet?*** Choose the appropriate response. If never, skip to question 9.

   b. How much does this bother you? Please select a number between 0 (not at all) and 10 (a great deal). Choose the appropriate response.

9. ***a. Does urine leak when you cough or sneeze?*** Choose the appropriate response. If never, skip to question 10.

   b. How much does this bother you? Please select a number between 0 (not at all) and 10 (a great deal). Choose the appropriate response.

10. ***a. Do you ever leak for no obvious reason and without feeling that you want to go?*** Choose the appropriate response. If never, skip to question 11.

    b. How much does this bother you? Please select a number between 0 (not at all) and 10 (a great deal). Choose the appropriate response.

11. ***a. Do you leak urine when you are asleep?*** Choose the appropriate response. If never, skip to question 12.

    b. How much does this bother you? Please select a number between 0 (not at all) and 10 (a great deal). Choose the appropriate response.

12. ***a. How often have you had a slight wetting of your pants a few minutes after you had finished urinating and had dressed yourself?*** Choose the appropriate response. If never, skip to question 13.

    b. How much does this bother you? Please select a number between 0 (not at all) and 10 (a great deal). Choose the appropriate response.

13. ***a. How often do you pass urine during the day?*** Choose the appropriate response.

    b. How much does this bother you? Please select a number between 0 (not at all) and 10 (a great deal). Choose the appropriate response.

14. ***a. During the night, how many times do you have to get up to urinate, on average?*** Choose the appropriate response. If none, skip to END.

    b. How much does this bother you? Please select a number between 0 (not at all) and 10 (a

great deal). Choose the appropriate response.

Thank you very much for answering these questions.

3.4.10 Lung Questionnaire

I. PURPOSE

The Lung Questionnaire includes American Thoracic Society COPD recommended guidelines for grading COPD severity and assessment of exacerbation-like respiratory events that can occur in individuals without COPD. These events are associated with significant health and socioeconomic outcomes. The questionnaire asks about childhood respiratory infections, which demonstrated a significant association with COPD among never-smokers in the CanCOLD Study, and waterpipe use, which is associated with increased respiratory symptoms, impaired lung function, and altered airway biology.

III. METHODS

General instructions:

This is an **interviewer-administered** questionnaire. Questions should be read to the participant verbatim as they appear on the form to ensure standardization. In addition, any introductory and transitional wording should be read verbatim.

The interviewer should read all choices to the participant and have the participant choose the appropriate response/s for each question.

Do not probe to make interpretations about a participant's specific symptoms. Ask questions as written and record answers as given by the participant.

Specific instructions:

Begin the questionnaire by reading to the participant the following introduction:
For each question below, select the number that best describes you currently:

1. ***I never cough…or…I cough all the time.***
   Choose the appropriate response (between 0 and 5) to the best estimate.

2. ***I have no phlegm (mucus) in my chest at all…or… My chest is completely full of phlegm (mucus).***
   Choose the appropriate response (between 0 and 5) to the best estimate.

3. ***My chest does not feel tight at all…or… My chest feels very tight***
   Choose the appropriate response (between 0 and 5) to the best estimate.

4. ***When I walk up a hill or one flight of stairs I am not breathless…or… When I walk up a hill or one flight of stairs I am very breathless.***
   Choose the appropriate response (between 0 and 5) to the best estimate.

5. ***I am not limited doing any activities at home…or… I am very limited doing activities at home.***
   Choose the appropriate response (between 0 and 5) to the best estimate.

6. ***I am confident leaving my home despite my lung condition…or… I am not at all confident***

leaving my home because of my lung condition.
Choose the appropriate response (between 0 and 5) to the best estimate.

7. ***I sleep soundly…or… I don't sleep soundly because of my lung condition.***
Choose the appropriate response (between 0 and 5) to the best estimate. The question should be answered for sleeping soundly or not sleeping soundly due to the participant's lung condition (not other sleep disturbances).

8. ***I have lots of energy…or… I have no energy at all.***
Choose the appropriate response (between 0 and 5) to the best estimate.

9. ***Have you ever had a period when you had breathing problems that got so bad that they interfered with your usual daily activities or caused you to miss work? Choose YES, NO, or DON'T KNOW. If YES, answer questions*** 9a-d. If NO, go to question 10

10. ***Were you hospitalized as a child for breathing problems prior to the age of 10?***
Choose YES, NO, or DON'T KNOW.

The following questions ask about use of a waterpipe to smoke tobacco, sometimes called a hookah, shisha, or nargile.

11. ***Have you used a waterpipe, hookah, shisha, or nargile to smoke tobacco more than 100 times in your life?*** Choose YES, NO, or DON'T KNOW. If YES, answer questions 11a-c. If NO, go to END.

3.5 Core Clinic Examination

3.5.1 Anthropometry

I. PURPOSE

Anthropometry was obtained in each of the previous MESA exams. The purpose is the same as for previous exams.

II. MATERIALS AND EQUIPMENT

- Stadiometer (Accu-Hite Measure Device with level bubble) (height ruler with triangle level is used at some centers)
- Detecto Platform Balance Scale in lbs/kg
- Gulick II 150 cm anthropometric tape
- Full length mirror
- Four 50-pound weights (certified prior to first MESA visit) to calibrate scale

III. METHODS

Methods for completing the Anthropometry portion of Exam 6 are the same as in Exam 1. Some important points are reiterated here.

General Instructions:

For all measurements, participants should wear light clothing but no shoes (thin socks or "pillow slippers" OK). Have participants completely empty their pockets and remove excessive amounts of jewelry that could affect the weight measurement. Provide lockers with locks for valuables.

Pregnant women should not be measured, regardless of gestational stage (check exclusion criteria for pregnancy). The Clinic Coordinator should ascertain pregnancy status, both for measurements and for subsequent coronary calcification measurement.

Specific Instructions:

1. Standing Body Height ~ procedure is the same as for Exams 1–5.

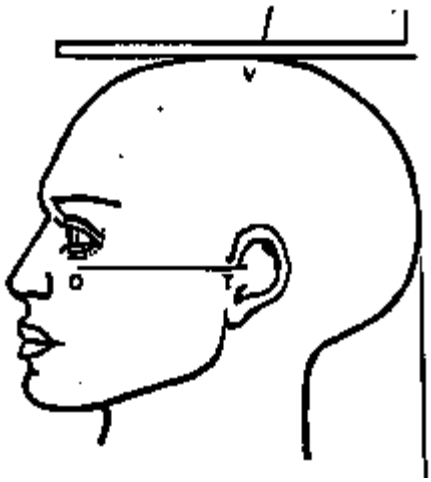
   1.1 Equipment
   - Stadiometer (Accu-Hite Measure Device with level bubble) (height ruler with triangle level used at some centers is adequate)

   1.2 Before measuring height, make sure the floor is level, the wall is at a 90 degree angle to the floor, the wall is straight, and the Stadiometer is mounted perpendicular to the floor.

   1.3 Record the results, to the nearest tenth (0.1) of a cm, in Box 1a on the Anthropometry Form.

   1.4 For accurate measurement of height, the participant must be standing in a vertical plane. To

achieve this position, have the participant stand erect on the floor or horizontal platform, with back against the vertical Stadiometer, heels against the wall, and feet or knees together—whichever come together first. Have the participant look straight ahead, with head in the Frankfort horizontal plane (Figure 1, below).



The Frankfort Plane includes the lower margin of the bony orbit (the bony socket containing the eye) and the most forward point in the supratragal notch (the notch just above the anterior cartilaginous projections of the external ear)—also referred to as the upper margin of the external auditory meatus (the hole in the ear).

Figure 1. Frankfort Plane for Measuring Body Height

1.5 Place the headboard over the crown of the head, with the headboard forming a right angle to the scale. The headboard should touch the scalp lightly.

1.6 Ask the participant to step out from under the headboard. Record the participant's height to the nearest 0.1 centimeter in Box 1a of the Anthropometry Form.

1.7 If you are unable to measure the actual height of the participant because the headboard does not rest directly over the scalp, estimate height to the nearest 0.1 cm, record in Box 1a of the Anthropometry Form and answer "yes" to the question, "Was there a modification in protocol?"

1.8 If any modification was made to obtain height, bubble in "yes" to the question, "Was there a modification in protocol?"

2. Body Weight ~ procedure is the same as for previous exams.

2.1 Equipment
- Detecto Platform Balance Scale in lbs/kg

2.2 Always balance the scale so that the indicator is at zero when no weight is on the scale. The scale should be on a firm, level surface. Instruct the participant to stand in the middle of the platform of the balance scale, with head erect and eyes looking straight ahead. Adjust the weight on the indicator until it is balanced. *Record the results, to the nearest 0.5lbs, in Box 2a.*

2.3 If the participant is too obese to stand securely on the scale's platform when looking straight ahead, he/she may stand sideways on the scale to take the weight measurement; facing to the side rather than the front will provide the participant a wider base and more stability.

2.4 If a participant has a prosthetic limb or breast prosthesis, measure weight with the limb on.

2.5 If a participant is frail or unsteady, measure weight while participant is lightly steadied by you or an assistant.

2.6 If a participant is unable to stand on the scale for a weight measurement, do not attempt a weight measurement. Answer "yes" to the question, "Was there a modification in protocol?"

2.7 If any modification were made to obtain weight, bubble in "yes" to the question, "Was there a modification in protocol?"

3. Girth Measurements ~ procedure is the same as for Exam 1.

3.1 Equipment

- Gulick II 150 cm anthropometric tape
- Full length mirror

3.2 Technique

- Do *not* take abdominal and hip girth measurements over loose clothing. It is ok if taken over light well-fitted clothes.
- If a participant is very large, you may have him/her hold one end of the tape while walking the tape around to obtain the measurement. If any circumference exceeds 150 cm, use the 250 cm tape measure. (Take care not to offend the person being measured, and change to the larger tape as discretely as possible.)

3.3 Abdominal Girth

Apply a Gulick II anthropometric tape horizontally at the level of the umbilicus and instruct the participant to breathe normally. Move to the participant's right side to take the measurement; do not take this measurement from the front. Be sure to keep the tape horizontal while making the measurement; use the wall-mounted mirror to assure horizontal placement on all sides.

Round abdominal girth measurement to the nearest 0.1cm and record in Box 3a.
If the circumference exceeds 150 cm, record "yes" for the question, ***"Was there a modification in protocol?"***

3.4 Hip Girth

Take the hip girth measurement from the participant's right side; do not take this measurement from the front. Instruct the participant to stand with his/her feet together. Measure hip girth at the maximum circumference of the buttocks. Check to see that the tape

is level in front and back.

Round hip girth measurement to the nearest 0.1cm and record in Box 3b.
If the circumference exceeds 150 cm, record "yes" for the question, ***"Was there a modification in protocol?"***

4. Comments/Modifications to the Protocol

If you have comments or if there have been modifications to the protocol as described above, answer "yes" to question 4 on the Anthropometry Form and record comments in the space provided. If there are no comments or modifications, answer NO to question 4.

5. Completing the "For MESA Field Center Use Only" section

Make sure to record the Technician ID#, Reviewer ID#, and Data Entry ID# is these fields at the bottom of the form.

6. Quality Control ~ Calibration Check of Scales and Equipment Check

6.1 Equipment:
- Four 50-pound weights (certified prior to first MESA visit) to calibrate scale
- Gulick II anthropometric tapes

6.2 Check scales for accuracy on a monthly basis.

6.21 Place two weights on the scale and record the numeric value obtained in the "Light Poise" column of the "Scale Calibration Checklist." Add two more weights and record the numeric value obtained in the "Heavy Poise" column.

6.22 The values obtained should be within ±1.0 pound of the expected weight. If either value exceeds this limit, the scale must be calibrated by the manufacturer or by the appropriate institution personnel.

6.23 When the scale is not in use, keep it balanced at 300 pounds. This keeps the tension off the internal spring mechanism.

6.3 Examine anthropometry tape measures on a weekly basis for sign of wear.

3.5.2 Seated Blood Pressure

I. PURPOSE

Blood pressure (BP) level is a major risk factor for coronary heart disease, congestive heart failure, and stroke. Heart rate reflects autonomic nervous system function and cardiovascular fitness. The measured BP level is subject to biological and observer variability. The purpose of a specific measurement protocol, or training and certifications of technicians, and of ongoing quality control is to minimize variability due to known exogenous factors and to reduce imprecision and biases in measurement.

The main advantages of the Dinamap® automated device are accuracy comparable to manual mercury sphygmomanometry, with reduced potential for observer biases and less demand on research assistants in terms of training and effort in data collection.

Seated Blood Pressure was obtained in the MESA "Baseline Exam" or Exam 1. The Dinamap® automated device will be used in Exam 6 for consistency and to reduce the potential for observer biases.

II. MATERIALS AND EQUIPMENT

- Dinamap® automated blood pressure device (Dinamap Monitor Pro 100®, which includes printer paper, power cable, and power converter.)
- Blood pressure cuffs in a variety of sizes (Dura-cuf Adult Assortment Pack® [#2699]).
- Measuring tape (for arm circumference).
- Watch or stop watch (to time five-minute rest and resting heart rate).
- Hand calculator (to average 2nd and 3rd BP readings).
- Copy of Critikon® chart for choosing correct BP cuff size (see Table 2).
- Information sheet on interpretation of BP from JNC VI (see Table 1).
- Resting Heart Rate/Blood Pressure Form.

III. DEFINITIONS

1. Sphygmomanometry: Measurement of blood pressure.

2. Oscillometric device: Method for measuring blood pressure that relies on the oscillation or fluctuation in arterial pressure generated by the cardiac cycle and transmitted to an inflated blood pressure cuff overlying an artery. This method differs from the auscultatory method, which relies on audible changes over an artery during deflation of an inflated cuff.

IV. CLASSIFICATION OF THE PARTICIPANT'S BLOOD PRESSURE WITHIN THE JNC 7 CATEGORIES AND CRITERIA FOR ALERTS AND REFERRALS

The 2004 Report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) defines categories of blood pressure and recommends follow-up according to the following criteria:

Table 1. Classification of BP in Adults Aged 18 Years or Older*.

BP Category	SBP (mm Hg)		DPB (mm
Normal	<120	and	<80
Prehypertension*	120-139	and	80-89
Hypertension**			
Stage 1	140–159	or	90–99
Stage 2	≥ 160	or	≥ 100

* When recommendation for follow-up of DBP and SBP are different, the shorter recommended time for recheck and referral should take precedence. This classification applies only to participants not taking antihypertensive drugs.

** Diagnosis of hypertension must be based on two or more readings taken at each of two or more visits following an initial screening.

SBP= systolic blood pressure. DBP= diastolic blood pressure.

1. Alert levels requiring **immediate referral** (send participant directly to a physician or hospital) for MESA participants are:

   - **Systolic BP >210 mm Hg**
   - **Diastolic BP >120 mm Hg**

2. Alert levels requiring *urgent referral* (*within one week*) are:

   - *Systolic BP 180–210 mm Hg*
   - *Diastolic BP 110–120 mm Hg*

3. Alert levels requiring follow-up within two months time, and, therefore, we recommend physician notification for systolic or diastolic BP above these levels.

   - BP >140/90 mm Hg

4. JNC 7 states that blood pressure classifications and referral recommendations are based on the average of two or more readings on two or more occasions. In MESA we intend to use the average of the 2nd and 3rd blood pressure readings (see below) in order to reduce the impact of reactivity (higher first reading) on the estimate of the value of the underlying blood pressure. Thus, in deciding whether a participant meets criteria for an alert level, the average of the 2nd and 3rd readings should be used. This will require on-the-spot arithmetical manipulation of the systolic and diastolic values. A hand calculator may be useful. The data forms include fields for these averaged values and for any actions taken.

V. METHODS

1. Preparation

   1.1 Record the date of the procedure and the Dinamap® number on the Seated Blood Pressure Form during the five-minute rest period.

1.2 Before the BP measurement procedure, explain to the participant what to expect and how long the procedure will take. The following script is suggested:

This part of the exam involves taking your resting blood pressure. It will take about 10 minutes. We would like you to sit with both feet on the floor and your arm supported on the table. We will have you sit quietly for five minutes. Then we will take your blood pressure three times, one minute apart, using an automated device. We will give you your blood pressure readings and some material to help you interpret them at the end.

2. Cuff Size Selection

2.1 Use the proper cuff size to avoid under- or over-estimation of the correct blood pressure. Selection of the proper sized cuff is based on the guideline that the length of the inflatable bladder in the cuff should be at least 40% of the arm circumference. Measurement of the bladder length in the Critikon® cuffs confirms that the chart in Table 3 conforms to this guideline. A copy of this chart should be available during the BP measurement procedure for easy reference. *Selection of cuff size should be based on the Critikon® chart in Table 2, and only Critikon® cuffs should be used.* If the participant's arm size falls in a range in which there is overlap of two Critikon® cuff sizes, use the *larger* cuff.

2.2 Measure the right arm circumference as follows:

- Ask the participant to bare the upper arm.
- Ask the participant to sit or stand holding forearm horizontal, i.e., parallel to the floor.
- Measure arm length from the acromion (bony extremity of the shoulder girdle) to the olecranon (tip of the elbow) using a metric tape.
- Mark the midpoint on the dorsal (back) surface of the arm.
- Ask participant to relax arm along side of the body.
- Draw the measuring tape snugly around the arm at the midpoint mark, keeping the tape horizontal. Only pull the tape snug enough so that the first red-bead marker can be seen. Tape should not indent the skin. If you can see both bead, the tape is too tight. *Record the arm circumference measured to the closest (0.1) cm in Field 1 on the Seated Blood Pressure Form.*
- Use the criteria in Table 2, below, to determine cuff size. *Check the cuff size used in Field 2 on the Blood Pressure Form by filling in the appropriate circle.*

Table 2. Cuff Size Indicated by Measured Arm Circumference

Arm Circumference*	Cuff Name**	Bladder Length (cm)
12-19	Child	8
19.1-25	Small Adult	10
25.1-33	Adult	13
33.1-40	Large Adult	17
40.1-50	Thigh	

* These circumferences are printed on the corresponding cuff for verification.

** Critikon Dura-cuf® nomenclature is also printed on the cuff.

3. Setting up the Dinamap® BP Machine

3.1 Load the printer paper by opening the flap on the side of the device. There is a diagram showing how to thread the paper on the inside of the door. There is a gray plastic wheel to the left of the roller. Just to the right of the gray wheel is a *gray plastic lever.* Gently flip this lever up. This releases the roller so that you can use the gray plastic wheel to turn the roller to thread the paper. Flip the gray lever down when finished.

3.2 To turn on the Dinamap® device, push the "Off/On" button on the front control panel (lower left).

3.3 After five seconds an initial message will appear on the LCD screen. It will consist of a WARNING and the instruction, "PUSH A FRONT PANEL KEY TO START."

3.4 In the main menu select PRINT using the gray toggle knob. In the next menu, select AUTO and then push the toggle knob. This will program the device to print the blood pressure measurements.

3.5 Do not touch the monitor again until you have completed steps 4–6, below, and you are ready to proceed with blood pressure measurement.

4. Positioning the Participant

4.1 The workstation should be free of excessive noise or distractions.

4.2 The participant should be seated and relaxed in a comfortable chair, to ensure that:
- He or she is sitting up (not slouched).
- Both feet are on the floor (legs/ankles not crossed).
- Right forearm is supported resting on the table.

4.3 The participant should not talk, eat, or drink during the procedure.

4.4 Ideally, the Dinamap output will not be visible to the participant during the measurement, as this may cause anxiety.

5. Application of the Blood Pressure Cuff

5.1 Place the appropriate cuff around the upper right arm so that the mid-height of the cuff is at heart level. Palpate the patient's brachial artery and place cuff so that the artery is aligned with the cuff arrow marked "artery."

5.2 Place the lower edge of the cuff, with its tubing connections, two centimeters above the natural crease across the inner aspect of the elbow.

5.3 Wrap the cuff snugly around the arm, with the palm of the participant's hand turned upward.

5.4 Secure the wrapped cuff firmly by applying pressure to the locking fabric fastener over the area where it is applied to the cuff.

5.5 Do not wrap the cuff too tightly around the arm. You should be able to insert the first joint of two fingers under the cuff. The cuff should be snug but not tight.

5.6 Be sure all air is squeezed out of the cuff before each inflation.

6. Rest Period

6.1 The participant should rest for five minutes (timed using a watch or stop watch) prior to the heart rate and blood pressure measurement.

6.2 When the five-minute rest period is over, but before the first blood pressure measurement is started, *record the time of day on the Seated Blood Pressure Form* (examples: 04:25 P [p.m.] or 11:38 A [a.m.]).

7. Blood Pressure Measurement

7.1 To begin the blood pressure procedure, access the Main Menu on the Dinamap by pushing the "Start/Stop" button at the lower right of the monitor. (Please note that the gray knob located at the upper right of the monitor allows you to change selections in the monitor screen, in a manner similar to a computer mouse or pointing device. Rotate the knob in order to move from one item to another in the monitor screen, and push it to select the desired option.)

Use the knob to select the set bp option from the menu and then press the knob (equivalent to clicking a mouse) to implement the selection. The next menu appears automatically.

Use the knob to select auto bp and then press the knob.

7.2 Immediately after you select AUTO BP the monitor will start the first blood pressure measurement. However, during this first inflation, select the window that has appeared to the right of AUTO BP and push the knob, so that there is a black number against a clear background in the window. Rotate the knob to select "1." This will select one minute as the interval between sequential blood pressure measurements. Push the knob again (colors in window will reverse) to implement the selection. (The device will retain this setting, even after it is turned off, so you will not have to repeat this step again.)

7.3 Palpate the radial pulse during inflation. The radial pulse should not be palpable at peak inflation pressure. If the participant's radial pressure remains palpable when the device begins to deflate, the device will complete its deflation procedure and then should automatically reset itself for a higher inflation pressure and repeat the measurement. In the unlikely event that this does not occur, manually reset the inflation pressure:

7.31 Rotate the knob until the window to the right of TGT PRESSURE is highlighted, push the knob and rotate it again until it reaches 210, and push it again to select. Repeat

the blood pressure measurement.

7.32 It is not necessary to repeat or prolong the five-minute rest period, if this happens, but explain the change in the procedure to the participant (e.g., "I think we need to use a higher inflation pressure—I'm just going to reset the machine").

7.33 If a higher maximal inflation pressure is needed, reset this parameter at 260 mm Hg, and, if necessary, at 300 mm Hg. Check carefully to be sure that the cuff is properly positioned on the participant's arm with the arrow at the brachial artery.

7.4 When the radial pulse is obliterated at maximal inflation, the first blood pressure measurement will be obtained. The device will automatically obtain the 2nd and 3rd measurements, at two-minute intervals.

7.5 *Record the three sequential blood pressure readings in Fields 4, 5, and 6 on the Seated Blood Pressure Form.*

7.6 After the 3rd measurement is obtained, return to the main menu and select TREND and then PRINT ALL. When printout is obtained and verified, proceed to TREND and then CLEAR. When the monitor requests confirmation, select YES. Paste or staple the printout in the ad-hoc page.

7.7 In order to keep the machine from continuing with further automatic blood pressure measurements go to the main menu, select SET BP and then MANUAL. There is no need to turn off the machine if another participant is ready. If for any reason the machine automatically starts an unnecessary inflation, push the "Start/Stop" button at the lower right hand corner of the monitor and then select MANUAL, as explained above. Remove the blood pressure cuff from the participant's arm and thank the participant for his/her time.

8. <u>BP Measurement Instructions for Participants With Short, Thick Arms</u>

8.1 Occasionally there will be a participant whose upper arm is too thick and short for the thigh cuff or on whom the thigh cuff pops open on inflation. The alternative procedure in this case is to obtain the resting blood pressure in the right *forearm.*

8.2 Measure the forearm circumference at the midpoint between the olecranon (elbow) and the ulnar stylus (wrist bone on pinkie side). Select the proper size cuff based on the forearm measurement. The blood pressure procedure is otherwise the same.

8.3 You must document on the Seated Blood Pressure Form that you have measured the *forearm blood pressure.*

9. <u>Reporting Blood Pressure Results to Participants</u>

9.1 The technician may verbally provide the participant with the blood pressure reading (the average of the last two pressures), *if asked,* after the procedure has been completed.

9.2 Alternatively, if the blood pressure is normal (<140/90), the technician may say that it is

normal, particularly if asked.

9.3 If the blood pressure is not normal (>140/90) but not at an alert level (>210 mm Hg), the technician should exercise the standard option of not discussing the interpretation or stating that it does appear to be high (or "somewhat elevated") but that, again, it will be discussed later.

9.4 If an alert level is identified, the technician should calmly notify the clinic coordinator when the procedure has been completed. (If symptoms of severe hypertension are present, the technician should notify the clinic coordinator immediately.)

VI. QUALITY ASSURANCE/QUALITY CONTROL PROCEDURES FOR DINAMAP PRO 100®

1. Once a week each device should be used simultaneously with a paired device to simultaneously measure the blood pressure in each arm of a non-smoker under the age of 50, in whom there is no reason to suspect that the blood pressure in the two arms should differ. Repeat the measurement three times.

2. If the paired blood pressure measurements agree within 4 mm Hg or less, for both systolic and diastolic BP, the devices are considered to be in calibration.

3. Investigate any systematic divergence, even if less than 4 mm Hg (e.g., by switching arms and/or pairing the devices with a third device).

4. If the two devices differ by more than 4 mm Hg, calibration must be done. It should be recognized that, if the cuff deflation rate is 2 mm Hg/sec and the heart rate is 60 bpm, divergences of 2–4 mm Hg would be expected, even if the device is in perfect calibration.

3.5.3 Pulse Oximetry

I. PURPOSE

The rationale for measurement oxygen saturation is to measure cardiopulmonary function.

II. MATERIALS AND EQUIPMENT

Pulse Oximeter: Devon Medical Handheld Pulse Oximeter PC-66

III. METHODS

Preparation

1. Resting oxygen saturation will be measured while the participant is resting for blood pressure measurement.

2. Explain the procedure to the patient

3. Verify that the probe is clean, dry and in good condition before applying it to the participant

4. Ask the participant to remove her nail varnish or acrylic nails that may impair the effective transmission of light (have some nail varnish remover on hand just in case).

Positioning the Participant

1. The workstation should be free of excessive noise or distractions

2. The participant should be seated and relaxed in a comfortable chair

3. The participant should not talk, eat, or drink during the procedure

Reading the pulse oximeter

1. Place oximeter on participant's finger during the beginning of the resting period prior to blood pressure measurements.

2. Verify that the probe is well positioned

3. Record the apparent median value obtained while observing the monitor over a one-minute observation period

For participants using oxygen

If the subject is using oxygen, the pulse oximeter should be placed on the subject's finger first. Next, the subject's oxygen should be discontinued while monitoring the oximeter for a period of five minutes. If the pulse oximeter reading falls to 82% or less, oxygen will be replaced and a

reading of 82% will be recorded as the subject‘s oximetry. The apparent median value obtained while observing the monitor over a one-minute observation period should be recorded.

Quality Assurance/Quality Control Procedures for Oximeter

1. Clean sensor/probe as per manufacturers‘ guidelines in between each patient use.
2. Calibration as per manufactures instructions
3. Daily quality control check on self
4. Carry spare alkaline batteries
5. To avoid any leakage from the batteries, remove them if the pulse oximeter is not in regular use
6. Report immediately to the Clinic Coordinator if the pulse oximeter appears to be malfunctioning

Certification requires five documented, correctly performed pulse oximetry measurements, following the MESA certification form

3.5.4 Phlebotomy & Urine Collection

I. PURPOSE

The purpose of the Phlebotomy and Spot Urine forms is to record information related to the blood draw and spot urine collection to facilitate the tracking of samples and to inform the central laboratory of samples collected and any issues that may affect processing

II. MATERIALS/EQUIPMENT

See separate Exam 6 Laboratory MOP for specific materials.

III. METHODS

General instructions

1.4 There are six possible blood draw configurations depending on the studies in which participants are enrolled.

1.5 Data entry software will create the appropriate Phlebotomy form automatically.

1.6 The process of labeling of tubes and cryovials for a given participant will be dictated by the specific version of the Phlebotomy form for that person.

1.7 Copies of the Phlebotomy form and the Processing form are included with the shipment of samples to the Central Laboratory.

1.8 The full lab section (3.9) includes the details about the blood draw and processing.

Specific Instructions:

1 Phlebotomy and Urine Collection Form

1.1 Print the participant's Phlebotomy and Urine Collection form immediately after he or she has signed the informed consent and the responses have been recorded in the Consent screen. The informed consent responses are necessary to print the correct version of the Phlebotomy Form for that participant.

1.2 Give the form to the phlebotomist or lab tech as soon as possible to inform him or her how to complete the setup of the sample tubes and cryovials, or if the prepared MESA setup is all that is needed.

1.3 Indicate whether or not the blood and urine collection were done.

1.4 If blood or urine was not collected, select the reason why not

1.5 Indicate whether or not the participant is selected as a QC subject.

1.6 After the blood draw has been completed, retrieve the completed Phlebotomy form and enter the information in the appropriate fields on the electronic data entry screen.

3.6 Cognitive Assessment

I PURPOSE:
Inclusion of assessment of cognitive functioning in the MESA cohort offers a number of significant advantages not only to MESA but more broadly to understand cognitive aging in what is rapidly becoming a more multi-ethnic population of older adults in the US. The battery of three tests described here will (1) allow for direct evaluation of relationships between underlying cardiovascular disease and cognitive aging; (2) provide unique data on cognitive aging among major ethnic groups including those contributing most to the rapidly growing population of older adults in the US (e.g. Hispanics, African-Americans, Asians); (3) put in place a platform of "baseline" cognitive data allowing for later augmentation through longitudinal exams for evaluating patterns of cognitive aging overt ie in these ethnic groups; and (4) contribute significantly to available data on patterns of performance in Hispanics and Asians, two groups for whom current normative data are based on small samples. MESA results would be among the largest samples for whom such cognitive data would be available across cultures and languages.

The MESA Cognitive assessment is meant to provide measures of cognitive function using standardized tools that produce scores that can be compared to standardized norms and to other studies. The scores themselves are not sufficient to determine presence of dementia or other clinical disorders, but rather may be used as a means to evaluate a range of abilities within the cohort. Scores are expected to decline with age; however, once adjusted for age evaluations may be used to determine risk of other conditions or as outcomes themselves. In the MESA Study, three tests have been selected to evaluate cognitive function as described below:

1. Global Cognitive Functioning: **Cognitive Abilities Screening Instrument (V.2)** (CASI; Teng et al, 1994). This instrument was explicitly developed for cross-cultural use and has a validated Chinese version (Li et al, 1994; Tsai et al, 2007). Though we are not aware of a formal validation for a Spanish version of the CASI itself, the content of the CASI draws from standardized tests (e.g., Modified Mini-Mental State [3MS] that have been validated in Hispanics (Bird et al, 1987; Valle et al, 1991). Indeed, CASI items were explicitly chosen for their cross-cultural applicability (Teng et al, 1994).

The CASI provides brief assessments of major domains of cognitive function including attention, concentration, orientation, short-term memory; long-term memory, language abilities, visual construction, verbal fluency, abstraction, and judgment which when summed provide a measure of global cognitive functioning (see Appendix of Teng et al, 1994 for copy of CASI). Importantly, the CASI has been used to screen for dementia as well as to track within-individual changes over time in cognitive functioning (Teng et al, 1994). We will increase the sensitivity of our battery by modifying one of the CASI items. Item # 14 asks participants to list as many 4-legged animals as possible in 30 sec up to a maximum of 10. The task assesses verbal (semantic) fluency. We will administer item #14 according to CASI instructions but we will allow the participant an additional 30 seconds to continue naming animals. This modification will eliminate potential ceiling effects and match precisely a widely used verbal fluency task thereby giving us an additional assessed cognitive domain in the battery. For the CASI total score only the number of words generated in the first 30" counts.

2. Speed of Processing [**Digit Symbol Coding Test**; Wechsler, 1996]. The DSCT, a subtest of the Wechsler Adult Intelligence Scale-III (formerly called the Digit Symbol Substitution Test), measures how quickly simple perceptual or mental operations can be performed, which along

with working memory (see next test) mediate a large proportion of age related variance in memory (Salthouse, 1991; Park et al, 1996), reasoning (Salthouse, 1991) and other cognitive abilities (Lindenberger & Baltes, 1994). For 120 seconds the participant fills in the symbols (e.g., +, >) that correspond with numbers according to a key provided at the top of the page.

3. Working Memory [**Digit Span Test** (Wechsler, 1**996)** is a sub-test of the Wechsler Adult Intelligence Scale-III). This test which is administered in two parts requires the participant to repeat spans of numbers that increase in length first forwards and then backwards. Translations into Spanish and Chinese are provided by the publisher (The Psychological Corporation).

3.6.1 Cognitive Abilities Screening Instrument

1. **INTRODUCTION:** The Cognitive Abilities Screening Instrument (CASI) consists of 25 test items and provides brief assessments of major domains of cognitive function including attention, concentration, orientation, short-term memory, long-term memory, language abilities, visual construction, list-generating ability, abstract thinking, and judgment which when summed provide a measure of global cognitive functioning. Importantly, the CASI has been used to screen for dementia as well as to track within-individual changes over time in cognitive functioning.

Administration time is approximately 15-20 minutes. The maximum total score is 100.

The CASI includes items derived from several screeners: Hasegawa Screening Test for Dementia (HSTD), The Mini-Mental State Examination (MMSE), and The Modified Mini-Mental State Test (3MS). In addition to providing CASI subscale and total scores, it is possible to compute comparable scores for the HSTD, the MMSE, and the 3MS.

The CASI was explicitly developed for cross-cultural use. Versions have been translated into Japanese, Chinese, Spanish, and French among other languages. For MESA, the Spanish, Chinese and English versions are being administered.

2. Equipment

- CASI Questionnaire
- Pen
- Stopwatch
- Soft-lead pencil with eraser
- Blank sheet of paper
- Five objects: toothbrush, spoon, key, comb, coin (quarter) for naming and recall
- Piece of blank cardboard (for covering the five objects during recall)

3. General Considerations

3.1 Examiners should thoroughly familiarize themselves with the testing procedures and the scoring criteria before using the CASI in formal assessment. The CASI record sheet contains highly condensed

information from this manual. Users of the record sheet must first study this manual carefully; otherwise misunderstandings of the condensed information on the record sheet can easily occur.

Tests should be administered in a **quiet place with minimal distractions**. Distractions could affect participant performance and should be noted on the record sheet.

In the administration of the CASI, **do not offer extra help or wait too long for responses**. Although sometimes it is appropriate to re-present or rephrase a question, in general if a participant gives an incorrect answer, says "I don't know," or is unable to give an answer, the examiner should just score accordingly and proceed to the next item.

Time limits are set for some items. **Subjects should never be told of any time limit on any item.**

Practicing the administration of the CASI is highly recommended and certification by the Coordinating Center is required. Written materials (the MOP), observations, and live practice will be helpful. Questions about administration of the cognitive tests should be directed to the CC staff.

Please note the following:

3.2 If the participant makes a mistake but is able to spontaneously correct him/herself, please give him/her credit for the answer.

3.3 The aim of the CASI is to assess the participant's best cognitive performance. Assisting a participant to be comfortable and free from distractions helps obtain optimal performance.

3.4 Ask the questions using the **exact wording** on the CASI form.

3.5 **Speak loudly and enunciate clearly**.

3.6 Write down the participant's answers whenever possible. If there is any question later on, it is easier to settle if the answers are written down.

3.7 Do **not** allow the participant to see the CASI score sheet as it may affect performance.

3.8 Do **not** give the participant feedback about his/her performance. When a participant asks if his answers are correct, you should tell him/her, "Sorry, I cannot tell you how you did on any item" the truth. In case the answer is incorrect, you may soften the impact by saying like "this item is meant to be difficult" or "many people have trouble with this one".

3.9 There are certain items that should only be said to the participant once, and should not be repeated even if the participant did not hear or was not paying attention. However, please do NOT tell the participant "I can only ask you this question once" before these items.

3.10 Use multiple choices ONLY if specified, for example, questions (5) and (12) both state "may provide 4 choices".

3.11 Prior to starting the CASI, do NOT say "There are no write or wrong answers…" However, you should say "These tests are designed to be challenging. We do not expect you to get every question right, so just do the best you can".

3.12 When timing the participant for certain items, try not to make it too obvious. The participant should not know that he/she is being timed.

3.13 Some participants may seem upset or defensive and make statements like, "Do you think I'm senile?" or "You must think I'm stupid.". You should answer them by saying , "We do not expect you to answer each question correctly, so try not to worry about how you are doing, just do your best."

3.14 When the informed consent is completed, please advise whoever is collecting it to NOT tell the date to the participant if asked. If necessary, the technician should enter the date him/herself.

4. Special Circumstances

4.1 Scoring for a Vision-Impaired Participant: If the participant's vision is very poor, please write "RAISE YOUR HAND" and draw the pentagons **on a separate white paper, very large, and with a thick black pen.** Sometimes, this will help the person to see better. If they are still unable to see, score 0 for all of these items and for **validity code "3 = probably invalid: poor eyesight".**

4.2 Scoring for a Hearing-Impaired Participant: Before starting the CASI, if it is determined that the participant has a hearing impairment, optimize the participant's hearing as much as possible by keeping room as quiet as possible and/or by speaking louder for the entire test. If the participant is still unable to perform some of the CASI items due to poor hearing, score these items as 0 and code that the CASI is **probably invalid due to poor hearing**. Certain items, like 17 a and b (repeating sentences), should **not** be repeated even if the participant was not able to hear the first time.

4.3 CASI Administration for a Participant who is Too Severely Impaired Cognitively to Take the Test: Begin by asking as many of the CASI questions as you can, and code them as "0" if the participant cannot provide the correct answer. This will still provide a score for comparison with others in the cohort.

5. ADMINSTRATION

5.1 Start Time of the Test: Enter the testing start time in military time right before asking the first question. At the end of the exam you will be asked to record end time.

5.2 Introductory Text: Prior to starting the CASI, it is very important to inform the participant that you will be performing a memory test and the reason why. The following simple explanation should be provided as an introduction to the CASI:

"In this next examination, we are asking you to perform tasks related to memory and other thinking abilities. Some of the questions I will ask you are easy while others are hard. Nobody gets all correct. I have to ask you ALL the questions, so just do the best you can."

This simple explanation helps to put the participants at ease and may prevent them from getting defensive if they miss certain items.

5.3 Questions 1: PLACE OF BIRTH: These items are a measure of long-term memory. It is assumed that all individuals have had repeated opportunities to learn and report their date and place of birth.

1. WHERE WERE YOU BORN?
    a. City/Town (Town/Village) _____ (2)
    b. State/Country _____ (2)

After the opening question, if the participant has provided only a part of the information, PROBE FOR THE MISSING PART(S).

Example: "Where were you born?" "Sunnyvale" "What state is it in?" "California"

If the participant was born in the US, state is sufficient. If he/she was born outside of the US, country will be accepted.

The computer screen will show state or country of birth that was collected at the MESA baseline exam. If it matches, mark it as correct.

We do not have information on city/town of birth. Therefore, this will be asked again at the end of the exam. If the same response is given easily, assume it is correct and mark it at that time

5.4 Questions 2: DATE OF BIRTH: These items are a measure of long-term memory. It is assumed that all individuals have had repeated opportunities to learn and report their date and place of birth.

2. WHEN WERE YOU BORN?
    a. Year _____
        i. Accurate = 2
        ii. Missed by 1-3 years = 1
        iii. Missed by > 3 years = 0
        iv.

    b. Month _____ (1) Date _____ (1)

Date of birth collected from the MESA baseline exam will be shown on the computer screen. Please score according to this information.

5.5 Question 3: AGE: HOW OLD ARE YOU?

3. Age _____

   i. Accurate = 2
   ii. Missed by 1-3 years = 1
   iii. Missed by > 3 years = 0

If the question is answered "I will be xx years old this year", e.g. someone born 12/12/1940 may say "I will be 70 this year" instead of saying "I'm 69 years old". If they are correct, give full credit for either answer.

5.6 Questions 4 and 5: COMMON KNOWLEDGE. This item is also intended to be a measure of long-term memory. It is assumed that the participant has had many opportunities to learn these facts.

4. HOW MANY MINUTES ARE THERE IN AN HOUR? _____ (2)
Or HOW MANY DAYS ARE THERE IN A YEAR?

If the participant correctly answers "minutes in an hour", skip asking "days in a year". If the participant fails "minutes in an hour", ask "days in a year". Credit 2 points (full credit) if EITHER is answered correctly.

5. IN WHAT DIRECTION DOES THE SUN SET? _____ (2)

If the participant seems confused, provide the four choices of north, south, east, west. If the participant POINTS in a direction or names a landmark (e.g. the sun sets in the direction of the xx mountain"), ask him/her: "Is that north, south, east or west?" If still incorrect, score 0.

5.7 Questions 6a and 6b: REPEATING THREE WORDS.

I AM GOING TO SAY THREE WORDS FOR YOU TO REMEMBER. REPEAT THEM AFTER I HAVE SAID ALL THREE.

SOCKS _____ (1) BLUE _____ (1) CHARITY _____ (1)

Say each word clearly at the rate of 1.5 seconds per word. If the participant repeats after each word, request at the end of your presentation "Repeat the three words again" and score according to the response to this request. When you present the three words for the participant to repeat, sometimes they interrupt you by asking "what did you say?" or "I did not hear that, can you say that again?" before you have finished saying all three words. When this happens, do not stop in the middle of the three words even when the participant asks "what?" Finish the three words and say "repeat what you think I said". Score the number of words correctly repeated.

Please remember that if the participant is able to repeat all 3 words the first time, you DO NOT have to repeat the three words three more times. If the words are registered the first time, this should be scored as spontaneous recall. If the participant cannot repeat all three words, re-present all three words UP TO THREE MORE TIMES. Then, whether or not the participant can repeat all three words, proceed to the next item. During the first RE-presentation of the three words, it is advisable to clarify the words in order to ensure understanding. For example "Let me say the three words again. They are… SOCKS –

something to wear, BLUE – a color, and CHARITY – a good personal quality. Now say the three words again.

After the participant has repeated the three words, do **not** tell him again "Now remember these words" He/she has already been told to remember them earlier. This is different from the same item on the Folstein mental status exam and this subtle difference is intentional.

Minor variations in these words are acceptable. Accept the word as correct whether it is in the singular or plural form. For example, accept "socks" for "socks".

5.8 Questions 7: DIGITS BACKWORD.

I SHALL SAY SOME NUMBERS, AND YOU REPEAT WHAT I SAY BACKWARDS. FOR EXAMPLE, IF I SAY 1-2, YOU SAY 2-1, OK? REMEMBER, YOU REPEAT WHAT I SAY BACKWARDS.

A. 1-2-3 (1) Coach for 3-2-1 if needed
B. 6-8-2 (2)
C. 3-5-2-9 (2) Skip this if A and B cannot be repeated backward.

For the first digit span only, if the participant cannot correctly repeat A. 1-2-3 backward, score as 0 but coach for the correct response of 3-2-1.

If the participant fails the first two digit spans, skip the third one and score it 0.

For each digit span, give credit only if the response is entirely correct; score 0 otherwise.

If the participant says the numbers forward only, do not clue further, score 0. If he/she says the numbers forward, then asks if he should say them backwards, you can say "yes". And score according to his next answer. If he./she say the numbers forward, then backwards simultaneously and correctly, give him/her credit.

5.9 Questions 8: FIRST RECALL OF THREE WORD.

WHAT THREE WORDS DID I ASK YOU TO REMEMBER EARLIER.

A. Shoes:	Spontaneous recall (3) After "one word was something to wear" (2) After "was it shoes, shirt or socks" (1) Still incorrect and does not know (0)
B. Blue	Spontaneous recall (3) After "one word was a color" (2) After "was it blue, black or brown" (1) Still incorrect and does not know (0)
C. Charity	Spontaneous recall (3) After "one word was a good personal quality" (2)

After "was it honesty, charity or modesty" (1)
Still incorrect and does not know (0)

The order in which the 3 words are remembers is NOT important.

For each word not spontaneously recalled, provide the **category** cue followed by the multiple choice cue, if necessary. Wait up to 3 seconds for spontaneous recall and category cued recall before providing the next level of cuing. When you give the participant 3 choices to choose from, allow up to 5 SECONDS for the response.

For category cuing, please be careful not to provide non-verbal cues (e.g. pointing to your shirt).

When you prompt "one word was a good personal quality", if the person does not understand what that means, you can explain "it refers to something good about a person".

If the participant starts out giving an incorrect answer in the correct category (e.g. reports "shoes" or "coat" when the correct answer is "shoes"), proceed to provide the three multiple choices and score 1 if the choice is correct. IN THIS SITUATION YOU SKIP CATEGORY CUING.

If the participant cannot get the correct answer from the multiple choices, score 0 and TELL HIM/HER THE CORRECT ANSWSER for the benefit of the second recall to be requested later.

If he/she has not reported all three words correctly without help (less than spontaneous recall), SAY ALL THREE WORDS CORRECTLY once more before proceeding to the next item.

Examples:

5.10 Questions 9: SERIAL SUBTRACTION OF 3. This item measures the ability to successfully perform a series of mental operations.

NEXT I'M GOING TO ASK YOU TO DO SOME MENTAL SUBTRACTION

A. FROM 100, TAKE AWAY 3 EQUALS HOW MANY?	Answer = 97
B. AND TAKE AWAY 3 FROM THAT EQUALS ?	Answer=94
C. TAKE AWAY 3 FROM THAT EQUALS?	Answer = 91
D. TAKE AWAY 3 FROM THAT EQUALS?	Answer=88
E. TAKE AWAY 3 FROM THAT EQUALS	Answer=85

The participant is supposed to KEEP MENTAL TRACK OF THE PREVIOUS ANSWER and to perform the next MENTAL SUBTRACTION from that. If the participant forgets the previous answer, and asks the examiner to provide the answer from the previous step, please comply but score the current step "0" even if the subtraction is correct. If the participant forgets the previous answer more than once, the same scoring rule applies each time.

After the first step, if the participant confirms "subtract 3 from 97?", you can say "yes". If he/she tries to write the answers, say "please try to do this in your head, don't write".

For the FIRST error in subtraction (this refers to the first error, not necessarily the first step): If the participant does not know the correct answer or gives an incorrect answer, SCORE 0 BUT SUPPLY THE CORRECT ANSWER. Here the first does NOT refer to the first step, rather it refers to the first time a mistake is made in subtraction. If the participant makes an error in subtraction, that step is scored 0; give him a point for the second step if he subtracts 3 correctly from that initial error.

DISCONTINUE after two consecutive 0's for any reason and score the remaining steps as 0.

SCORING: For each step, score 0 for an incorrect subtraction from the previous (corrected) answer; also score 0 if the participant requests the examiner to repeat the answer from the previous step even if the subtraction for the current step is correct.

Example.

5.11 Questions 10-12: TEMPORAL ORIENTATION.

WHAT IS TODAY'S DATE?

YEAR:	Accurate (4) Missed by 1 year (2) Missed by 2-5 years (1) Missed by 6 or more years (0)
MONTH:	Accurate or within 5 days (2) Missed by 1 month (1) Missed by 2 or more months (0)
DAY	Accurate (3) Missed by 1 or 2 days (2) Missed by 3-5 days (1) Missed by 6 days or more (0)

Today's date will be shown on the computer screen. After the opening question and the participant's response to it, PROBE FOR ITEMS NOT REPORTED .

IF HE/SHE ATTEMPTS TO LOOK AT HIS WATCH, PHONE OR A CALENDAR, tell him "Please try without looking".

Scoring: Answers are scored in a graded manner according to closeness of the response to the correct answer. Follow the criteria listed above. The year is scored completely separately and the month/date are scored together.

WHAT DAY OF THE WEEK IS TODAY?	Correct (1) Incorrect (0)

For day of the week, don't provide choices.

WHAT SEASON OF THE YEAR IS IT ?	Accurate within 1 month (1) Missed by > 1 month (0)

For season, do not accept "Christmas season" or similar responses, but it is permissible to provide the names of the four seasons for the subject to choose from.

Scoring: Give 1 point if the answer is correct or if the change of the season occurred (will occur) within 1MONTH and the participant reports the last (next) season.

See CHART to assist in correct response.

5.12 Questions 13: SPATIAL ORIENTATION.

WHAT STATE ARE WE IN? (2)

WHAT CITY/TOWN/VILLAGE ARE WE IN (2)

Score 2 points for the correct answer.

IS THIS PLACE A CLINIC, STORE OR HOME? (1)

You may replace clinic with hospital if that is the location of the exam. Use either, not both. If testing occurs at another location, i.e. senior citizen's service center, adult daycare center, church, etc, substitute it for the middle alternative (store).

IF YOU ARE PERFORMING THE CASI IN A NURSING HOME OR CAREHOME, SUBSTITUTE IT FOR THE THIRD OPTION (HOME).

5.13 Questions 14: GENERATING ANIMAL NAMES.

WHAT ANIMALS HAVE FOUR LEGS? TELLME AS MANY AS YOU CAN.

Start timing at the end of the request. If the participant says "All animals have 4 legs" say "tell me their names" but do not re-start the timing.

Discontinue after 30 seconds. Do not tell the participant about the time limit.

Write all names provided by participant into the space provided on the form. SCORE 1 POINT FOR EACH CORRECT ANIMAL NAME (excluding duplicates).

IF THE PARTICPANT GIVES NO RESPONSE IN 10 SECONDS AND THERE ARE STILL AT LEAST 10 SECONDS OF REMAINING TIME, gently remind him ONLY ONCE "What (other) animals have 4 legs?"

After the first incorrect answer, remind the participant "I want you to name four-legged animals".

Do <u>not</u> provide hints like "can you think of animals in the zoo or on a farm". Also, don't say "you should name 10 animals" or keep prompting "one more" until they get all points. IT'S IMPORTANT THAT WE BE CONSISTENT IN HOW THIS IS ASKED AND IN PROMPTING.

Scoring: Score one point for each correct animal name. Different names for the same animal of different ages or sexes receive no credit (e.g. kitten and cat, puppy and dog, deer and doe). If a participant says "bear", "brown bear" and "polar bear", give only 1 point. Accept marginal answers such as monkeys, chimps, baboons, etc. Donkey and mule are different and can be awarded 1 point each. Imaginary animals such as "unicorn" can be accepted as long as they have 4 legs. "Man" should receive 0 points.

IGNORE INCORRECT ANSWERS, count only the correct answers. IF THE SAME ANIMAL NAME IS REPEATED MORE THAN ONCE, IT SHOULD ONLY BE COUNTED ONCE.

5.14 Questions 15: SIMILARITIES

This item measures abstract reasoning ability.

THE NEXT SET OF QUESTIONS IS ABOUT HOW THINGS ARE ALIKE TO EACH OTHER. FOR EXAMPLE, AN 'ORANGE' AND A 'BANANA' - THE WAY THAT THEY ARE SIMILAR IS THAT THEY ARE BOTH FRUIT. SAY:

A. AN ARM AND A LEG ARE BOTH? Body parts, limbs, extremities (2)
Long, bend, muscles, bones, etc (1)
Incorrect, tells difference (0)

B. LAUGHING AND CRYING ARE BOTH? Expressions of feelings/emotions (2)
Other correct answer (1)
Incorrect/tells difference (0)

C. EATING AND SLEEPING ARE BOTH? Necessary body functions (2)
Other correct answer (1)
Incorrect/tells difference (0)

A: For the first pair (arm and leg) only: If the participant's answer is anything less than 2 points, score them either 0 or 1 as appropriate COACH FOR A 2-POINT ANSWER, i.e. tell him/her "What I'm trying to get at is: an arm and a leg are both parts of the body, or limbs, or extremities". Even though you scored him/her 0 or 1, this coaching serves as another example before going on to the next pair. However, do NOT coach if he/she scores 0 or 1 on the remaining two pairs.

For B and C: NO COACHING. If the participant gives an incorrect similarity, or tells the difference, or says "they are different" or "I don't know" , just score 0 and proceed to the next part.

Scoring: ARM and LEG: 2 points = Body parts
Limbs
Extremities
Appendages
"They are part of a human"

1 point = Long
Bend
Have muscles
Have bones
"They move"

	"You use them both"
	Skin color
	Pairs
	Have flesh
	Have nails
0 points =	Don't know
	They're different
	Have fingers
	Other incorrect
LAUGHING and CRYING: 2 points =	Must mention "emotions" or "feelings"
	Sentiments
	Sentimental
1 point =	Expressions (alone)
	Reactions
	Human
	Make sounds
	Natural instinct
	Behavior
0 points =	Don't know
	They're different
	They're opposite
	It's a habit
	Sometimes you cry when you laugh
	Sometimes you laugh when you cry
	Things you do
	Senses
	Other incorrect answer
EATING and SLEEPING: 2 points =	"Necessary" or "essential" bodily functions
	Things that you have to do
	For subsistence
	For survival
	Anything implying "necessary"
	Basic needs
	For living or for live cycle
1 point =	"Bodily function" alone without necessary
	Refreshing
	Relaxing
	Nourishing
	Things you do everyday
	It's a habit
	I enjoy both
	They both feel good
	Natural instinct
	Natural or natural doings

	What a person does For your health
0 points =	Don't know They're different They are opposite Other incorrect answer

In general, be lenient in awarding 1 point. Participants are given credit as long as they can see beyond the differences and come with a reasonable similarity.

5.15 Questions 16: JUDGMENT.
This item assessed common knowledge. SAY:

A. WHAT ACTIONS WOULD YOU TAKE IF YOU SAW YOUR NEIGHBOR'S HOUSE CATCHING FIRE?

Score number of appropriate answers up to 2

One point for each CATEGORY of correct action:

- Call 911, inform the fire or police depts. or other appropriate authority
- Try to save or alert the residents
- Try to help put out the fire
- Safeguard own property/family
- Alert other neighbors
- Try to help

If the participant stops before earning 2 points, ask once only: WHAT ELSE MIGHT YOU DO? If the participant does not know, do not give examples.

B. WHAT ACTIONS WOULD YOU TAKE IF YOU LOST A BORROWED UMBRELLA?

Score 1 point for each category of actions

- Inform/apologize
- Replace/compensate

If the participant says "I'll look for it", ask: "What would you do if you cannot find it?" and score according to his/her next answer.

If the participant answers "I would forget about it, it's only an umbrella", score 0 points.

C. WHAT WOUD YOU DO IF YOU FOUND AN ENVELOPE THAT WAS SEALED, ADDRSSED AND HAD A NEW STAMP?

Score according to the answer provided:

2 points = Mail it
1 points = Try to locate the owner
0 points = Inappropriate action

If the participant asks "Where did I find the envelope?" you can say "on the street", then score according to his next answer.

If the participant says "I would not do anything because it's none of my business" or "I would not touch it because it's a federal offense to tamper with the US mail" or "I would look inside of the envelope", score 0 points. These answers may not mean that a person is demented, but they are not the answers usually given and may indicate impaired judgment form other causes. We should try to be consistent here.

If the participant answers "I would take it to the police station", please score 1.

"Give it to the mailman" = 2 points
"Take it to the Post Office" = 2 points

5.16 Questions 17: REPEATING SENTENCES.
This item assesses attention and the ability to follow a command. SAY:

REPEAT EXACTLY WHAT I SAY**:**

A. HE WOULD LIKE TO GO HOME, NOW REPEAT…

Say the sentence in a normal pace (about 2 seconds). Score 2 points if correct, 1 point if 1-2 words are missed/wrong, and 0 if 3 or more missed/wrong words are cited. READ THE FOLLOWING:

B. THIS YELLOW CIRCLE (1)
IS HEAVIER (1)
THAN BLUE SQUARE (1)

Say the sentence in about 3 seconds. IT SHOULD BE SAID AS A CONTINUOUS SENTENCE, not broken up into three parts. This is intended to be an anomalous sentence without the article "the" before "blue square".

Do not say "I will not repeat this statement again". Do not stop in the middle of a sentence even when the participant asks "What?" Finish the sentence and say "Repeat what you think I said".

For both A and B, take off a point for extra words.

Examples.

5.17 Questions 18: READ AND OBEY "RAISE YOUR HAND". This item tests the ability to follow a simple written command. The command is printed in all capital letters approximately 2.5 cm in height within the top third of a sheet of paper. Point to the command and say "PLEASE DO THIS". Keep the paper close to the surface of the desk.

Score: 3 points = Raises hand without prompting
2 points = Raises hand after prompting
1 point = Reads correctly but does not raise hand
0 points = Can neither read nor obey

If the participant does not respond, repeat the instruction once, and if he does it then you can still give the 3 points. If the participant merely reads the command aloud, say "PLEASE DO WHAT IT SAYS". Do NOT say "Please raise your hand". If he/she does it at this point, give 2 points. If he/she still doesn't do it, but only reads it aloud, give 1 point. READING ALOUD IS NOT REQUIRED.

ALLOW UP TO 5 SECONDS for a response at each stage.

If the participant askes "which hand?", reply "either one".

As soon as he/she raises his/her hand, say "THANK YOU, YOU CAN PUT IT DOWN NOW".

5.18 Questions 19: WRITING "HE WOULD LIKE TO GO HOME". This item tests the ability to correctly spell and write five simple and common words. Tell the participant:

I WOULD LIKE TO HAVE A SAMPLE OF YOUR HANDWRITING. WRITE
"HE… WOULD… LIKE… TO …GO… HOME"

Allow either cursive or printing. Say each word of the sentence slowly and distinctly. If the participant seems to have trouble remembering the sentence, dictate word by word as the participant writes. It is ok to repeat individual words.

Allow up to 1 minute for response. If at the end of one minute the participant is still working on the task in earnest, allow him/her to finish for the sake of maintaining rapport and morale, but note how many words are finished . Do not credit parts finished after 1minute. DO NOT TELL the participant there is a time limit on this or any other item.

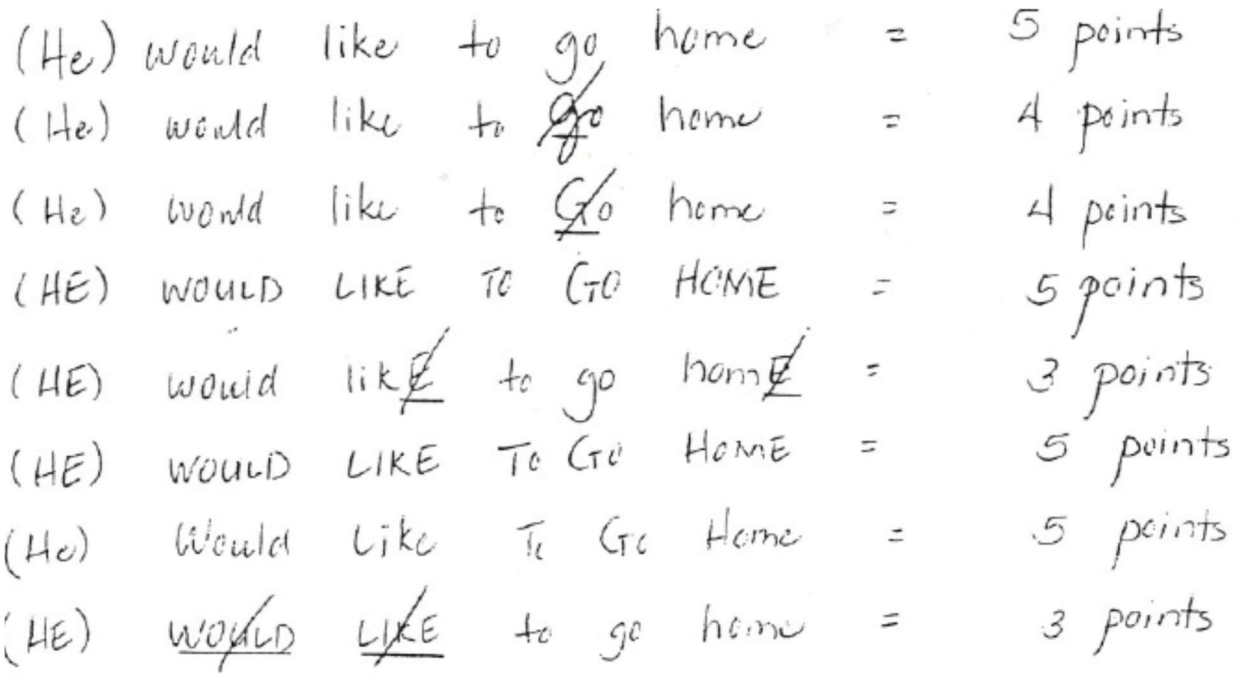
Scoring: 1 point for each word except do not score the first word (He) of the sentence. Score each word according to whether or not it can be readily identified without the context. For each word, score 0 if there is a spelling error or mixed capitalization. Do not give credit if the "i" does not have the dot. Do not penalize if the participant prints all letters in the uppercase. Do not take points off for extra words in the sentence.

Depending on a person's education or habit, capital letters are often written differently. For example, the capital letter "G" can be written the following ways.

Therefore, in order to decide whether or not a letter is capitalized or not, please consider the size of the letter relative to the size of the other letters in the word.

For the word "like", the dot does on the "i" does not necessarily have to be exactly above the "i". Give 1 point if it is a bit off-centered.

EXAMPLES:



NOTE ON THE FORM THE HAND WHICH THE PARTICIANT USES TO WRITE THIS SENTENCE.

5.19 Question 20: COPYING PENTAGONS. Show the sample pentagons and say:

PLEASE COPY THIS

For right-handed persons, present the sample on their left side. For left-handed persons, present the sample on their right side. This way the sample will not be blocked by the drawing hand. You can observe which hand the person writes with at Question 19 (writing the sentence).

Only say "Please copy this" and do not say "make it the same shape" or "please copy these pentagons" since that provides an extra cue.

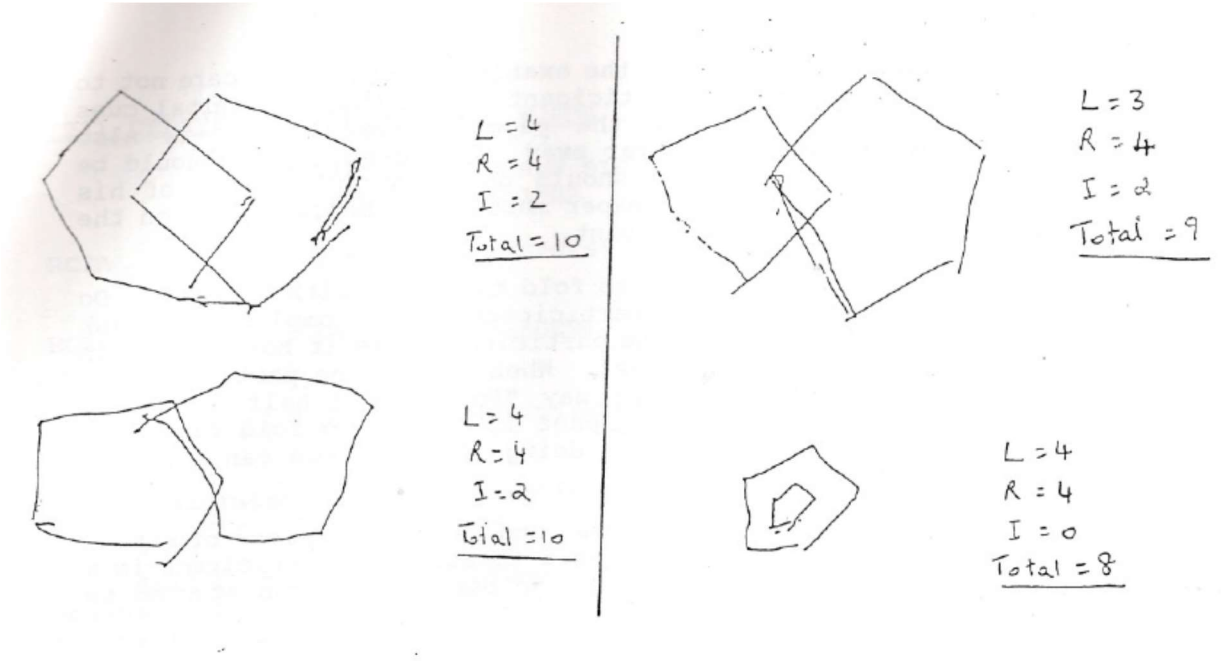
Allow up to ONE MINUTE for response, then move on to the next item. DO NOT tell the participant there is a time limit on this or any other item. If at the end of one minute the participant is still working on the task in earnest, consider allowing him/her to finish for the sake of maintaining rapport and morale. Note how much has been completed after 1 minute. For scoring, do not credit parts finished after one minute.

Sometimes the participant is not satisfied with the product and wants to try again. This is permitted but do NOT re-start the timing. At the end of one minute, score for the BETTER product. DO NOT PROMPT HIM/HER TO TRY AGAIN, BUT LET HIM/HER DO SO IF DESIRED.

Scoring: Scoring will be done for the left and right pentagons and for the intersection. The pentagons will have a maximum of 4 points and the intersection 2.

Pentagons: 3 points……if it is five-sided but the longest side is longer than twice the length of the shortest side. Do not penalize for non-straight or crooked lines, or minor gaps or over-shoots at the corners, that seem to be caused by poor motor control. Also, DO NOT PENALIZE FOR EXTRA LINES DRAWN.

EXAMPLES:



5.20 Questions 21: FOLLOWING THREE-STAGE COMMAND.
This item tests the participant's ability in understanding, remembering, and executing a three-part oral command. Please hold a piece of paper in front of your chest (not near the participant) and say:

TAKE THIS PAPER WITH YOUR (Left) (Right) HAND (1)
FOLD IT IN HALF, AND (1)
HAND IT BACK TO ME (1)

The three parts of the command are spoken clearly and without interruption in approximately 6 seconds. THIS ITEM SHOULD BE SAID AS A CONTINUOUS SENTENCE and not broken up into 3 parts. If the participant interrupts with "What did you say?" or similar, continue to finish the command, then say "Do what you think I asked you to do".

Use a blank piece of rectangular-shaped paper (about half the size of a standard 8.5" x 11" sheet) for this test.

The first stage of the command asks the participant to take the piece of paper with his NON-PREFERRED HAND (the hand not used in the preceding wring and drawing tasks).

The examiner holds the piece of paper in hand, in plain view of the participant, while giving the command. Some participants tend to reach for the paper right after hearing the first part. When this happens, the examiner should temporarily move his hand away from the participant to be out of reach while continuing to state the next two parts of the command without interruption.

After saying the command, the examiner should take care not to move the paper toward the participant to provide non-verbal cues for the participant to take the paper. However, it is also important NOT TO HOLD IT TOO FAR AWAY. The participant should be able to reach it easily and should not have to get out of his chair to reach it. Also, the paper should not be laid down on the table but given to the participant.

Some participants attempt to fold the paper with one hand. Do not disrupt them if you think the participant can accomplish the task despite clumsiness. If the participant asks if both hands can be used for folding the paper, answer "yes". When asking the participant to fold the paper in half, do NOT say "fold it in half with both hands". However, if the participant is trying to fold the paperwith one hand and is having trouble doing it, say "you can use both hands for this".

After the participant has taken and folded the piece of paper, the examiner should NOT move his hand toward the participant in a gesture to receive the paper UNTIL the participant has started to hand the paper back.

DO NOT REPEAT ANY PART OF THE COMMAND. If the participant requests the examiner to do so and it is desirable to oblige for the same of maintaining rapport, score according to the responses executed before the repeat presentation of t he command.

IN THE MIDDLE OF THE TASK, if the participants asks "should I give this to you?", say "Do what you think I said before" and score according to his/her response.

Scoring: 1 point for each part of the command. The use of the non-preferred hand is required only for the first part.

A. No credit if the participant uses the preferred hand
B. No credit if the participant folds the paper more than once. No credit if he/she tears the paper in half.
C. No credit if the participant simply puts the paper down instead of handing it back to the examiner. No credit if he/she shoves it toward or throws it toward the examiner. He/she MUST HAND it back to get credit for the third part of the command.

SPECIAL CIRCUMSTANCES: e.g. paralysis of one hand. Usually you should ask the participant to take the piece of paper with his non-preferred hand (hand that is NOT used for writing and drawing). However, there may be occasional exceptions to this rule. For example, if the person has paralysis of his/her right arm and used his left hand to draw/write previously, he obviously can't take the paper with his/her paralyzed hand, so you can t ell him/her to take the paper with his left hand, even though this is the preferred hand.

5.23 Questions 22: DELAYED RECALL OF THREE WORDS.

WHAT THREE WORDS DID I ASK YOU TO REMEMBER EARLIER?

A. Shoes: Spontaneous recall (3)
After "one word was something to wear" (2)
After "was it shoes, shirt or socks" (1)
Still incorrect and does not know (0)

B. Blue Spontaneous recall (3)
After "one word was a color" (2)
After "was it blue, black or brown" (1)
Still incorrect and does not know (0)

C. Charity Spontaneous recall (3)
After "one word was a good personal quality" (2)
After "was it honesty, charity or modesty" (1)
Still incorrect and does not know (0)

Administer this item even if the participant scored 0 on the First Recall (Question 8). Scoring is the same.

Follow the testing procedure for Question 8, First Recall. However, do NOT REPEAT the correct answer no matter what the participant scores.

The order in which the three words are remembered is not important. When you prompt "One word was a good personal quality", if the person does not understand what that means, you can explain "it referees to something good about a person".

5.24 Questions 23: NAMING BODY PARTS.

This section tests whether or not the participant can PROMPTLY name five parts of the body. Please say:

WHAT DO WE CALL THIS PART OF THE (FACE) (BODY)?

The examiner asks the above while pointing directly to the appropriate part on his/her own body: "What do you call this part of the fact (pointing to the middle of the forehead)…and what do you call this part of the body (pointing to the chin)… and this part of the body (pointing to shoulder)…and this part (pointing to the elbow)….and this part (pointing to the wrist)."

Allow 2 seconds for each body part. Score 1 point for each correctly identified:

A. Forehead (1) (accept brow)
B. Chin (1) (accept jaw)
C. Shoulder (1)
D. Elbow (1)

E. Wrist (1)

If the participant cannot name a part within 2 seconds or if the answer is incorrect, do not help or question again; just score 0 and move on to the next part.

For forehead, accept brow. Do NOT accept head, eyebrow, or temple.
For chin, accept jaw.

If the participant gives you a wrong answer, but manages to correct himself right away, give him the points. If he says "arm" instead of "shoulder", you can clarify by saying saying "what do you call the part that moves?" If he still says "arm", score 0.

5.25 Questions 24: NAMING OBJECTS .
This item assesses if the person can PROMPTLY name five common objects. Please say:

WHAT IS THIS?

Spoon (1)
Coin (1) accept coin, quarter, 25 cents, 2 bits
Toothbrush (1)
Key (1)
Comb (1)

Present one item at a time and ask the participant to name it. Lay the objects directly in front of the participant where they are easily visible. If the participant cannot name an object in 2 seconds, put it in the participant's hand and ask "What do you call this?" If he/she still cannot name it, wait 4 seconds, say (for key) "It is a key…say key". Asking the participant to repeat is to check if they register the input and can say the word.

Avoid any items with outstanding colors. Do not use keys or coins that are small (in the US use a quarter).

The exact order of presenting the objects in not important.

If the participant describes the object, ask "What do you call it?" or "What is its name?"

For coin, accept "coin" or the name of the specific denomination of the coin (quarter or 25 cents or 2 bits). Do not accept "money". If the participant says "money", ask "what is the specific name for this kind of money?", and score according to his/her response.

For toothbrush, do not accept "brush" as correct. If the participant says "brush", ask "what is the specific name for this kind of brush?" and score according to his/her response. By asking for the specific name of the object, we can differentiate between the participant not being able to name things correctly and just being global by using a general name rather than a specific one.

If the participant gives an incorrect name, tell the correct name and ask the participant to repeat it.

After naming each item, put it back down in front of the participant on a clean, uncluttered surface.

Scoring: 1 point for each correctly named object without coaching by the examiner. If the participant recognizes the item (describers it s use) but cannot name it, score 0.

If the participant gives you a wrong answer but manages to correct him/herself right away, give him/her the points. Please make sure that he can see the objects well. If his/her vision is very poor, hand him the objects, and if he/she can name them correctly, give the points.

5.26 Questions 25: IMMEDIATE RECALL OF FIVE OBJECTS .

After all five objects from the previous naming have been replaced back in front of the participant, say:

PLEASE REMEMBER THESE FIVE OBJECTS

WAIT 5 SECONDS and then cover all five objects with a blank piece of cardboard (something opaque and stiff that will hide all visual cues from the objects) and ask:

WHAT FIVE OBJECTS DID I JUST SHOW YOU?

Do not give the participant longer than 5 seconds even if he/she asks to see the objects again.

Terminate testing when t he participant has reported five objects (including incorrect names) or when the participant cannot recall any additional item in 5 seconds.

Score 1 point for each correctly name object recalled:

Spoon (1)
Coin (1) accept coin, quarter, 25 cents, 2 bits
Toothbrush (1)
Key (1)
Comb (1)

While before, "money" and "brush" were not acceptable answers – HERE THEY ARE ACCEPTABLE. Please provide a point for each if named as such.

5.27 CLOSING . Thank participant for completing the exam

THOSE ARE ALL THE QUESTIONS WE HAVE ON THIS EXAMINATION. THANK YOU FOR COMPLETING THEM FOR US.

5.28 Recording Time test Ended and Validity.

5.28.1 Finish time: Remember to fill in the time that the exam was completed in military time.

5.28.2. Validity: At the end of the test, enter whether or not the CASI was a valid assessment of the participant's cognitive abilities. The CASI should be scored as invalid only if the impairment interferes with the total score. If the participant is hard of hearing but his hearing impairment does not interfere with the score, you should code "1 = valid". The total score does not have any relation to validity, e.g. a

low score due to dementia does not mean that the test is invalid, and a high score does not necessarily mean that the test is valid. **If not valid,** pick the reason that the test was invalid. Only one reason should be coded. If there are 2 or more reasons that the CASI score is not valid, pick the most important reason. You can write in the other reasons, but do not circle more than 1 number as only 1 entry can be put into the computer**. If you are unable to perform the CASI at all, because of severe dementia or agitation, code "3", because of sever deafness, code "4", because of non-verbal conditions either due to coma or aphasia, code "5", because of any other reason code "6" and specify.**

5.28.3 Validity and CASI Status Questions must always be completed unless the participant refused the CASI completely**.**

3.6.2 Digit Symbol - Coding

1. **INTRODUCTION.** This test is part of the WAIS-III battery and was formerly called the Digit Symbol Substitution Test. It assesses speed of mental processing, learning and working memory.

2. **Materials**
   Answer sheet
   Stopwatch
   Two No. 2 graphite pencils without erasers
   Digit Symbol Scoring Template

3. **Description**

For Digit Symbol – Coding[2], the examinee copies symbols that are paired with numbers. Using a key at the top of the form, the examinee copies each symbol in a box under its corresponding number. The examinee's score is determined by the number of symbols correctly drawn within the 120 seconds,

DSC begins with an explanation of the task and completion of sample items. Timing begins with the participant's attempt at coding after learning the task. **Discontinue after 120 seconds.**

4. **General Directions**
   4.1 A smooth drawing surface must be provided. If the table has a rough surface, the Record Form should be placed on a clipboard, a piece of cardboard, or another flat surface.

   4.2 To introduce the test, say:

In this section, I'm going to ask you to copy some symbols.

4.3 If the examinee asks what she/he should do if they make a mistake, encourage them to continue to work as fast as they can. However, do not discourage examinees from making spontaneous corrections unless they do so repeatedly and it impedes their performance.

   4.3 If, after completing a row, an examinee tries to complete the next row in reverse order, remind the examinee to start at the beginning of the row and not to skip any.

5. **Item Instructions**

Turn to the Digit Symbol – Coding page in the Record Form. Fold the Paper Form so only Digit Symbol – Coding is showing, and place it in front of the examinee. Hand him or her a pencil without an eraser, point to the key above the test items, and say:

Look at these boxes. Notice that each has a number in the upper part and a special mark in the lower part. Each number has its own mark.

Point to 1 and its mark in the key, then 2 and its mark. Then point to the seven squares located to the left of the heavy black line and say:

Now look down here where the squares have numbers in the top part but the squares at the bottom are empty. In each of the empty squares, but the mark that should go there. Like this.

Point to the first Sample Item, then point back to the key to show its corresponding mark, and say:

Here is a 2; the 2 has this mark. So I put it in this empty square, like this.

Write in the symbol. Point to the second Sample Item and say:

Here is a 1; the 1 has this mark (point to the second Sample Item, then to the mark below the 1 in the key)**, so I put it in this square.**

Write in the symbol.

Point to the third Sample Item and say:

This number is a 3; the 3 has this mark (point to the third square and to the mark below the 3 in the key)**, so I put it in the square** (write in the symbol)**.**

After marking the first three Sample Items, say:

Now you fill in the squares up to this heavy line.

If the examinee makes an error on any of the Sample Items, correct the error immediately and review the use of the key. Continue to provide help if needed. Do not proceed with the subtest until the examinee clearly understands the task.

When the examinee completes a Sample Item correctly, offer encouragement by saying **Yes** or **Right**. When all the Sample Items have been completed, say:

Now you know how to do them. When I tell you to start, you do the rest of them.

Point to the first square to the right of the heavy line and say:

Begin here and fill in as many squares as you can, one after the other without skipping any. Keep working until I tell you to stop. Work as quickly as you can without making any mistakes.

Sweep across the first row with your finger and say:

When you finish this line, go on to this one.

Point to the first square in the second row. Then point to the heavy black line and say:

Go ahead.

Begin timing.

If the examinee omits an item or starts to do only on type (e.g., only the 1's), say:

Do them in order. Don't skip any.

Point to the first item omitted and say:

Do this one next.

Provide no further assistance except to remind the examinee to continue until instructed to stop.

At the end of 120 seconds, say **Stop.**

6. Scoring

Record 1 point for each correctly drawn symbol completed within the 120-second time limit. ***Responses to the seven Sample Items are not included in the examinee's score.*** Do not give credit for items completed out of sequence.

Use the Digit Symbol Template to check the examinee's responses and record the score on the Record Form.

A response is scored as correct if it is clearly identifiable as the keyed symbol, even if it is drawn imperfectly or if it is a spontaneous correction or an incorrect symbol.

Maximum Score: 133 points

3.6.3 Digit Span Test

1. General Directions. This test, also a part of the WAIS III, is a working memory test involving repeating spans of numbers forward and then other spans backward. Please use the scripts, coaching and scoring as follows:

2. Digits Forward

2.1 After saying the instructions, administer the Digit Spans in order

2.2 Do not repeat a span once read.

2.3 Administer both spans of the same length regardless of how the participant performs.

2.4 Say the digits at a rate of 1 digit about every 1 second.

2.5 Use a monotonic voice without inflections at the end.

2.6 Do not 'chunk' spans (e.g., 34-729) when you read them

2.7 Discontinue after failure on BOTH trials of any item (e.g. 5a and 5b).

2.7. **SCRIPT**

I am going to say some numbers. Listen carefully, and when I am through say them right after me. For example, if I say 7-1-9, what would you say?

- If the participant responds correctly, 7-1-9, say "**That's right**" and proceed to Item 1.
- If the participant fails the example, say "**No, you would say 7-1-9. I said 7-1-9 so to say it forward you would say 7-1-9. Now try these numbers. Remember, you are to say them forward. 3-4-8.**
- Whether the participant succeeds or fails with the second example (3-4-8), proceed to Item 1. Give no help on this second example or any of the items that follow.

2.8 **Scoring**. Each span is scored 0 or 1. Give 1 point if the participant passes the trial and no points if the participant fails the trial. ONLY DISCONTINUE THE TEST WHEN PARTICIPANT HAS FAILED BOTH TRIALS OF THE SAME SPAN LENGTH (e.g. 5a and 5b).

3. Digits Backward

3.1 Administer the digit spans in order.

3.2 Do not repeat a span once read.

3.3 Administer both spans of the same length regardless of how the participant performs.

3.4 Say the digits at a rate of 1 digit about every 1 second.

3.5 Do not 'chunk' spans (e.g., 34-729) when you read them

3.6 Use a monotonic voice without inflections at the end.

3.7 **SCRIPT**

Now I am going to say some numbers, but this time when I stop I want you to say them backwards. For example, if I say 7-1-9, what would you say?

- If the participant responds correctly, 9-1-7, say "**That's right**" and proceed to Item 1.
- If the participant fails the example, say "**No, you would say 9-1-7 I said 7-1-9 so to say it backwards you would say 9-1-7. Now try these numbers. Remember, you are to say them backwards. 3-4-8.**
- Whether the participant succeeds or fails with the second example (3-4-8), proceed to Item 1. Give no help on this second example or any of the items that follow.
- Discontinue after failure on BOTH trials of any item.

3.8 **Scoring**. Same as Digit Forward. Each span is scored 0 or 1. Give 1 point if the participant passes the trial and no points if the participant fails the trial. ONLY DISCONTINUE THE TEST WHEN PARTICIPANT HAS FAILED BOTH TRIALS OF THE SAME SPAN LENGTH (e.g. 5a and 5b).

3.7 Spirometry

MESA Lung III and MESA Lung Non-Smokers Pulmonary Function Manual of Procedures

July 13, 2016 - Version 1.0

Prepared by the MESA Lung Pulmonary Function Reading Center

3.7.1 BACKGROUND

3.11.1.1 The MESA Lung Study III

The MESA Lung Study III is measuring spirometry among over 2,000 MESA participants who previously enrolled into the MESA Lung Study. The MESA Lung Study III is examining the role of lung perfusion in chronic obstructive pulmonary disease (COPD) and emphysema. Spirometry is measured in the MESA Lung Study III to define obstructive and restrictive lung disease, COPD, and to measure decline in lung function since Exams 3, 4 and 5. COPD is now the third-leading cause of death in the US and much of the world; however, few preventative strategies are available for COPD besides smoking cessation and avoidance.

3.11.1.2 The MESA Lung Non-Smoker Study

The MESA Lung Non-Smoker Study is measuring spirometry among 650 non-smokers in MESA. The MESA Lung Non-Smoker Study is examining why COPD occurs in non-smokers. Spirometry is measured in the MESA Lung Non-Smokers Study to define COPD.

Combined Protocol for the MESA Lung Study III and Non-Smoker Study
The MESA Lung III Study and the MESA Lung Non-Smoker Study will perform spirometry following a single, uniform, standardized protocol that is designed to be well-integrated into MESA Exam 6. We therefore have one Manual of Procedures for spirometry for MESA Lung Study III and MESA Lung Non-Smoker Study and you don't need to worry about which of the two lung studies a given participant is enrolling into when performing spirometry. Both studies also include a lung CT scan. The details of the lung CT scan are included in the MESA CT Manual of Operations. The additional procedures are summarized in the table on the following page.

Procedure	**MESA Lung III** (n=~2,000, all FC)	**MESA Lung Non-Smoker** (n=650, all FC)
Spirometry Pre-bronchodilator Post-bronchodilator	 X if airflow obstruction	 X if airflow obstruction
Lung CT scan Non-Contrast Contrast	X 1,000 1,000	X 650 0
Selection form/questionnaire	X	X

3.11.1.3 Spirometry

Spirometry is the simplest, most precise, and least expensive test for the assessment of pulmonary function. Low lung function is a major independent predictor of morbidity and mortality from cardiovascular, pulmonary and all causes.

The important spirometry measurements are the forced vital capacity (FVC), which is greatest forced volume of air exhaled from a maximal inspiration to a complete exhalation; the forced expiration volume in one second (FEV_1), which is the volume of air exhaled in the first second of the FVC maneuver; and the ratio between these two values: FEV_1/FVC. A low FVC defines restrictive lung disease whereas a low FEV_1/FVC ratio defines obstructive lung disease. These measurements were made in MESA Exam 3, 4, and 5. In MESA Lung III and MESA Lung Non-Smoker Studies, we shall perform these measurements at Exam 6 following the same protocol. Maximal inspiratory pressure (MIP) and diffusing capacity for carbon monoxide (DLCO) will **not** be measured again.

Participants with airflow obstruction in the MESA Lung III and MESA Lung Non-Smoker Studies will receive a bronchodilator, after which "post-bronchodilator" spirometry will be performed. The bronchodilator is very helpful in differentiating the two main types of obstructive lung disease. Asthma is characterized by airflow obstruction which is intermittent and which is generally reversible with a bronchodilator; COPD is characterized by airflow obstruction which is chronic and does not fully reverse with a bronchodilator.

Two professional societies publish widely recognized spirometry guidelines: the American Thoracic Society (ATS) and the European Thoracic Society (ERS), and a combined ATS + ERS spirometry guideline was published in 2005. The original authors of this manual were members of the spirometry guidelines committee. The instruments and methods in this manual conform to these guidelines and exceed their accuracy and repeatability recommendations.

The spirometers, software, and quality assurance program are the same as in the original MESA Lung Study, the 4th National Health and Nutrition Examination (NHANES IV), and the Hispanic Community Health Study (HCHS)/SOL. This standardization of methods makes the results of these large government-funded studies directly comparable.

Spirometry results are very dependent on an adequate effort by the participant performing the test. The participant must be instructed to completely inhale and forcefully exhale throughout the entire expiratory maneuver. If the participant does not produce an adequate effort, the results are not valid. It is therefore **essential** that you explain, demonstrate, and evaluate each maneuver to coach the best possible effort from the participant.

Although the OMI software provides technical feedback to the technician, the technician still must instruct and demonstrate the test procedures to the participant. In addition, the technician must observe the results (flow-volume curves, volume-time curves, test values, and computer quality assessments) to determine the best coaching instructions to provide to the participants. This requires that the technician be familiar with what constitutes a valid test including unacceptable maneuvers as well as provide appropriate coaching instruction. There is no substitute for a well-motivated and well-trained technician.

The testing room is quiet and private, without distractions. No other tests are conducted in the room during spirometry testing. The ambient temperature in the testing room is maintained between 65-78ºF. Ask for air conditioning if the room becomes uncomfortable due to high humidity or high temperatures.

3.7.2 EQUIPMENT AND SUPPLIES

- SensorMedics model 1022 dry-rolling seal volume spirometer is fitted by OMI with a digital volume encoder, temperature sensor, and RS232 serial computer interface (you should have from Exam 3/4/5).
- OMI spirometry software is installed on a notebook computer with Windows.
- Calibration syringe, 3.00 liters, Han Rudolph model # 5530 (you should have from Exam 3/4/5).
- Spirometer hoses, 3 feet long
- Disposable mouthpieces, nose clips
- Albuterol metered-dose inhalers (MDIs) and spacers

Note: Although this spirometry system is much larger than spirometers commonly used for clinical practice (office spirometers), it is more accurate. The volume accuracy of this system is better than 1.5 percent, which exceeds the ATS-ERS recommendation (accuracy within 3.5%).

3.11.2.1 Advantages of the Sensor Medics Zero Return Spring

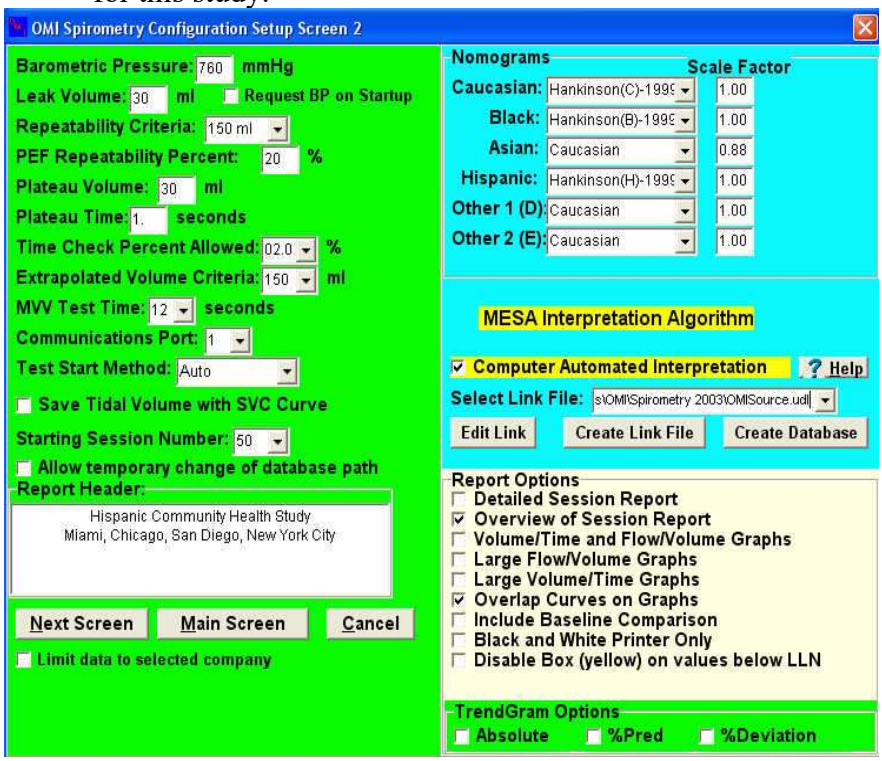
- The spirometer's piston is returned to the zero position at the end of each maneuver by the zero return spring, reducing the time required to test a participant.
- Any leak in the spirometer or between the participant and his/her mouthpiece is easily detected because of the obvious loss in volume as a result of the positive pressure (0.4 cmH_2O) generated by the return spring
- There is a clear indication when the participant comes off the mouthpiece.
- The spirometer is always stored with minimal volume in the spirometer, which eliminates the development of a "blip" due to seal memory within the measuring volume.

3.11.2.2 Initial Equipment Setup

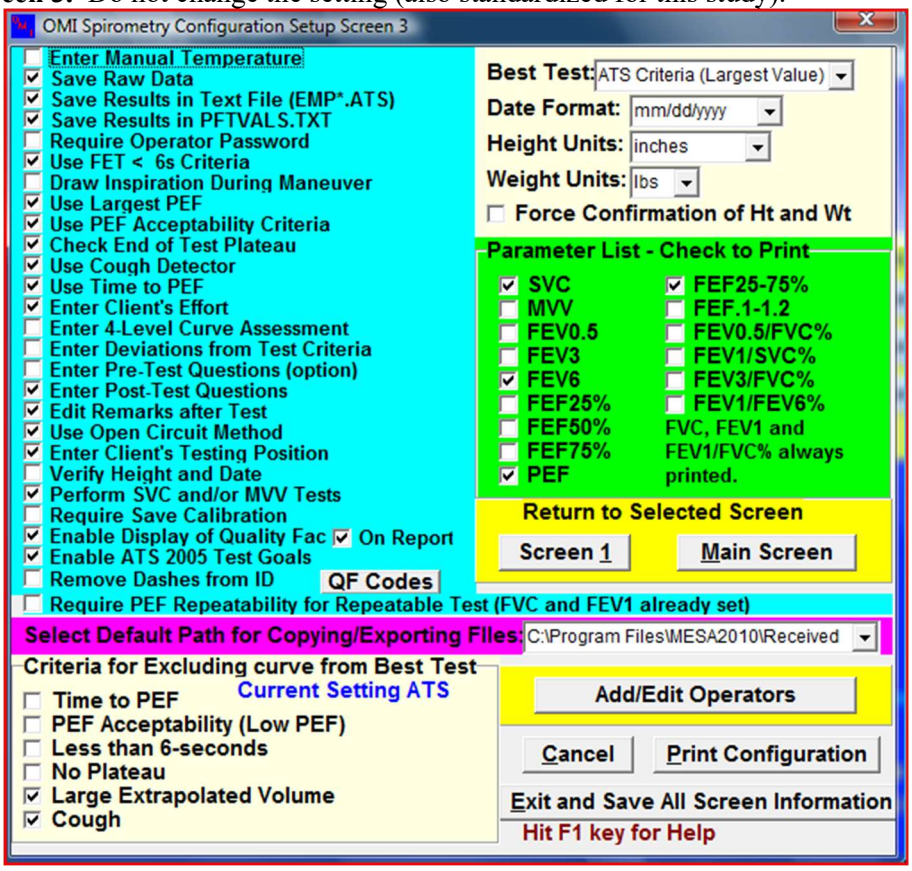
1. Set up the equipment and connect cables on a solid desk or table. Make sure that the rod on the rolling barrel (at back of unit) can slide backwards without hitting a wall or other object.
2. Connect the power cords to a grounded electrical socket.
3. Turn on the spirometer.
4. Power up the laptop computer.
5. Use the OMI Setup Program (desktop icon).
   - Double click on "OMISetup" windows icon.
   - The initial password to enter the setup program is 'omisetup'
   - There are three screens showing user, spirometer and other information. Details are given in the appendix.

Setup Screen 1.

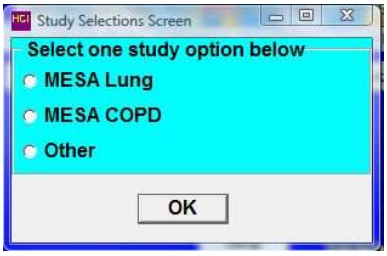
Setup Screen 2. Please don't change the settings on this screen, which have been standardized for this study.



Setup Screen 3. Do not change the setting (also standardized for this study):



3.11.2.3 Daily Leak and Calibration Checks



Perform a leak and calibration check before each day of testing.

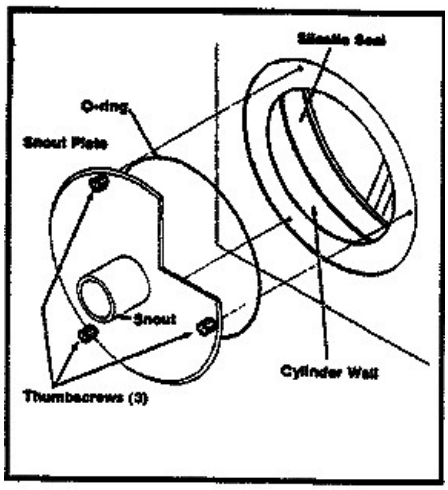
1. Double click "OMIWSP.exe" windows icon.
2. Select MESA Lung (for both studies)
3. Enter your initials
4. Select "Calibration"
5. Select Leak Test from pull-down "Calibration" menu.
6. A leak test is performed by checking that the negator (return spring) is engaged and then adding 3 liters of air into the spirometer with the calibrating syringe.
7. Click on "Start Timing". The computer then monitors the spirometer volume for 60 seconds and determines if the volume is maintained. A progress bar shows the time left until completion of the leak test.
8. The result of the leak test are written to a calibration/leak test log file, including the date and time of the test, by clicking on the "Save" button. A warning is displayed if a leak larger than the 20ml is observed.
9. Select "Perform Cal/Leak Check" button on the main screen or in the "Calibration" menu.
10. Check that the "Current Volume" is zero.
11. Fill the calibrating syringe and connect it securely to the spirometer hose.
12. Click on "OK" or type any key, inject the full 3-liters from the syringe into the spirometer, and then pull back on the syringe. (NOTE: When injecting air from the syringe, do not "slam" the

syringe at the end of the injection by pushing the air out too vigorously as this may cause erroneous calibrations.)

13. The computer determines the volume injected. You then verify the calibrating syringe's volume and the computer compares this volume with the volume measured by the spirometer. The computer displays the difference between the syringe and spirometer-determined volume in both absolute volume and as a % Error.
14. Detach the calibration syringe and store it near the spirometer.
15. View Calibrations: The "View Calibrations" menu item allows you to view all previous calibration results.

3.11.2.4 How to Clean the Spirometer

1. Clean the inside of the spirometer at the end of each day.
2. Wear gloves. Disassemble the spirometer for cleaning. Unplug the power cord. Remove the snout plate by rotating the three thumbscrews counterclockwise until the snout plate is free. It is not necessary to remove the blue adaptor from the snout for cleaning. Carefully reach inside the cylinder and slowly push back the piston.
3. Wipe the snout plate, O-ring and cylinder wall with a germicidal disposable cloth. Do not use alcohol, acetone, other volatile agents or abrasive cleaners on the rolling seal.
4. Allow the interior of the spirometer to dry thoroughly (perhaps overnight) before reattaching the snout plate.



5. Examine the O-ring for any irregularities. If damaged, replace it. Lubricate the O-ring lightly with stopcock grease. Fit the O-ring into the groove on the back of the snout plate.
6. Position the snout plate so that the three thumbscrews are aligned with the three holes on the spirometer housing. Tighten only "finger-tight".

How to Clean the Hoses

The hoses and accessories will be cleaned and disinfected at regular intervals.

1. Tubing will be cleaned and disinfected daily using a solution of Detergezyme and water according to the following protocol.
2. Add one ounce of Detergezyme to every gallon of water (can be cold or warm but not hot) in the 5-gallon bucket.
3. Rinse hoses after use in this solution. Hoses that are not rinsed soon after use (i.e., saliva or mucous has dried) should be soaked in this solution for 10 minutes (IT'S ONLY NECESSARY TO SUBMERGE HOSES FOR 10 MINUTES IF THEY'VE DRIED (EG LEFT OVER THE WEEKEND WITHOUT CLEANING)).
4. Ideally, re-rinse hoses with water.
5. Hang hoses up to dry using clothes pegs.

3.7.3 HOW TO TEST PARTICIPANTS

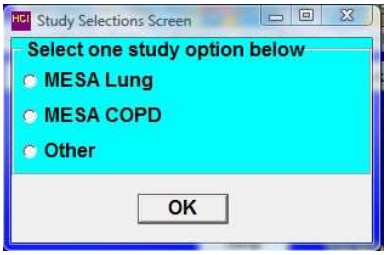
You should first complete the first page for the Spirometry Completion Form. The spirometry exclusion criteria at the end of the manual should have already been applied to every participant.

In addition, if the participant is selected for a post-bronchodilator test, you will prompted to ask some additional questions before a decision about administering the bronchodilator is rendered by the spirometry software. Anyone meeting spirometry exclusion criteria will not start spirometry. The albuterol exclusions (which you will be prompted to administer by spirometry software) must be checked before administering the bronchodilator (albuterol).

The accuracy of spirometry depends on your skills, which influence the effort exerted by the study participant. Consequently, it is crucial that the examination protocol be observed consistently. The participant must be carefully prepared and "coached."

The spirometry program is started by clicking on the spirometry icon located on the desktop.

Before you can do any testing, you must first select the study into which the participant is selected and consented. If the participant is **selected for and consented into** the MESA Lung III Study or the MESA Lung Non-Smoker Study, then select the "MESA Lung" button. Selecting this box implies that the participant will be asked to receive albuterol if they have airflow obstruction. You can change the Study Selection with the last menu item under Files (Change Study Selection). The Study Selection screen is shown below:

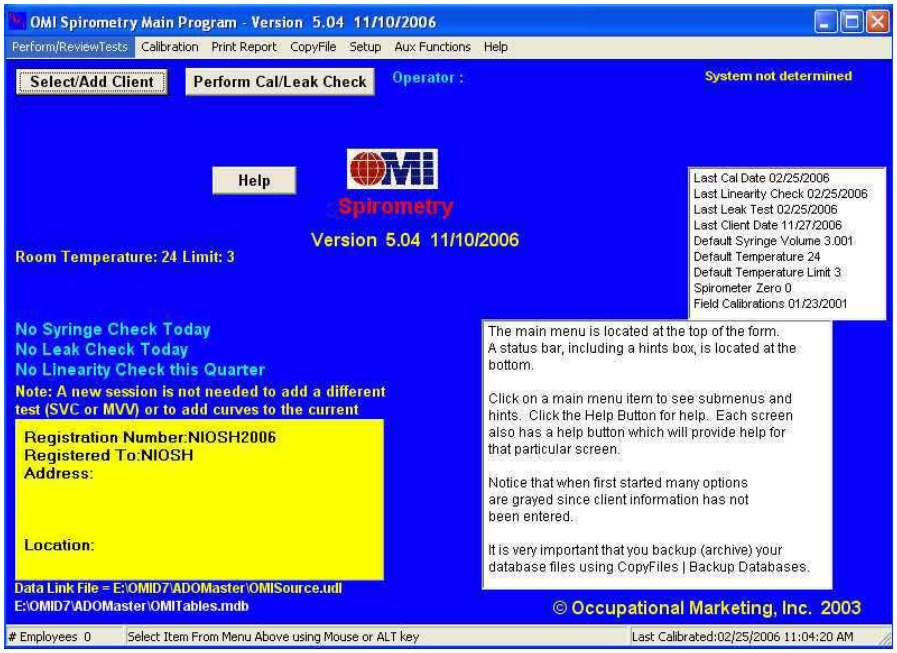


3.11.3.1 Spirometry Instructions, Preparation and the FVC Maneuver

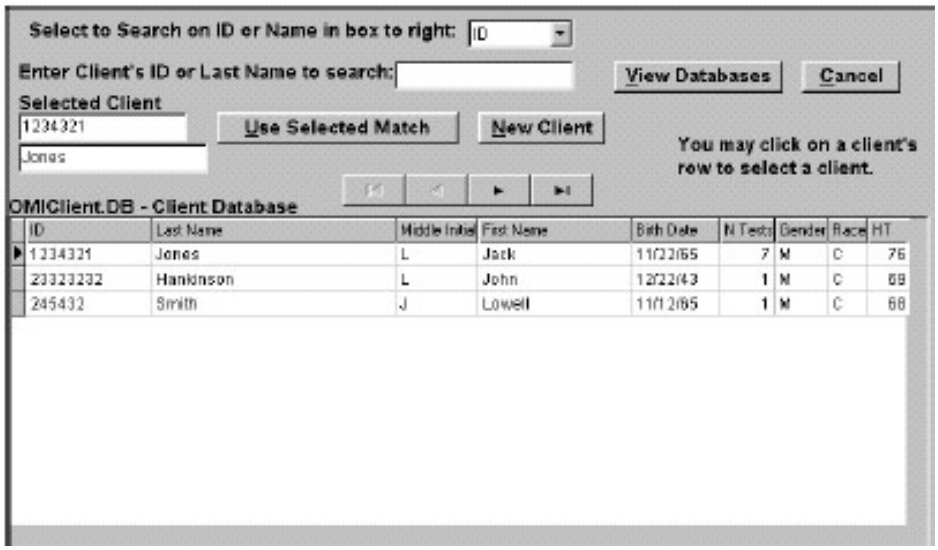
Tight clothing**, such as a tie, vest, belt, or body-shaping garment which might restrict maximal breathing efforts, should be loosened. Dentures, if they are loose, should be removed and placed in a clean denture cup, since they prevent a tight seal from being formed around the mouthpiece. If dentures are not loose, leave them in place.**

2. Select "Perform/Review Test" main heading and/or "Select/Add Participant" button

3. Bring up Participant Screen

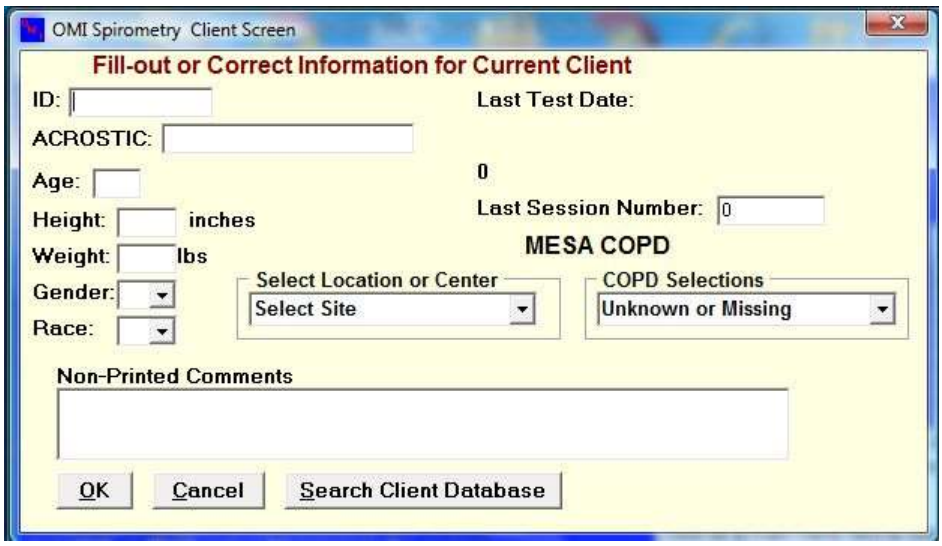


4. You should use the "Use Selected Match" function rather than having to choose to enter a "New Participant." Information for almost all participants will be preloaded. To search for a participant, select to search on ID or ACROSTIC; then start typing the ID or ACROSTIC in the search field. The bottom grid will display the closest match to the partial ID or ACROSTIC as it is entered. If the ID is not there, select "New Client." Before any participant is tested, demographic information must be confirmed and edited if necessary.



5. Edit/Paste/Enter participant information. The participant's information including ID, ACROSTIC, age, gender, race/ethnicity and height should be preloaded and appear in the

screen. Verify that the information is correct (particularly age and height) and, if it is, click "OK." Other information on the screen does not need to be entered. If the preloaded information is wrong, double-check ID and ACROSTIC match the participant then update the incorrect information. Please use the information as recorded on the Exam 5 Anthropometry form for height and weight. For a participant who is not preloaded into the software (which should be rare and only occur for those that have moved Field Center), enter ID, ACROSTIC, age, gender, race/ethnicity and height. For participants not preloaded in the software, you may also need to select your site or center.

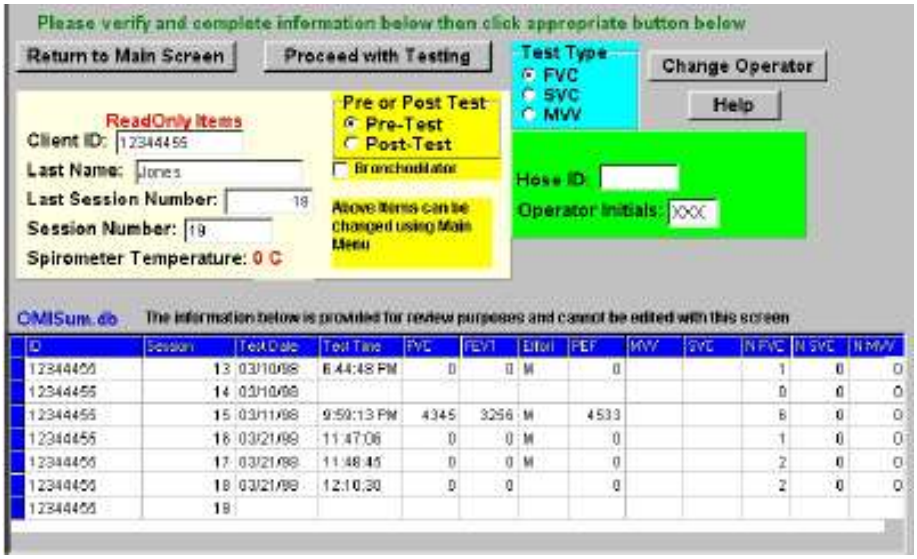


6. Wash your hands.
7. Attach a clean breathing hose.
8. Explain the purpose of the FVC and the need for extra effort from the participant to get maximal results. Say "I want to measure how much and how fast you can breathe out" and explain that you want the participant to take a very, very deep breath, blast out and then breathe out all the way out.
9. Demonstrate a deep inspiration: exaggerate body language, eyes wide, shoulders back, on tiptoes. Demonstrate proper placement of the mouthpiece stick out your tongue and place the mouthpiece on top of it. Blast out.
10. Ask the participant to sit during the examination. Encourage them to sit up straight. If participant wants to stand during the examination, they may do so.
11. Place nose-clip on their nose. It may be removed between trials. If the nose-clip falls off or is uncomfortable, try another one, or the participant may hold his nose during each maneuver.
12. Have the participant do a trial deep breath in and blast out. The following instructions may be helpful:
    1. "Take a great big breath of air as far as you can inhale." (Phase I)
    2. "Put the mouthpiece into your mouth and seal your lips tightly around it."
    3. "Blast your air into the tube as hard and fast as you can." (Phase II; the exhalation should be made with the lips tight around the mouthpiece with maximal force and speed.)
    4. "Keep on blowing out the same breath of air, until I tell you to stop." (Phase III; for the trial maneuver, stop the participant after a 1-2 seconds of Phase III rather than 6 or more seconds of the real maneuver).

Review the procedure and correct any problems from the trial.

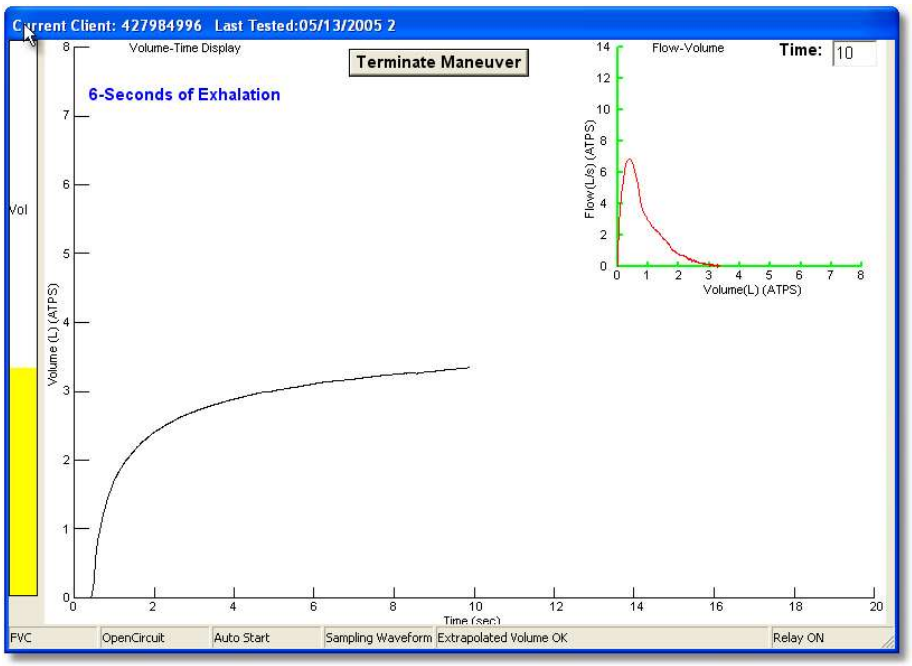
3.11.3.2 The FVC Maneuver

Click “Perform FVC Test”



Select “Proceed with Testing” and a “Volume-Time and Flow-Volume Graph” screen appears. A window prompts “Start Test?” When ready, click “OK.”

The message “Wait, Checking Spirometer” appears in red on the screen. AFTER THE MESSAGE DISAPPEARS, instruct the participant to take a deep breath, place the mouthpiece in his/her mouth, and **BLAST the air out!** Watch participant.

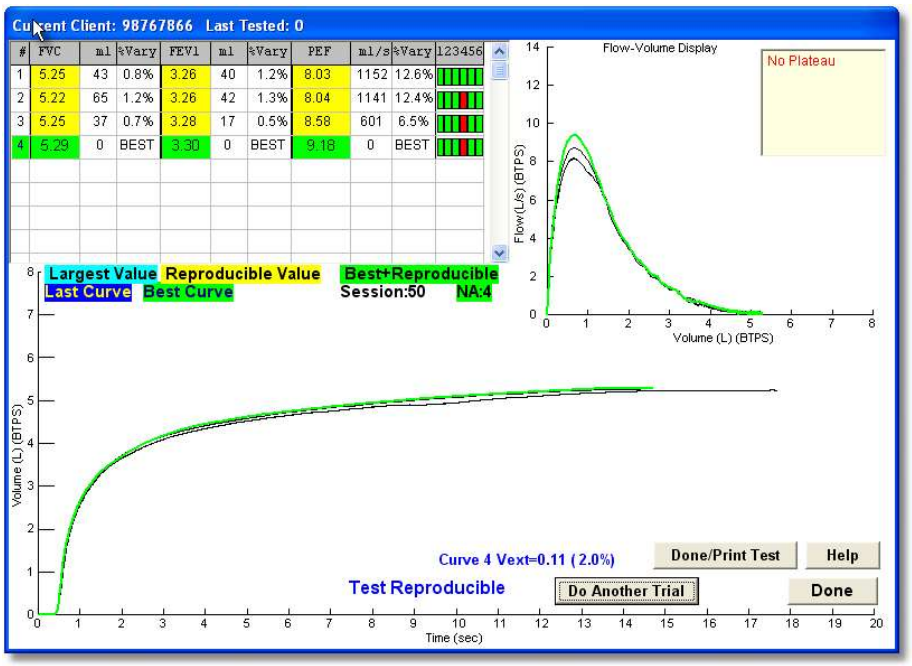


Quietly coach the participant to exhale until the "Plateau Achieved" message is displayed and the bar on the left side turns green. Just say, "Keep going…you are still getting more air out." It is *not* helpful for them to "squeeze out the air." Help the participant to move the mouthpiece away from their face (to reduce the risk of cross-contamination).

Indicate standing or sitting, and your impression of the participant's effort.

Press "Calculate Curve".

A result screen is then displayed, including Trial Number, FVC, FEV_1, and PEF (peak flow). After the second and successive trials, differences from the largest observed values and the 6-item acceptability code are displayed. All of the flow-volume and volume-time curves are also displayed superimposed. The last maneuver is highlighted in dark blue and the best curve is lime green. All of the remaining curves are black. Any deleted or unacceptable curves are red. The quality assessment information should be used to judge whether a curve should be accepted or rejected. Click on the quality code box for a description of the acceptability codes. A repeatability message is displayed.



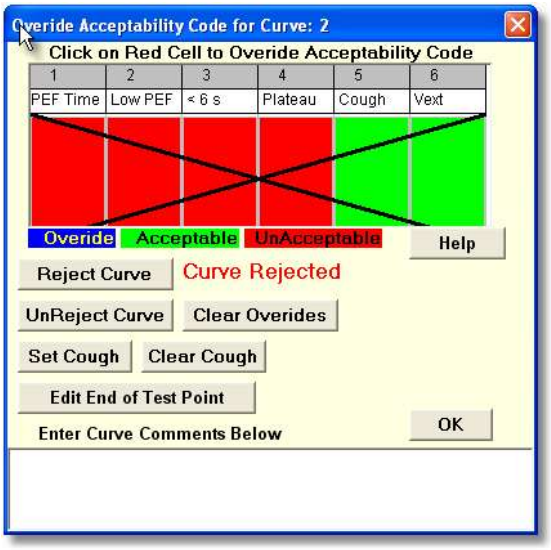
The Quality code box - A more detailed view of the maneuver values is shown below. The largest values for FVC, FEV_1, and PEF are indicted by "BEST" to the right of the value in the "%Vary" column. An important goal of testing is to match the largest and second largest FVC and FEV_1 within 150 ml of each other. This is called repeatability.

To obtain the best test session quality grade (an A), the FEV_1 and FVC must match within 100 ml. A scroll-bar on the right can be used to scroll up or down when more than 8 maneuvers have been done (but this will rarely be necessary).

#	FVC	ml	%Vary	FEV1	ml	%Vary	PEF	ml/s	%Vary	123456
1	5.25	43	0.8%	3.26	40	1.2%	8.03	1152	12.6%	
2	5.22	65	1.2%	3.26	42	1.3%	8.04	1141	12.4%	
3	5.25	37	0.7%	3.28	17	0.5%	8.58	601	6.5%	
4	5.29	0	BEST	3.30	0	BEST	9.18	0	BEST	

For experienced technologists ONLY:

How to over-ride the acceptability criteria: Click on the quality code box (extreme right column), and a popup window is displayed, allowing you to over-ride any acceptability code or reject a curve. The repeatability criteria are then re-applied and a message as to whether the test is reproducible is displayed. For acceptability codes, a red bar indicates the criterion is unacceptable. Click on the "Reject Curve" button if you wish to reject a curve, "Set Cough" button if you feel the computer did not correctly detect a cough, "Clear Cough" button if you feel the computer incorrectly label the curve as having a cough. Any code that is "over-ridden" is colored in blue instead of red.

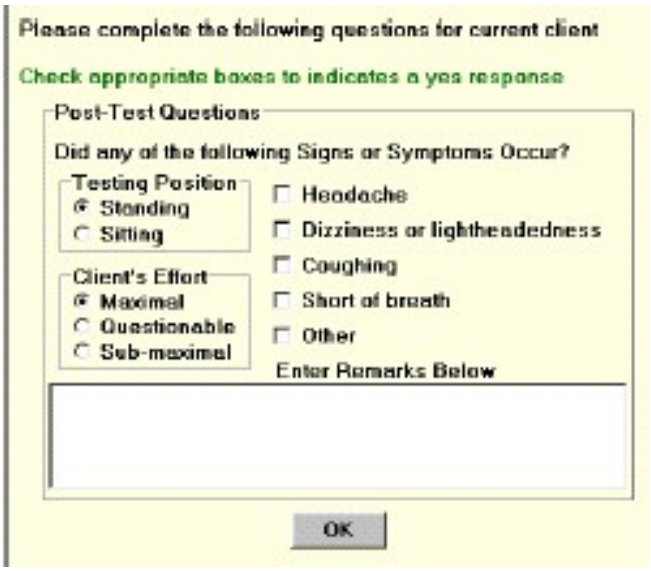


Criteria for an acceptable maneuver: no hesitation or false starts; the volume of back-extrapolation (Vext) less than 5% of the FVC or 0.15 L (whichever is greater). No coughing during the first second; no glottis closure, no mouthpiece obstruction by tongue or dentures. There should be a plateau at the end of the volume-time graph; and the maneuver should last at least 6 seconds.

Criteria for a repeatable test session: after three acceptable maneuvers, the two highest values for FVC and FEV1, taken from acceptable forced expiratory maneuvers, must show minimal variability. The two largest FVC values should agree within 150 ml; the two largest FEV1 values should agree within 150 ml. Testing should continue until three acceptable tests (all green in the code box) and repeatability criteria are met (yellow values), until a maximum of eight tests have been performed, or until the participant cannot or should not continue. To obtain the highest quality rating, the FEV1 and FVC repeatability must be within 100 ml.

Proceed or Done: You decide to proceed to perform another maneuver ("Do Another Trial"), or to stop performing additional FVC maneuvers ("Done").

Post Test Questionnaire: After test completion, the "Post Test Questionnaire" screen will appear. On this screen, indicate the testing position, participant (client) effort, and add comments, if you wish. Then click "OK."


Please complete the following questions for current client
Check appropriate boxes to indicates a yes response
Post-Test Questions
Did any of the following Signs or Symptoms Occur?
Testing Position
Standing
Sitting
Client's Effort
Maximal
Questionable
Sub-maximal
Headache
Dizziness or lightheadedness
Coughing
Short of breath
Other
Enter Remarks Below
OK

3.11.3.4 Coaching Breath-holding for the Lung CT Scan

Accurate and precise CT scanning of the lungs requires a deeeeeeep breath-hold in exactly the same way that accurate and precise spirometry requires a deeeeeeeep breath in Phase One of the spirometry maneuver. The lung CT scan is italicized in this section because, while the CT tech will ask the participant to take a deep breath for the cardiac scan also, the accuracy and precision of the cardiac scan is less dependent on the deep breath than is the lung CT scan. Hence, we are particular focused on getting a really deeeeeeeep breath for the lung scan.

Please therefore prepare the participant for the lung CT scan by telling them, after completing spirometry, that they will need to take as deep a breath as they can for the lung CT scan, just like they did for spirometry. The only difference is that they will hold the deep breath for about 10 seconds during the lung CT scan and then breathe out normally – instead of 'blasting out' for the FVC maneuver. Please demonstrate for them (emphasizing the deep breath and hold) and have them practice (unless they are too tired after spirometry).

There are several reasons why we wish you to explain the breath-hold for the lung CT scan to the participant. Both you and the CT techs have been trained and certified in MESA Lung spirometry and lung CT scanning, respectively. However, you have established a relationship with the participant, you know how important breathing is for these tests, and you speak the participant's language. The CT tech does not know the participant as well, is sometimes more focused other aspects of the CT protocol, and may not speak the participant's language.

The Lung CT Reading Center has produced videos to show you the lung CT scan being performed. Please watch the 6-minute video at:

http://www.youtube.com/watch?v=aEocwG08iq0

You will be asked for a username and password:

username: iowaimagingtraining
password: iowait2010

(please note that the actor portraying the CT tech was over-aggressive in his portrayal of coaching breath-holding).

If you are interested, there is additional (optional) background information on the measures that we obtain from the lung CT scans at the link below (same username and password):

http://www.youtube.com/watch?v=_Jz_rVNZBQM

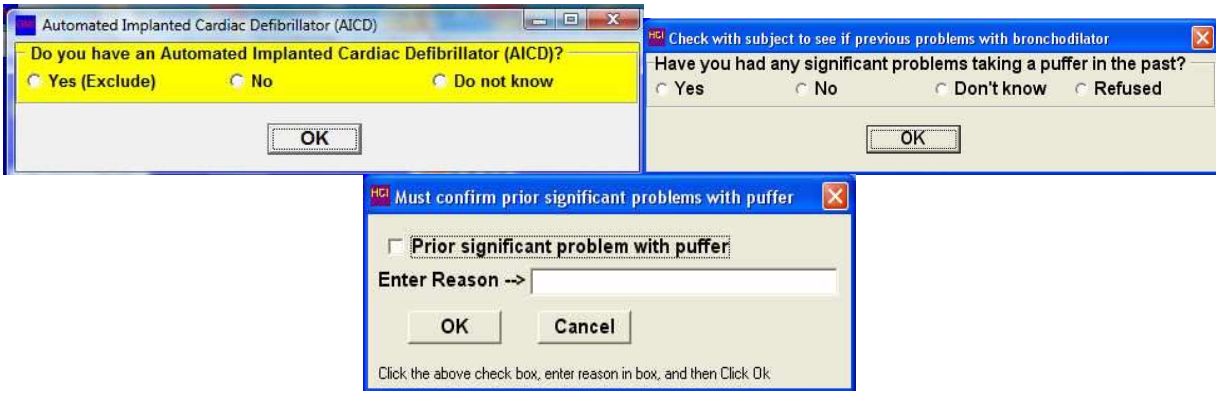
There is no certification test for this section. Thank you for your help!

3.7.4 POST-BRONCHODILATOR TESTING

The MESA Lung III and MESA Lung Non-Smoker participants who have airflow obstruction will be offered post-bronchodilator spirometry to determine if the airway obstruction is reversible (indicating that asthma is more likely than COPD). These participants will also undergo post-bronchodilator SVC testing. For this purpose, airway obstruction is defined as a FEV1/FVC below the Lower Limit of Normal (LLN) calculated using the NHANES III reference equations *or* FEV1/FVC below 0.70. Selected participants will receive albuterol if they have no contraindications to albuterol administration (see Spirometry and/or Albuterol Exclusions Section).

The following screen will appear if the participant is selected for post-bronchodilator spirometry and has no contraindication based on information collected earlier in the exam. These screens are to check to see if the subject has had an automated implanted cardiac defibrillator or any SIGNIFICANT problems with a bronchodilator puffer in the past. Ask the participant about "any SIGNIFICANT problems taking a puffer in the past" and show the puffer to the participant (this is much faster than trying to explain what a puffer is; the puffer is immediately recognizable to participants who have taken them in the past).

NOTE: Bronchodilators frequently cause a brief coughing spell. Cough is a normal response to a bronchodilator. Cough should NOT be considered a significant problem with a puffer. In other words, if a participant reports cough following bronchodilator administration, click "No" and proceed with bronchodilator testing.

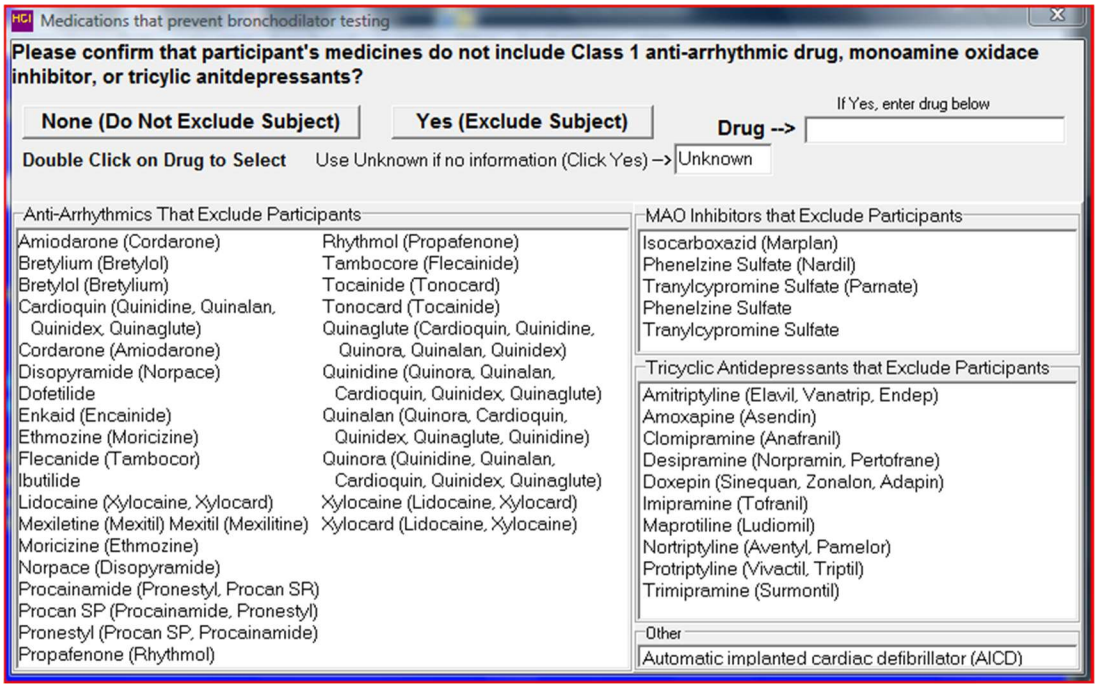


The screen (above-left) will appear for anyone who meets the study criteria for a bronchodilator test. Note the participant can refuse the bronchodilator test at this point by selecting "Refused." If you click "Yes", you must verify your selection by clicking the "Prior significant problem with puffer" checkbox (above right) and by entering the prior significant problem in the text box. Doing so will abort the post-bronchodilator testing protocol.

You will also be asked to check the participant's medications to make sure that they are not taking one of the medications on the lists provided (see panel below).

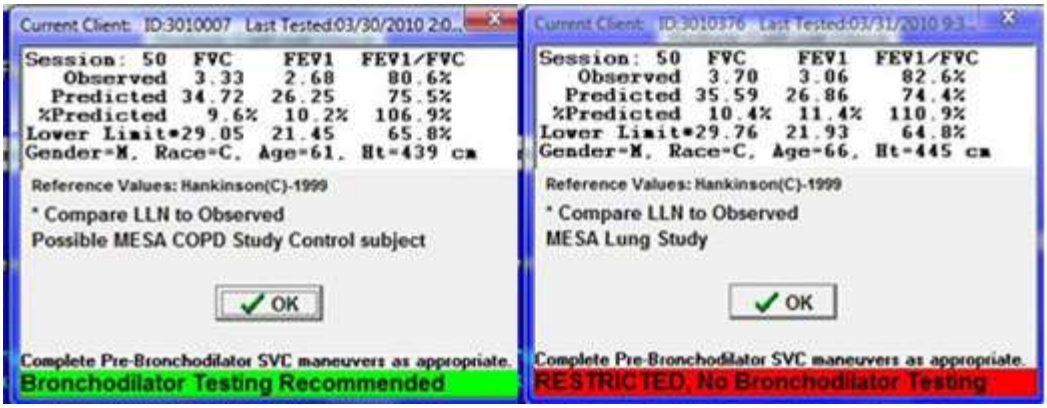
NOTE: Although these lists are long, all of these medications are prescribed rarely – even in patients with cardiac disease and depression. Anti-arrhythmics are prescribed only for a few patients with or at risk for severely abnormal heart rhythms (i.e., NOT for the much more common "heart disease" [coronary heart disease] and generally not for atrial fibrillation). MAO inhibitors and tricyclic antidepressants are both older types of antidepressants that are rarely prescribed for depression these days. Tricyclic

antidepressants (particularly amitriptyline [Elavil]) are still occasionally prescribed for chronic nerve pain.

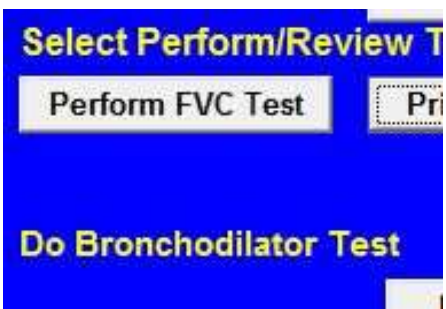


If you check "Yes (Exclude Subject)", you should enter the "Drug" by typing it or double-clicking on a drug from the bottom panels. If the participant did not bring their medications AND does not know what medications they are taking AND has abnormal heart rhythm, depression or chronic pain, enter "Unknown" for the Drug and click "Yes (Exclude Subject)."

One of the two following panels will then appear. If a participant is selected for and has no contraindications to bronchodilator testing, the "Bronchodilator Testing Recommended" box (left) will appear and you should proceed with bronchodilator testing (Section 4.1). If a subject has a contraindication for a bronchodilator, the "RESTRICTED, No Bronchodilator Testing" message will appear instead (right). Note that the screens below appear after completion of the pre-bronchodilator FVC maneuver – see text at bottom of screens below.



Appendix B shows a flow chart for determining whether albuterol is administered for a post-bronchodilator test. After administering

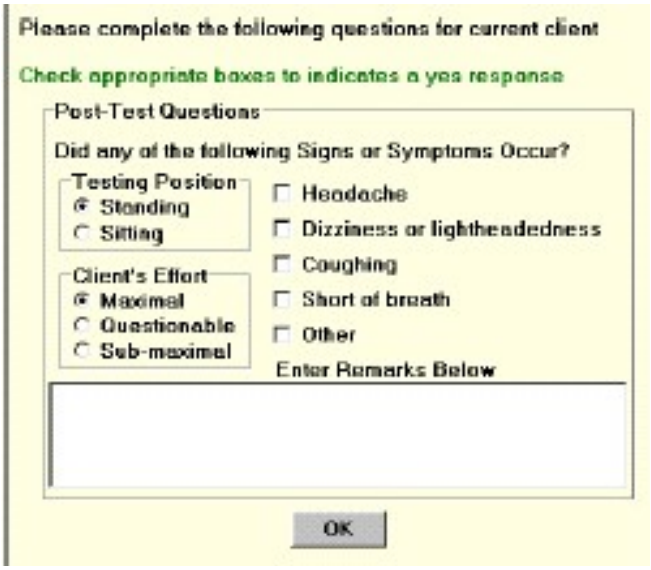


albuterol, perform first the SVC Test and then the FVC Test as before. Notice that a message that you should be performing a post-bronchodilator test will appear on the main screen.

If you have any concerns about administration of albuterol in a given participant, if you believe the participant should not have been selected for albuterol administration or if you have other questions or uncertainty about albuterol administration, then contact the either PI (Dr. Barr or Dr. Smith) for further assessment prior to proceeding.

Wait 10 minutes after administration of the albuterol and then repeat the FVC maneuver as described in Section 3.2 above (3-8 more attempts).

Post Test Questionnaire: After test completion, the "Post Test Questionnaire" screen will appear. On this screen, indicate the testing position, participant (client) effort, and add comments, if you wish. Then click "OK."



When the SVC Test has been completed click the Ok on the above button and you will be returned to the main screen where the "Perform FVC Test" button will now be visible. Proceed with performing the post-bronchodilator FVC test.

3.11.4.1 How to Give Albuterol

1. Shake the MDI. Point it away from faces, and then activate it once to verify aerosol delivery.
2. Attach a clean spacer
3. Hold the MDI and spacer in front of the participant's open mouth.
4. Ask the participant to exhale
5. As the participant inhales ***slowly***, activate the MDI while instructing the participant to continue to inhale slowly and completely. Count to five slowly.
6. Instruct the participant to hold his breath 5 seconds and then to exhale slowly.
7. Wait one minute and repeat above steps to administer another puff of albuterol.
8. Wait 10-15 minutes and then repeat spirometry
9. Click on the main menu item "Perform/Review Test"

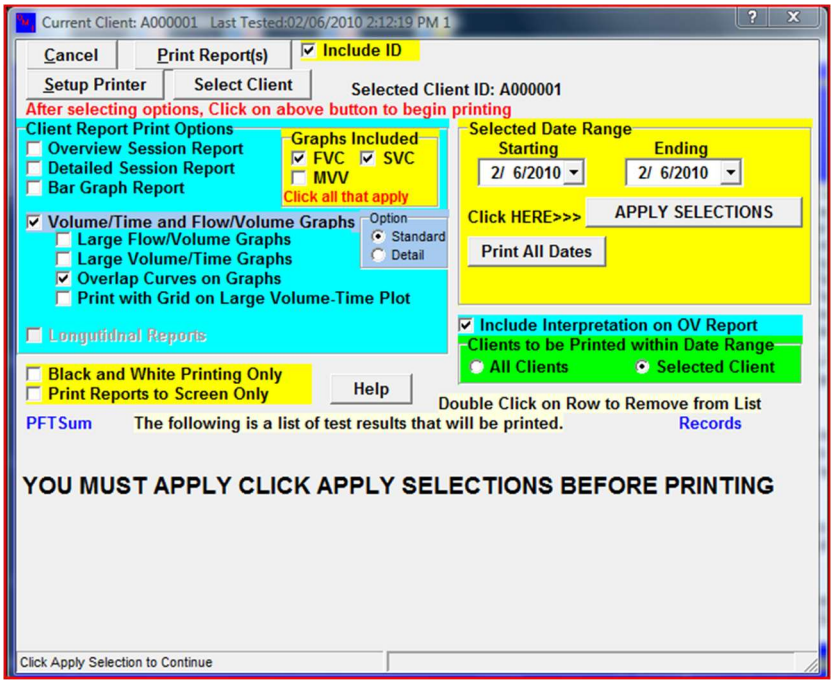
10. Click on “Add Post Bronchodilator Test”
11. Perform FVC test as previously described
12. Click on main menu item “Print Report”
13. Click on “Print Participant Report” menu item
14. Click “Print All”
15. Click on “Apply Selection” button
16. Click on check box “Print report to screen only” so that it is checked
17. Click “Print Report” button

3.11.4.2 Possible Side-Effects of Albuterol

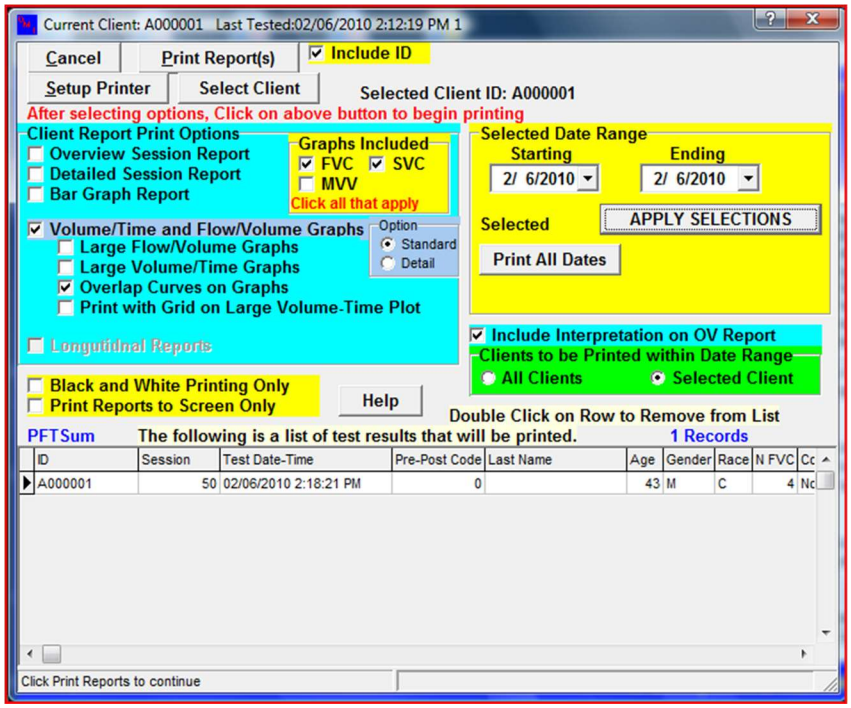
Albuterol is a mild stimulant, like caffeine, so some people (especially those who don’t drink coffee or tea regularly), may experience mild nervousness, lightheadedness, a slight tremor, or a headache for up to an hour after inhaling albuterol. These are not worrisome symptoms and will subside before the end of the visit. Albuterol may also increase the heart rate, but does not cause arrhythmias, even in older people. Albuterol is used by tens of thousands of patients with asthma or COPD daily to relieve shortness of breath.

3.7.5 HOW TO PRINT A REPORT

At the end of each test session, use the "Print Report" main menu item to print all test results. The "Print Current Test" menu item under "Perform/Review Test" is used, while participant information and results are still current in the computer. The right mouse button can also be clicked to display a popup menu with the "Print Current Test" menu item. Notice both the FVC and SVC check boxes are checked. You must click "Apply Selections" to complete the selection of tests to be printed.

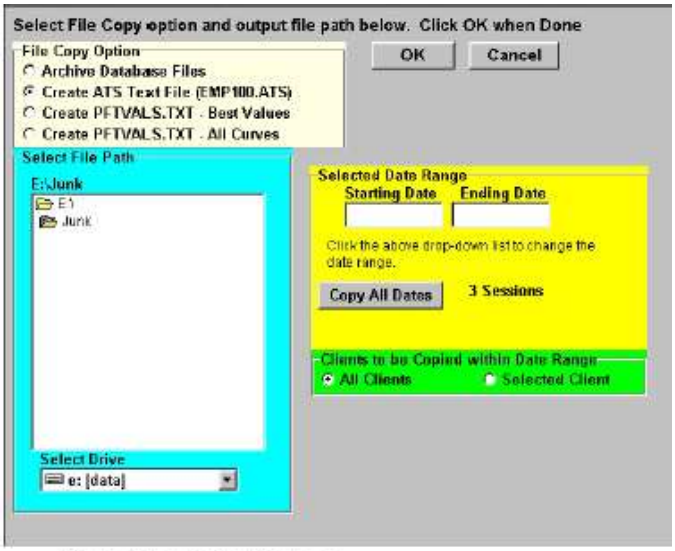


After Clicking "Apply Selections" the Test to be printed will appear in grid box. Click "Print Reports" to send the results to the printer.



3.11.5.1 Copy File

The “Copy File” main menu item provides you with a convenient means of backing up the data files. The sub-menu items under “Copy File” allow you to select several types of files to copy, some with selected date range limitations. You may select the output path using a file dialog box or use the default setting established in the setup program. The text files (EMP100.ATS and PFTVALS.TXT) can be limited by specified date range or for a selected participant. The backup files allow you to backup all the database files - compressed into one PKZIP compatible file. Again, the use can select the path for this file or the default path established in setup will be used. When you click the “OK” button, the list of database files is shown in the left list box, and as each individual file is placed in the backup zip file, it is listed in the right list box. Progress bars for both the individual files and for all files are shown. A default name of “OMIBackup.Zip” is used unless you specify another file name. The computer checks to see if the file already exists and prompts you to replace of update the file or exit and rename the backup file.



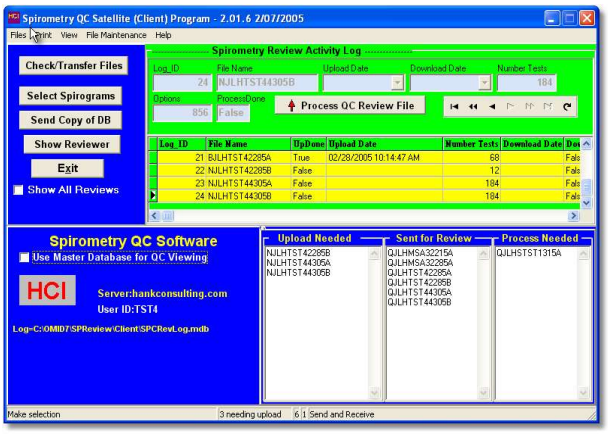
Copy Text File Screen

3.11.5.2 Send File for Review every Friday

The "Send File for Review" menu item, located under "Copy File" on the main screen is used to send data to the quality control center within the main spirometry program. Clicking on "Send File for QC Review" or the "SpRevParticipant" desktop icon runs the program which will select participant spirograms to be sent for review.

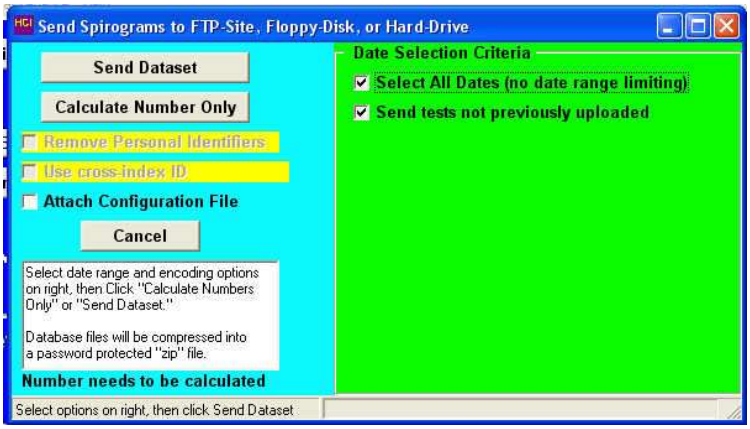
Copy File Menu - Send File for QC Review

Start Send File Program - Clicking on Send File for QC Review or desktop icon will execute the transfer program, see below. The yellow grid in the middle of the screen shows a list of files uploaded to the QC Reviewer and the transmission dates. Click on "Send Copy of DB" button to send a copy of the latest results to the QC Reviewer. The first time you run the program, you will be asked to select your field site (see figure on right).

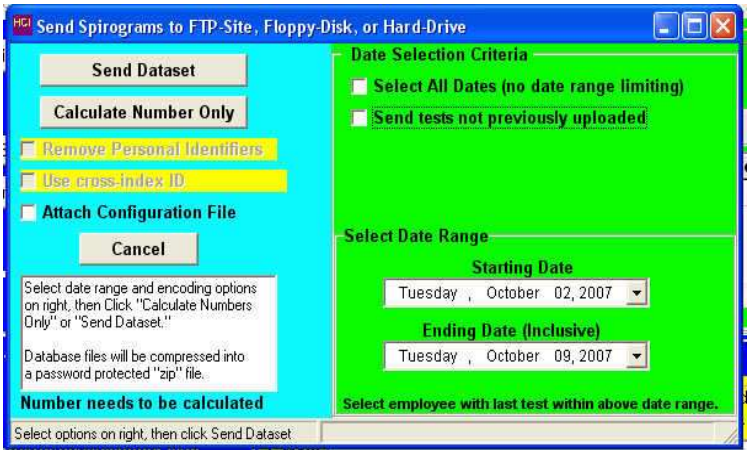


File Selection Program - Main Screen Select Site (User ID)

Selecting Date Range - The Send Copy of DB button will cause the send spirograms selection screen to appear. Use the Standard option below (both boxes on right checked). However, you may need to select the dates or date range of tests to include in the transmission if you need to resend some tests. The default starting date is the day after the date of your last transmission and the default ending date is the current date. The default settings of Remove Personal Identifiers and Use cross-index ID should remain checked.

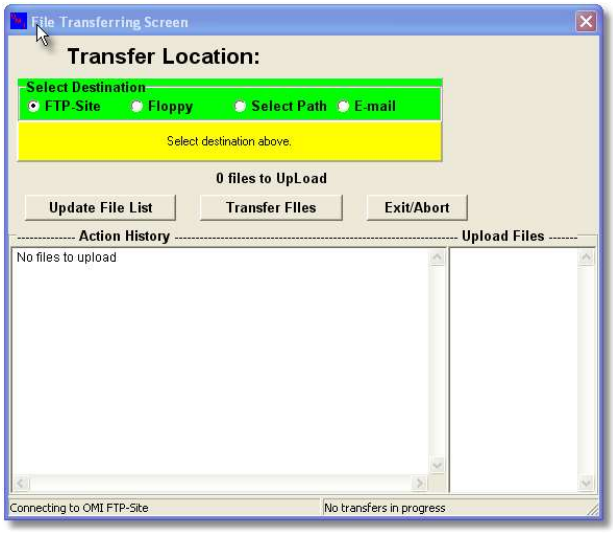


Send Spirograms Selection Screens (Standard)



Send Spirograms Selection Screen (by Date)

Transmitting Data - After verifying that the dates are correct, click the "Send Dataset" button to continue the transmission of the spirograms (spirometry results). If you receive a warning message that you are about to a replacing an existing file, click OK as this file is no longer needed. The Transfer Location screen will appear where you can select where you want the file to be sent. You should copy the file to a USB memory stick via the "Select Path" option. Transfer the file on the USB memory stick to the MESA computer then email to the Spirometry Reading Center The default is to use the Select Destination option shown in the screen below (FTP-site).



File Transfer Option Screen
After the file has been transmitted, you may exit the File Transfer Option Screen and the File Selection Program and return to the main spirometry screen.

3.7.6 QUALITY ASSURANCE

Upon completion and review of each batch of incoming data, you will be notified quickly of any errors with calibration and procedures. Each month, statistics will be compiled for each technician summarizing the quality of the tests done and the results of calibration checks. The reports may indicate that you may need additional training.

3.11.6.1 Training

Technicians from each Field Center will be trained centrally. Training will also include completion of a web-based spirometry training course, including answering all the review questions. Chapter 5 (hand-measurements) is optional. Retraining may be done by an experienced on-site technician.

3.11.6.2 Certification

The examination includes a formal web training, 50 multiple choice questions (written exam), and a practical demonstration of skills including leak and calibration checks, cleaning, and testing of a naive participants. A passing score of at least 70 points is necessary for certification for the written exam. Only certified technicians will perform pulmonary function testing in this study. A web-training account can be obtained from john@hankconsulting.com.

In addition, the slides from the spirometry training are on the MESA Lung website, http://www.uwchscc.org/MESALung/MesaLung2.aspx under the link, "Spirometry for MESA Lung Webinar - February 2010." These should be reviewed, if not seen in Central Training, and provide a useful reference as the study goes on. The user name and password for the MESA Lung website are the same as for the main MESA website.

PF technicians should test at least one person (participant, another technician or staff member) per week between the training session and the start of recruitment. To retain certification, technicians must test at least ten participants each month.

Certification of new technicians following the initial central training sessions may be performed by the project coordinator. The written exam is available on the training web-site, and the first 5 PF test performed will be observed by a certified PF technician or project coordinator and then examined by the PF Center and found to be satisfactory before the new technician is certified.

3.11.6.3 Site Visits

The results of the first 50 spirometry test sessions performed by each technician will be closely examined by the QC Supervisor (John Hankinson). Copies of suboptimal quality test sessions with comments for improvements will be sent to you the same day as they are evaluated.

A site visit to each of the four clinical centers may be made during the first three months of recruitment. Complete calibration, leak, and linearity check, and spirometry testing of at least three participants by each technician will be observed. Copies of suboptimal quality test sessions will be reviewed. More efficient methods as well as protocol violations will be discussed during the site visits and later in a written report.

3.11.6.4 The Need for Spirometry QC

Examination of spirograms from the Framingham study revealed that more than 18% were of clearly unacceptable quality. Two more recent studies, with over 12,000 adults each, found that 40-50% of the spirometry maneuvers were of unacceptable quality. Manual measurements from spirograms are tedious and prone to error and deviations in test performances and lack of regular leak checking and calibration can result in loss of study data.

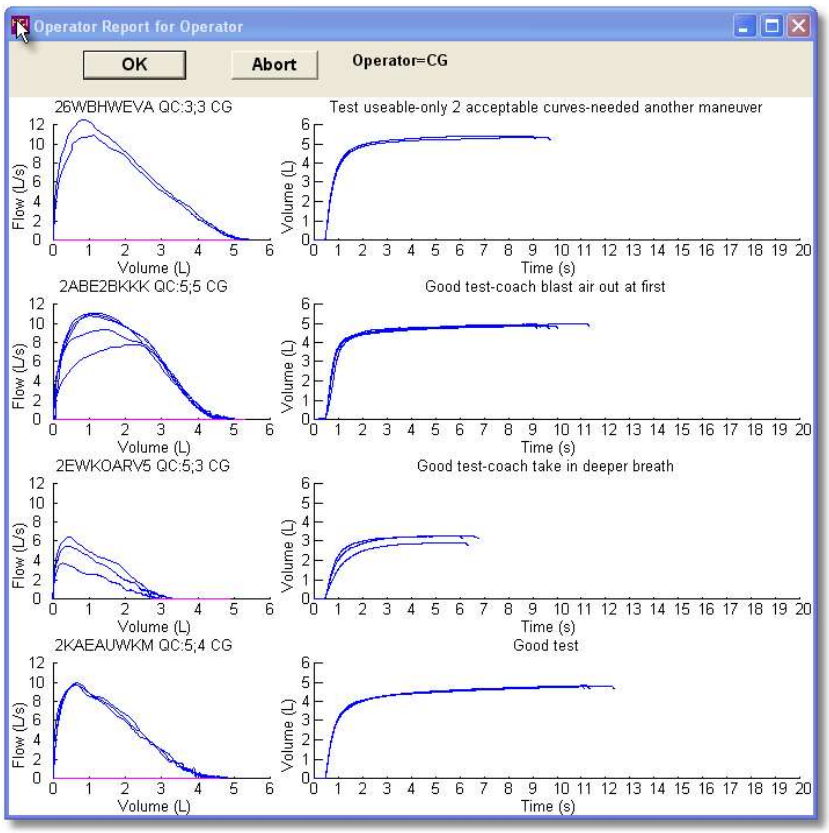
Evaluations of commercially available spirometers emphasize the importance of spirometry quality control procedures. Factors affecting spirometry quality include:

1. Participant
2. Maneuvers
3. Technician
4. Equipment
5. Analysis

3.11.6.5 Implementation of QC Procedures

There are five separate levels of quality control implemented for spirometry testing which address the five factors known to influence the results:

1. Daily spirometer leak and calibration checks using a 3.00 liter syringe as the "gold standard" check maneuver immediately after it is performed.
2. Eight computerized checks of FVC maneuver acceptability and repeatability check every maneuver immediately after it is performed.
3. The PF technician is trained to recognize the patterns of acceptable maneuvers, watching the participant during the performance, and reviewing the colorfully displayed flow-volume curves on the computer monitor.
4. The results of the leak and calibration checks and the best 3 FVC maneuvers are stored and sent to the PF Reading Center for review by the PF QC Supervisor. Monthly reports are compiled for each technician's performance.
5. Results from all of the above are taken into account during the analysis of the data by the PF Reading Center. The calibration factors, PF tech's impression of the participant and the maneuver quality, and the QC supervisor's impression of test session quality are all integrated to obtain the final FEV_1 and FVC results reported to the Data Coordinating Center. An operator report will be sent by e-mail to each technician periodically and at a minimum at the completion of testing at a study site. The operator report (password protected "pdf" file) contains copies of all tests performed by a technician with flow-volume, volume-time curves, FVC and FEV_1 quality factor codes, and specific comments (see below).



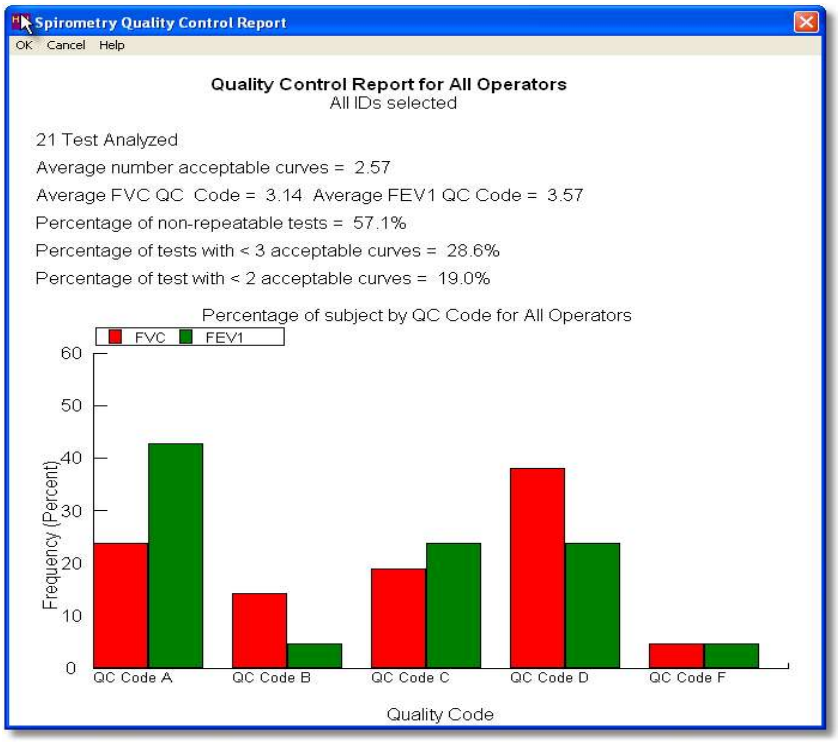
6. The following statistics are reported each month by the quality supervisor:
   - Average number of acceptable maneuvers, by technician.
   - Percentage of participants with non-repeatable tests results, by technician.
   - Percentage of participants with. less than 3 acceptable maneuvers, by technician
   - Percentage of participant with less than 2-acceptable maneuvers, by technician.
   - Average FVC quality score, by technician.
   - Average FEV_1 quality score, by technician.

   Quality grades (A-F) are computed for FEV_1 and for the FVC (quality codes) based in part on the number of acceptable maneuvers. An acceptable maneuver for FEV_1 quality purposes is no cough or large extrapolated volume. At least 6-seconds of exhalation and a plateau in the volume-time curve (30 ml in one second) are needed for an acceptable quality FVC. However, a maneuver that does not have a plateau but the exhalation is longer than 15-seconds is considered acceptable.

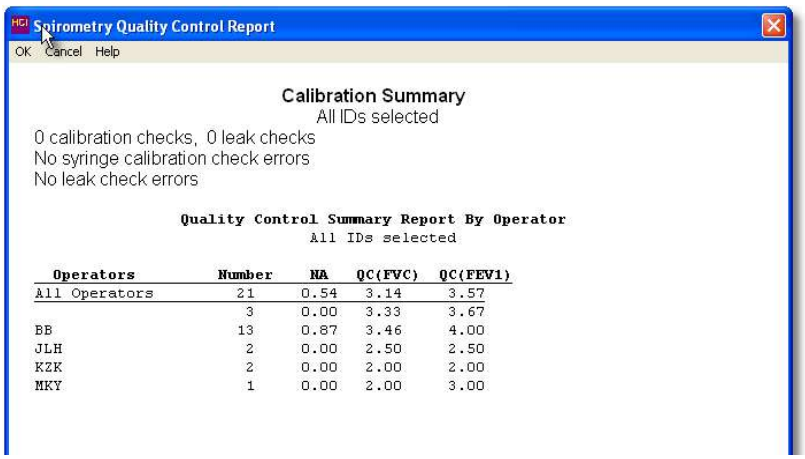
   Test session QC grades are assigned as follows:
   A = 3-acceptable curves, plus largest and second largest value within 100 ml
   B = 2-acceptable curves, plus largest and second largest value within 150 ml
   C = 2-acceptable curves, plus largest and second largest value within 200 ml
   D = 1 acceptable curve plus no end of test requirement for FVC QF
   F = no acceptable curves

The QC supervisor may assign a slightly higher QC grade for participants with obvious airways obstruction where it is difficult to obtain a plateau or reproducible test. A lower grade may also be assigned if a curve is judged to be unacceptable because the FVC or FEV_1 cannot be accurately measured.

7. In addition to the quality control summary report, a calibration summary report is also provided. Trends of average FVC and FEV_1 quality scores will be monitored during the study to determine if quality issues need to be addressed. Sample quality control reports (individual technician reports are similar to the All Operators report) are shown below:



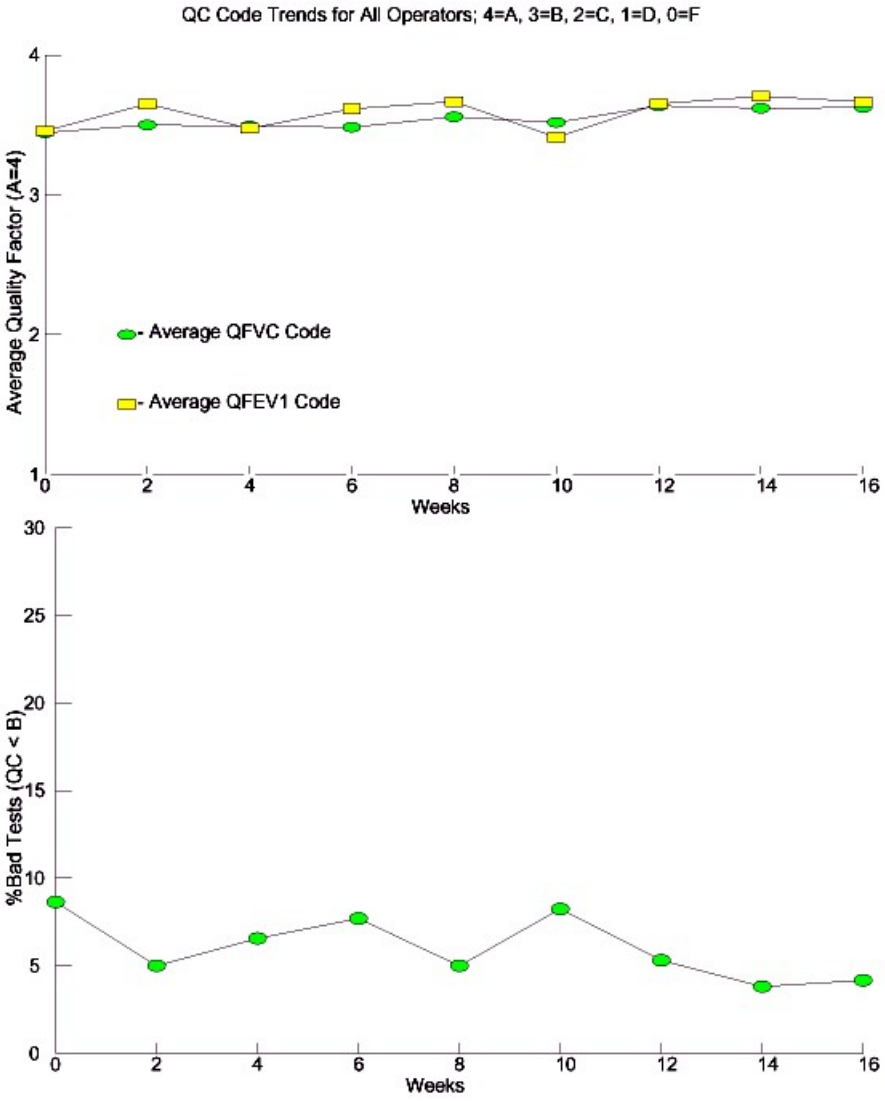
Quality Control Report - All Operators Combined



Calibration and Quality Control Summary Report

Trend Period 10/1/2003 to 2/15/2004 (18 weeks)

Week	N	QFVC	QFEV1	%Bad	Week	N	QFVC	QFEV1	%Bad	Week	N	QFVC	QFEV1	%Bad
0	81	3.44	3.46	8.6%	2	80	3.50	3.65	5.0%	4	61	3.49	3.48	6.6%
6	91	3.48	3.62	7.7%	8	120	3.56	3.67	5.0%	10	85	3.52	3.41	8.2%
12	132	3.64	3.65	5.3%	14	105	3.62	3.70	3.8%	16	24	3.63	3.67	4.2%



Quality Control Trend Analysis

3.7.7 SAFETY PROCEDURES

All equipment must be plugged into a grounded electrical outlet.
To minimize cross-contamination:

- Use a clean hose for each participant
- Use disposable mouthpieces
- Keep the participant's mouth higher than the spirometer snout.
- Participants do not inhale from the spirometer.
- The spirometer and accessories will be cleaned and disinfected at regular intervals.
  5. Tubing will be cleaned and disinfected daily (see Section 2.5)
  6. Instruments will be cleaned at the end of each testing session (see Section 2.4)
  7. Seal will be inspected and cleaned at the same time.

For participants that do not understand English, Spanish Versions of the exam instructions will be provided.

In rare cases, a participant may hyperventilate and feel dizzy during the examination. Ammonia capsules are available in the event of a participant becoming faint. A participant who feels faint should be guided onto the chair with head down towards knees and encouraged to breathe slowly and deeply until recovered. A physician should be summoned whenever a participant fails to recover normal breathing, faints or reports feeling ill.

3.7.8 REFERENCES

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3.7.9 Appendix A: The OMIWSP Setup Program

There are three configuration screens. It is important that these configurations are selected, otherwise the data needed for the study and subsequent analyses may not be stored.

B. Screen 1

Registration Information
Registration Number- set by OMI
Address: your address
Location: your location
Computer ID: take your pick
Maintenance Mode – Disabled

Spirometer Information
Spirometer make: SensorMedics
Spirometer Model: 1022
Spirometer Serial Number: to be entered

Screen 2

Report Header - (enter up to 4 lines)
Site Name
Site address
Phone #
Spirometry Report

Adjustable Parameters
Barometric Pressure - 760
Leak Volume – 20ml
Repeatability Criterion: 150ml
PEF Repeatability Percent - 20
Plateau Volume -40
Plateau Time - 1
Time Check Percent Allowed - 02.0
Extrapolated Volume Criteria - 150
MVV Test Time - 12
Communications P ort - 1
Test Start Method - Auto
Starting Session Number - 50
Automated Interpretation - Yes
Interpretation Level - 95%
Interpreter Algorithm - MESA
Selected data path - C:\Program Files\OMI\Database
Use Program Dr. for Cal Path - No
Allow temporary database path change – No

Nomograms	Scale
Caucasian – Hankinson-1999	1.00
Black- Hankinson-1999	1.00
Asian- Caucasian	0.88
Hispanic – Hankinson-1999	1.00
Other 1 - Caucasian	1.00
Other 2 - Caucasian	1.00

Report options
Detailed Session Report - No
Overview of Session Report - No
Volume/Time & Flow Volume Graphs - No
Large Flow/Volume Graphs - No
Large Volume/Time Graphs - No
Overlap Curves on Graphs - Yes
Include Baseline Comparisons - No
Black & White Printer - No
Disable Box (yellow) if below LLN - No
Absolute Values Trend - Yes
Percent Predicted Trend - No
Percent Deviation Trend - No

Screen 3

Adjustable Parameters Backup File Path - C:\Program Files\OMI\OMI Spirometry

Enter Manual Temperature - No
Save Raw Data - Yes
Enter Participant's Testing Position - Yes
Save Results in Text File - Yes
Verify Height and Date - No
Save Results in Enhanced Text File - Yes
Perform SVC and/or MVV Tests -Yes
Require Operator Password - No
Require PEF Repeatability - No
Use FET < 6s Criteria - Yes
Draw Inspiration – No
Use Largest PEF - Yes
Use PEF Acceptability Criteria - Yes
Check End of Test Plateau - Yes
Use Cough Detector - Yes
Use Time to PEF - Yes
Enter Participant's Test Effort - Yes
Enter 4-Level Curve Assessment- No
Enter Deviations from Test Criteria - No
Enter Pre-Test Questions - No
Enter Post-Test Questions – Yes
Edit Remarks after Test - Yes
Use Open Circuit Method - Yes
Other Options
Best Test - ATS Criteria (Largest Value)
Date Format - mm/dd/yyyy
Height Units - inches Weight -lbs.
Force Confirmation of Ht & Wt. – No

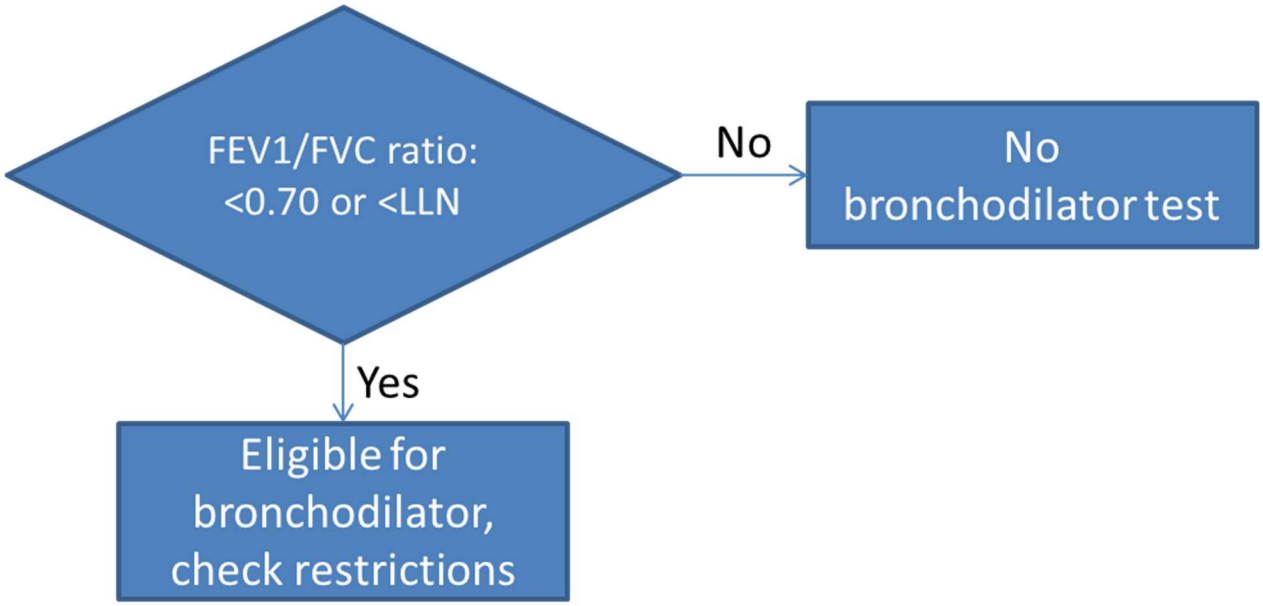
Parameter Print List

SVC – Yes
MVV – No
$FEV_{0.5}$ – No
FEV_3 – No
FEV_6 - Yes
$FEF_{25\%}$ - No
$FEF_{50\%}$ - No
$FEF_{75\%}$ - No
PEF - Yes
$FEF_{25-75\%}$ - No
$FEF_{0.1-1.2}$ - No
$FEV_{0.5}$/FVC% - No
FEV_1/SVC% - No
FEV_3/FVC% - No
FEV_1/FEV_6% - No

Exclusion Criteria

PEF Repeatability - No
Time to PEF - No
<6-seconds - No
No Plateau - No
Large Vext - Yes
Cough - Yes

3.7.10 Appendix B: Flow Chart for Determination of Post-Bronchodilator Test



3.7.11 CONTACT INFORMATION

PERSONNEL

R. Graham Barr, M.D., Dr.P.H. (MESA Lung PI)
622 W 168th St, PH9, East Rm 105
New York, NY 10032-3720
Phone: 212-305-4895
Email: rgb9@cumc.columbia.edu

Benjamin M. Smith, M.D., M.S. (MESA Lung Non-Smoker PI)
622 W 168th St, PH9, East Rm 105S
New York, NY 10032-3720
Phone: 514-616-5133
Email: bs2723@cumc.columbia.edu

John Hankinson, Ph.D. (Spirometry Reading Center co-I)
Suite 103, PMB 505
1860 Barnett Shoals Rd
Athens, GA 30605
Phone: (706) 742-8986
Email: john@hankconsulting.com
Spirometry Information and Installation Web Site: http://occspiro.com/mesa
User ID: **mesa**
Password: **[FEV1ratio**] be sure to include brackets

3.7.12 EQUIPMENT

SensorMedics / Viasys / CareFusion
(manufactures the dry-rolling seal spirometer)
22705 Savi Ranch Parkway
Yorba Linda, CA 92887-4645
phone (714) 283-1830 or (800) 520-4368

Occupational Marketing, Inc (OMI)
(OMI added the computer interface to the spirometer and provides software support)
11211 Kathy Freeway Ste, 420, Houston, Texas 77079
phone (800) 869-6783; 281-492-8250

Hans Rudolph, Inc. (makes the calibration syringe)
7200 Wyandotte, Kansas City, MO 64114
Phone (816) 363-5522

3.7.13 SUPPLIES

The following items will be provided centrally. Specifications and contact details are provided for your information.

Nose Clips: "Snuffer" Alliance Tech Medical. Contact person Romney Fischer, 800-848-8923, Order number 555 0047, #100.

Hoses: # 1011-xx Clean-Bor Tubes 1-3/8" (35mm) ID, 34" (Box of 50 1011-34-BULK) Available at http://www.vacumed.com/zcom/product/Product.do?compid=27&prodid=682.

Mouthpieces: White disposable cardboard mouthpieces, Catalog number 1027-250 (250 in a box); Nominal size: 34 mm ID, 36.5 mm (1-3/8") OD, 2.5" long Vacumed.com; 1-800-235-3333

Small mouthpieces: Pink disposable cardboard mouthpieces, Catalog number 1023-100 (100 in a box), Nominal size: 25 mm ID, 27.2 mm (1-1/16") OD, 2.5" long Vacumed.com; 1-800-235-3333

Spacers: Cardinal Health order number 001427. 5 ft tubes, segmented. 800.964.5227
Cut these into six inch lengths to make disposable spacers for the albuterol MDIs

Detergent: Detergezyme (enzymatic presoak and cleaning solution). Metrex Corp. #10-4500, 1 gallon bottle. Cardinal Health

Stop-cock grease (if needed): Any silicone-based variety (available at local hardware stores). Do not use petroleum-based grease.

3.7.14 DEFINITIONS AND SYMBOLS

ATPS is the condition of air inside the spirometer - Ambient Temperature and Pressure, and Saturated with water vapor. The ambient temperature of the spirometer is usually lower than body temperature; this has the effect of cooling and contracting the volume of air exhaled into the spirometer.

ATS is short for American Thoracic Society, the scientific branch of the American Lung Association - the Easter Seal folks. The ATS promotes accurate spirometers by recommending spirometry standards.

BACK EXTRAPOLATION (Vext, EV or BEV) is the standard method used to determine "time zero" when measuring the FEV_1. The amount of slowly exhaled volume at the start of the maneuver excluded from the FEV_1 by this technique is called the back extrapolated volume (BEV or EV). The BEV should be less than 5% of the vital capacity, otherwise the maneuver is considered to have started too slowly.

BD is bronchodilator. We are using the classic rapid-onset, short-acting bronchodilator: albuterol.

BTPS stands for Body Temperature (usually 37 degC) and Pressure, and Saturated with water vapor (100% humidity), which is the condition of air inside the lungs before it is exhaled into a spirometer. ATS standards require that volumes and flows be reported as if they were under these conditions.

CALIBRATION SYRINGE is a large metal cylinder with a rubber sealed piston used to check the volume accuracy of spirometers. The ATS recommends that it be 3.00 liters in size.

COPD stands for Chronic Obstructive Pulmonary Disease, a general term for lung disease caused by cigarette smoking - a mixture of emphysema, bronchitis, and hyperreactive airways.

DIAPHRAGM is the large, dome-shaped muscle between the lungs and the abdomen. Its strength is measured by the MIP test.

EV (see Back Extrapolation)

FET is short for Forced Exhalation Time. The FET should be at least ten seconds for the FVC maneuver to be considered acceptable, otherwise the FVC may be underestimated. Unfortunately, the FET cannot be seen on a flow-volume curve, and must be displayed separately.

FEV_1 is the most important spirometry variable, short for Forced Expiratory Volume in one second. It is convenient to think of it as the average flow rate during the first second of the FVC maneuver. It is reduced with airflow obstruction.

FEV_1/FVC RATIO is the most sensitive and specific index of airways obstruction measured by a spirometer. It is normally above 70%.

FLOW-VOLUME CURVE is the graph obtained from a forced exhalation maneuver plotted with flow on the vertical axis and volume on the horizontal axis. When compared with the traditional spirogram, it has the advantage of allowing easy recognition of unacceptable or poorly reproducible maneuvers and disease patterns.

FVC is the Forced Vital Capacity, the volume of air exhaled during the maneuver named after it. The participant takes as deep a breath as possible and then quickly exhales as much air as possible. The FVC is reduced with restrictive disorders.

OBSTRUCTION is a decrease in maximal airflow rates caused by airway narrowing. The FEV_1/FVC ratio and the FEV_1 are both decreased.

PEF stands for Peak Expiratory Flow, the highest flow measured during the FVC maneuver. It is a good index of effort used at the onset of the maneuver. It can be seen on a flow-volume curve but not on a spirogram.

***PF* (or PFT)** is short for Pulmonary Function (lung tests).

Post-BD is short for spirometry done after albuterol.

PRED is short for the predicted value of a PF parameter. It is determined from the regression equation from a large population study of supposedly normal people.

RESTRICTION is a decrease in lung volumes. Scarring of lung tissue (fibrosis), heart failure, pneumonia, and simple obesity are some of many causes. The FVC is reduced while the FEV_1/FVC ratio is normal or increased.

SPIROGRAM is an older term for the volume-time graph produced by water-sealed spirometers.

VOLUME-TIME TRACING is the graph produced directly by volume-sensing spirometers. It is traced by a pen connected to the spirometer bell with volume on the vertical axis.

Vext (see Back extrapolation)

3.7.15 METHODS SUMMARY

Daily Procedures

Calibrate Instruments
- Power-up workstation
- Check spirometer water level
- Run leak and volume checks (CAL)

Identify each participant
- Select participant's ID number (STATIONS)
- Administer spirometry questionnaire
- Verify name, age, and height (NEW then INF)

Perform Spirometry Test (FVL)
- Demonstrate FVC maneuver
- Attach clean tube & mouthpiece
- Obtain 3 acceptable FVC maneuvers
- Review maneuver quality
- Obtain another 2-5 FVC maneuvers

When indicated, administer albuterol and perform post-BD spirometry

Add comments (FIN)

Clean Equipment
Clean the breathing hoses
Rinse and dry the hoses overnight

Weekly Procedures (Friday afternoon):

- Upload week of spirometry data to PF Reading Center via e-mail
- Clean the breathing hoses
- Check the spirometer for leaks
- Rinse and dry hoses over the weekend

3.7.16 Spirometry and/or Albuterol Exclusion Criteria

Questionnaire Exclusion Items on Completion Form:

1. Have you had a heart attack, a stroke, or eye surgery in the last 3 months?
   Yes – STOP (Do not perform spirometry or administer albuterol)
   No – Proceed

2. Have you had any significant problems doing spirometry in the past?
   Yes (Do not perform spirometry or administer albuterol)
   No – Proceed

3. [FOR PTS SELECTED FOR BRONCHODILATOR ONLY] Have you had any significant problems taking a puffer [SHOW ALBUTEROL METERED DOSE INHALER] in the past?
   Yes (OK to perform spirometry but do not administer albuterol)
   No – Proceed

Automated Exclusion Item:

1. Systolic blood pressure ≥ 200 mmHg or diastolic blood pressure ≥ 110 mmHg – assessed earlier in Exam and leads to exclusion from all exam components, including spirometry and bronchodilator administration.

Other Albuterol Exclusions Items Assessed by Spirometry Software:

1. Report of use of Class 1 anti-arrhythmic drug, monoamine oxidase inhibitor, or tricylic antidepressant (assessed on the Medication history form) leads to exclusion from bronchodilator administration. All of these drugs are very rarely prescribed and the risk of inhaling albuterol is theoretical. If any of the following prescribed medications are reported on the Medication form, **avoid giving albuterol**:

   Anti-Arrhythmics:
   Amiodarone (Cordarone)
   Bretylium (Bretylol)
   Bretylol (Bretylium)
   Cardioquin (Quinidine, Quinalan, Quinidex, Quinaglute)
   Cordarone (Amiodarone)
   Disopyramide (Norpace)
   Dofetilide
   Enkaid (Encainide)
   Ethmozine (Moricizine)
   Flecanide (Tambocor)
   Ibutilide
   Lidocaine (Xylocaine, Xylocard)
   Mexiletine (Mexitil) Mexitil (Mexilitine)
   Moricizine (Ethmozine)
   Norpace (Disopyramide)
   Procainamide (Pronestyl, Procan SR)
   Procan SP (Procainamide, Pronestyl)

Pronestyl (Procan SP, Procainamide)
Propafenone (Rhythmol)
Rhythmol (Propafenone)
Tambocore (Flecainide)
Tocainide (Tonocard)
Tonocard (Tocainide)
Quinaglute, Quinidine, Quinalan, or Quinora
Xylocaine (Lidocaine, Xylocard)
Xylocard (Lidocaine, Xylocaine)

MAO Inhibitors:
Isocarboxazid (Marplan)
Phenelzine Sulfate (Nardil)
Tranylcypromine Sulfate (Parnate)
Phenelzine Sulfate
Tranylcypromine Sulfate

Tricyclic Antidepressants:
Amitriptyline (Elavil, Vanatrip, Endep)
Amoxapine (Asendin)
Clomipramine (Anafranil)
Desipramine (Norpramin, Pertofrane)
Doxepin (Sinequan, Zonalon, Adapin)
Imipramine (Tofranil)
Maprotiline (Ludiomil)
Nortriptyline (Aventyl, Pamelor)
Protriptyline (Vivactil, Triptil)
Trimipramine (Surmontil)

2. Also avoid giving albuterol to patients with an automatic implanted cardiac defibrillator (AICD).

3.7.17 Spirometry Completion Form

3.11.17.1 Purpose

Page 1 of the Spirometry Completion Form is designed to evaluate if subjects are medically able to perform spirometry (Questions 1 and 2), to assess potential short-term influences on spirometry (Questions 3 and 4), and to document completion of spirometry (Question 5).

3.11.17.2 Materials/Equipment

None.

3.11.17.3 Definitions

None.

3.11.17.4 Methods

General Instructions

This is an interviewer-administered form. Please administer questions before starting spirometry exam. The questions can be answered by filling in a bubble or a blank with a number or word. Most questions are self-explanatory. Specific instructions are given for some questions.

Specific instructions

Q.1. Have you been told that you had a heart attack, stroke, or eye, chest or abdominal surgery in the last 3 months?

- If the participant answers "yes" that they have been told that he/she had a heart attack or stroke in the LAST 3 MONTHS or surgery on the EYE, CHEST or ABDOMEN in the LAST 3 MONTHS, fill in the bubble next to "Yes" and DO NOT PROCEED with spirometry. Answer Questions 5 and 8 only, and fill in your Technician ID number at the bottom of page 2. If the participant reports a transient ischemic attack (TIA) in the last 3 months, follow the same procedure and do not perform pulmonary function testing. If the participant had a more remote heart attack/stroke/TIA or more remote eye/chest or abdominal surgery, in general it is fine to proceed with spirometry. We presume that participants will complete spirometry sometime in their clinic visit after blood pressure measurement. Participants with very high blood pressure (>210/120 mmHg) will therefore be excluded by the MESA protocol from performing pulmonary function testing. If not sure, consult MESA-Lung Principal Investigator Dr. Barr or Spirometry Consultants Drs. Enright and Hankinson before performing the test.
- If the participant has NOT been told that he/she had a heart attack or stroke in the last 3 months, proceed to Question 2.

Q.2. Have you had any significant problems doing spirometry in the past?

Ask if the participant has had any significant problems doing spirometry in the past. If the participant has never done spirometry in the past, answer 'no.' If the participant has done spirometry in the past and did have a significant problem, then answer 'yes' and describe the problem in the comments box. If the problem was indeed significant and likely to recur with retesting, DO NOT PROCEED with spirometry. Complete Questions 5, stating the reason that spirometry were not performed. If you are uncertain if the problem is significant and/or likely to

recur, consult with the Project Coordinator, Field Center Principal Investigator, and/or MESA-Lung Principal Investigator (Dr. Barr), and/or MESA Lung Non-Smoker Principal Investigator (Dr. Smith), or Spirometry Consultants (Drs. Enright and Hankinson) before performing the test.

Q.3. Did you have any caffeinated coffee, tea, or cola, or other caffeinated drink, in the past 2 hours?

Select "yes" or "no" or "don't know". This question is asked for information purposes only; proceed with spirometry regardless of answer.

Q.4. Did you smoke a cigarette, pipe or cigar during the last hour?

Select "yes" or "no". This question is asked for information purposes only; proceed with spirometry regardless of answer.

Q.5. Pre-Bronchodilator Spirometry was:

- If pre-bronchodilator spirometry was completed, fill in the bubble next to "**Completed**," and record the time at completion (hours AND minutes, AND fill in a bubble next to am or pm). FOR THE PURPOSE OF THE COMPLETION FORM ONLY, COMPLETED IS DEFINED AS THE PARTICIPANT COMPLETING AT LEAST ONE CURVE (MANEUVER).
  (note that we do not based the definition of "complete" on whether or not the curves are reproducible)
- If pre-bronchodilator spirometry was not completed, fill in the bubble next to "**Not completed. If not completed,**" specify the reason(s) why the spirometry was not completed. Select one or more from the provided options "refused" "physically unable" "cognitive unable" "equipment problem". For other reasons the spirometry was not completed, check "Other" and specify in the provided blank.

Continue with Page 2 on the **Spirometry Completion Form** on the following page.

Q.6. If selected for albuterol?

- Participants may be selected for albuterol by the spirometry software if they have airflow limitation. See Appendix B for details.
- Administer 2 puffs of albuterol as per Section 4 above and record the time. After 10-15 minutes, proceed with post-bronchodilator spirometry as per Section 4 above and complete Item 7 on completion of post-bronchodilator spirometry.
- If the spirometry software does not select the participant for albuterol, check off the "**No**" box, do not administer albuterol and skip to end.

Q.7. Participants Selected for Albuterol and Post-Bronchodilator Spirometry:

- If post-bronchodilator spirometry was completed, fill in the bubble next to "**Completed**," and record the time at completion (hours AND minutes, AND fill in a bubble next to am or pm). "Completed" is defined as in Item 5 above.
- If post-bronchodilator spirometry was not completed, fill in the bubble next to "**Not completed. If not completed,**" specify the reason(s) why the spirometry was not completed. Select one or more from the provided options "refused" "physically unable" "cognitive unable" "equipment

problem". For other reasons the spirometry was not completed, check "Other" and specify in the provided blank.

Heart Monitor Patch

3.7.18 Introduction and Background

Atrial fibrillation (AF) is the most common sustained arrhythmia seen in clinical practice. In AF, the top two chambers of the heart (the atria) quiver (or fibrillate) rather than contracting effectively. AF can last for seconds, minutes, hours, days, or can be permanent, and is associated with substantially elevated risks of stroke, cognitive decline, dementia, arterial emboli, heart failure, and cardiovascular death. Existing studies of AF rely on clinical recognition of AF when a patient presents with symptoms, but studies in patients with implanted monitoring devices such as pacemakers or defibrillators indicate that a large proportion of AF episodes produce no symptoms at all (subclinical AF). Therefore, relying on patient symptoms to identify AF seriously underestimates the incidence of AF. Convenient new external electrocardiogram (ECG) patch monitors now make possible extended ambulatory monitoring at reasonable cost, and permit identification of subclinical AF and estimation of AF burden.

The MESA Atrial Fibrillation study will examine AF and AF burden and how these relate to brain and heart structure as well as cognitive function in a subset of MESA participants. The study will recruit a total of 1500 MESA participants who will have cognitive function testing at Exam 6 and will then have two 14-day ECG monitoring episodes. These monitoring episodes will occur using an ECG patch monitor called the Zio Patch, which detects the presence of atrial fibrillation and other arrhythmias. To evaluate brain structure, participants will have a brain MRI 18 months later.

3.7.19 Eligibility and Exclusion Criteria for the MESA AF Study

A subset of 1500 MESA participants will be recruited for the MESA AF Study during Exam 6. Individuals of all ages, race/ethnicity groups and both sexes will be invited to participate, including Spanish and Chinese language speakers.

To be included in the MESA AF Study, participants must be willing to complete at a minimum the following components:

> Participants who don't have a past history of AF must be willing to complete the Zio Patch, the cognitive function testing, AND the brain MRI.
>
> Participants who have a past history of AF must be willing to complete at least 2 components, including the Zio Patch. In other words, they must be willing to complete EITHER all 3 components, OR the Zio Patch plus the brain MRI, OR the Zio Patch plus the cognitive function testing.

The FC staff do not need to implement these requirements; the software will do so in the clinic based on the information MESA has about a past history of AF.

We recognize that there will be some participants who are intending to do the brain MRI but become unable or unwilling to do so 18 months after Exam 6 because of a newly acquired contraindication to MRI. Regarding how to decide whether a participant has "completed" the cognitive function testing, we consider completing the CASI to be the minimum.

Exclusions relevant to the MESA AF study are:

Exclusions relevant to the MESA AF study:

1) Brain MRI
   a. Metal implants with a battery or that send electrical signals are NOT OK for the brain MRI. These include:
      i. Pacemaker
      ii. Defibrillator (also called AICD-- automatic implanted cardiac defibrillator)
      iii. Insulin pump
      iv. Nerve stimulator (implanted in brain or spinal cord)
      v. Cochlear implant
   b. Other metal implanted during surgery is sometimes OK:
      i. Joint replacements are generally made from titanium and are OK for brain MRI
         Hip replacement is OK
         Knee replacement is OK
      ii. Spinal fusion is OK if the metal is titanium (not stainless steel). If the participant doesn't know what metal was used, please exclude him/her from the brain MRI.
      iii. Metal plates and screws are OK if the metal is titanium (not stainless steel). If the participant doesn't know what metal was used, please exclude him/her from the brain MRI.
      iv. Brain (cerebral) aneurysm clip is NOT OK
      v. Stents located outside the brain (in arteries of the heart, pelvis or leg) are generally OK. We will ask the participant the type and location of the stent just BEFORE the brain MRI to confirm that it is OK. If the participant is uncomfortable with this plan, it's probably better for him/her not to do the brain MRI.
   c. Exposure to metal fragments around the eyes are NOT OK for brain MRI
   d. Weight over 300 lbs is an exclusion because the participant may not fit in the scanner
   e. Severe claustrophobia is an exclusion because the participant may become overly anxious in the scanner
   f. Inability to lie flat is an exclusion because the participant will need to lie still on his/her back for 40 minutes.

2) Heart rhythm monitor
   a. A history of allergy to skin adhesives is an exclusion.
   b. Unwillingness to shave upper left chest (in participants with hair on their chest) is an exclusion.
   c. Implanted electronic devices including nerve stimulator, cochlear implant, or infusion pump are NOT OK and are exclusions. However, please note that pacemakers or defibrillators (AICD) are OK for heart monitoring; the Zio Patch will not interfere with the pacemaker or defibrillator (AICD).

If the participant has an upcoming MRI, CT scan, or mammogram for their own health care, the heart rhythm monitor should be rescheduled for after those tests have been completed. It's possible that the Zio Patch would be detected at an airport by TSA screening. The Zio Patch booklet includes a statement for

the participant to show TSA personnel if the patch is detected, but if the participant knows they will be traveling by air, it would be best to reschedule the heart rhythm monitoring after or around the air travel. These situations are asked about in the MRI Exclusion Form.

3.7.20 Supplies:

For Patch #1:

Zio Patch monitor kit
Spare demo Zio Patch to use for demonstration
Sleep/Wake Log form
Spanish/Chinese-language Subject Instructions & Button Press Log booklets, Start Guides, and Sleep/Wake Log forms, if appropriate for your participant
Gown
Gloves

3.8 Heart Rhythm Monitor: Introduction

The Zio Patch is a single-use continuous recording ECG monitor that is much easier for the participant than a Holter monitor. It is worn for up to 14 days at a time, through normal daily routines such as light exercise, showering and sleeping. It is latex free, 100% recyclable, and each device is brand new for every participant. Participants will have Zio Patch #1 applied by clinic personnel at the end of the Exam 6 day, or as determined by individual Field Center schedules. At the end of the 14-day wear period, the participant will return the Zio Patch in a prepaid mailing box, along with a Sleep/Wake log, to the manufacturer for reading. Once patch #1 is received for reading, the CC will advise the FC to mail a second patch to the participant, who will apply it to their own chest. At the end of the second 14-day monitoring period, the participant will return patch #2 by mail to the iRhythm company. The data recorded on the second patch are analyzed and reported in the same manner as the first. The two monitors will provide a total of up to 28 days of ECG monitoring. It is important that all the Zio Patches, whether worn or not and even if defective, be returned to the iRhythm company in the supplied mailing box. Neither clinic staff nor participants should throw any Zio Patch away; they must all be returned.

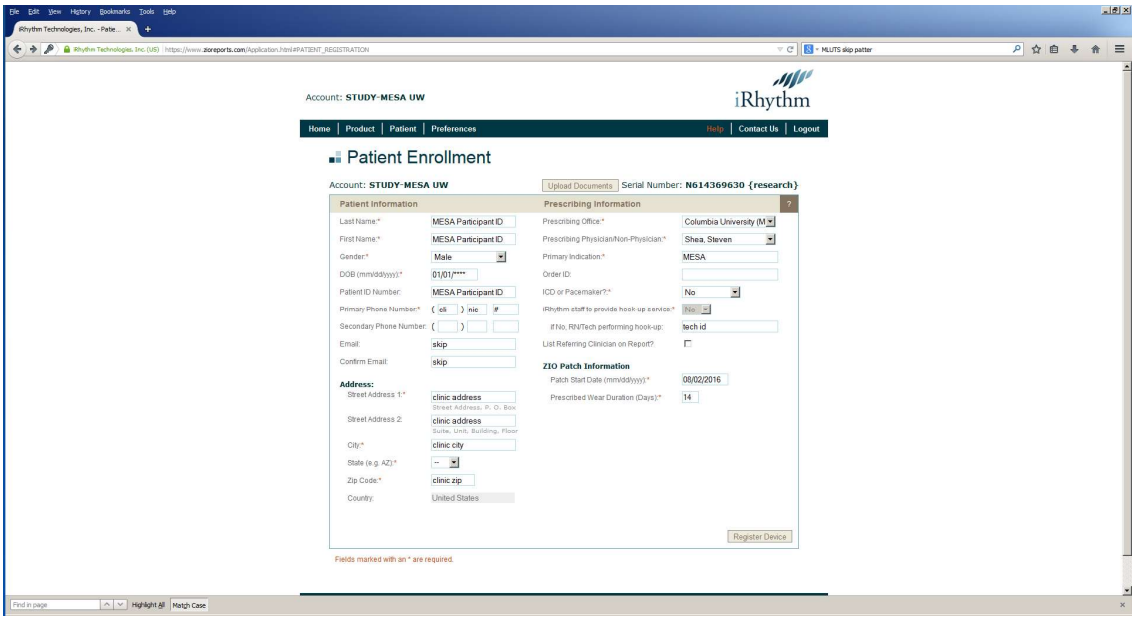
3.8.1 Online Participant Enrollment for Zio Patch #1

Register the participant with iRhythm online at www.Zioreports.com. The participant's MESA ID number and the device serial number should be recorded here. To register the participant and patch #1 online:

1) Log-in to ZioReports (www.Zioreports.com) using your email address and individual password.
2) Select the "Patient" tab in the header menu and then select "Register New Patient". (Note: The "Patient List" option will allow you to view all registered participants at your site, the device status (received or not), and also view/save patient reports in a PDF format.)
3) Enter the Zio Patch serial number (found on the sticker on the outside of the pouch containing the Zio Patch).
4) You will now see the Patient Enrollment screen. Enter the following information (See Image 1):
    a. Last Name: Enter MESA Participant ID
    b. First Name: Enter MESA Participant ID

c. Gender: Select "Male" for everyone, regardless of gender (we are doing this to limit the identifying information provided)
d. DOB: Enter 01/01/____ with actual year of birth.
e. Patient ID number: Enter MESA Participant ID
f. Primary Phone Number: Enter your site's phone number
g. Address: Enter your site's address
h. Prescribing Office: Select your site
i. Prescribing Physician/Non-Physician: Select your Primary Investigator
j. Primary Indication: Enter "MESA"
k. ICD or Pacemaker: Leave as "No," or select "Pacemaker," "ICD," or "both" as appropriate
    i. If ICD and/or pacemaker are present: a "Precaution" window opens. Click "Acknowledge and Continue". Then skip "Mode", "Lower Rate Limit" and "Upper Rate Limit."
l. iRhythm staff to provide hook-up service: "No" is already selected
m. if No, RN/Tech performing hook-up: Enter your MESA Tech ID
n. Patch Start Date: Enter patch start date in MM/DD/YYYY format.
o. PrescribedWearDuration (Days): Enter "14"

5) After all required information is entered, select "Register Device" in the lower right hand corner. This will complete the registration of the device.



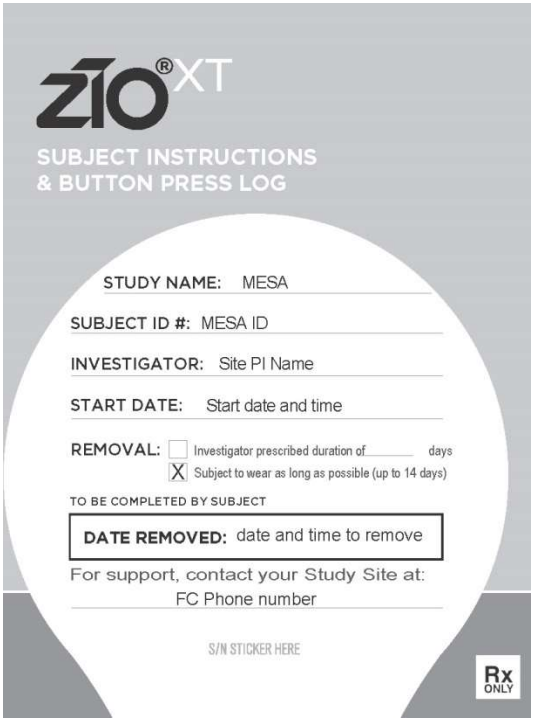
3.8.2 Prepare the Booklet and Sleep/Wake log for Patch #1

Prepare materials for Patch #1, usually ahead of time. The patches have a 6-month shelf life, and the expiration date is marked on the outside of the Zio Patch box. As you prepare patches for participants,

make sure to use the Patch with the soonest expiration date to ensure using patches before they expire. Open the gray Zio Patch box; remove and open the foil pouch. On the outside of the pouch are three serial number stickers. Inside the pouch is a kit including a razor, skin abrader, 4 packets of rubbing alcohol, a Skin Prep and Placement Card that contains the Zio Patch, and a Subject Instruction Booklet.

Put one serial number sticker on the front of the Booklet. Put another serial number sticker on the Sleep/Wake log. Save the 3rd serial number sticker in the participant's paper chart at the Field Center, in case you need it later.

Fill in the front page of the Booklet with "MESA", the MESA ID, site PI name, start date and time, check the box for "Subject to wear as long as possible," enter the date and approximate time you want the participant to remove the patch (14 days after the date of application, at approximately the same hour you applied it), and enter the Field Center phone number.

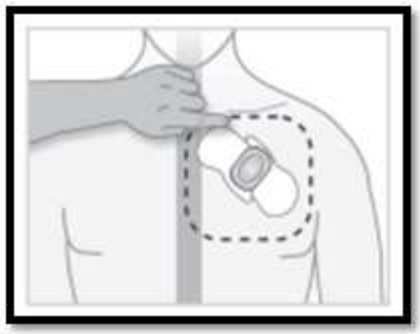


On the Sleep/Wake Log, enter the participant's MESA ID and the date of patch application, and the dates of the next 14 days. Fold it in quarters with the print showing. Keep it with the box so you can show it to the participant.

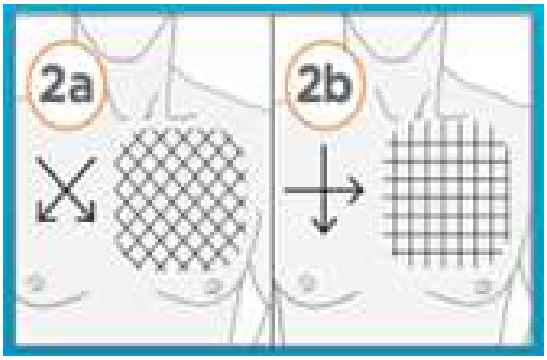
3.8.3 How to Prepare the Skin and Apply the Zio Patch

Proper skin preparation is crucial for accurate heart rate recording of the Zio Patch. The preparation process has several steps which must be followed to ensure good signal recording and quality. The participant must be standing or sitting upright, with their arms at their sides. The participant should be wearing a gown with the opening in the front, so that you have good access to the area of skin that need to be prepared.

Next, determine placement of the Zio Patch without removing the backing on the device. Placement of the device on the upper left chest is the same for both male and female participants. Position the device one finger width below the collarbone, with the edge of the device next to the sternum on the flattest part of the participant's chest. Avoid the armpit or breast tissue. The arrow on the device should be pointing up. Once you have determined the appropriate placement for the device, proceed with skin preparation.



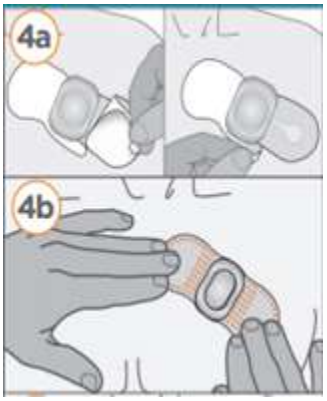
Successful use of the Zio Patch depends upon proper preparation of the application area. Prepare an area on the chest from the sternum to the armpit and from the collarbone to just above the nipple line. Shave any hair with the razor provided. Next, the area must be abraded using the provided abrader using 40 strokes: 10 horizontal, 10 vertical, and 10 on each diagonal. IMPORTANT: Please make sure you shave/abrade the whole area that the Zio Patch will be applied to. If you avoid the area close to the armpit or lower on the breast, the patch will not stick to the skin in these areas, there will be poor signal quality, and the patch may come off early.



The abrasion step is critical to remove the top layer of skin cells to ensure optimal Zio Patch adhesion and signal quality. Clean the whole area using two or three of the alcohol prep pads supplied. This removes any skin cells loosened during the abrading process, as well as any natural oils or lotions found on the skin's surface. Failure to follow these steps may cause skin irritation, decrease signal quality, or decrease device wear time.

After the area has been fully prepped, turn the Zio Patch over so that the serial number faces up. Remove the clear backing from the two wings. Without touching the exposed adhesives, apply the Zio Patch to the skin on the area mapped out earlier. With the white top labels "1" and "2" still attached, press firmly upon the device to the skin for two minutes.

After 2 minutes, remove the two white top labels. Start with the side marked 1, and pull in the direction of the arrows. As you pull, have your fingers follow the label and continue pressing down on the Zio Patch. Repeat this process for the tab marked 2. Once the tabs are removed, continue pressing on the Zio Patch for two minutes, working the adhesive onto the skin. Emphasize pressing around the edges of the adhesive, the wings, and along the button.

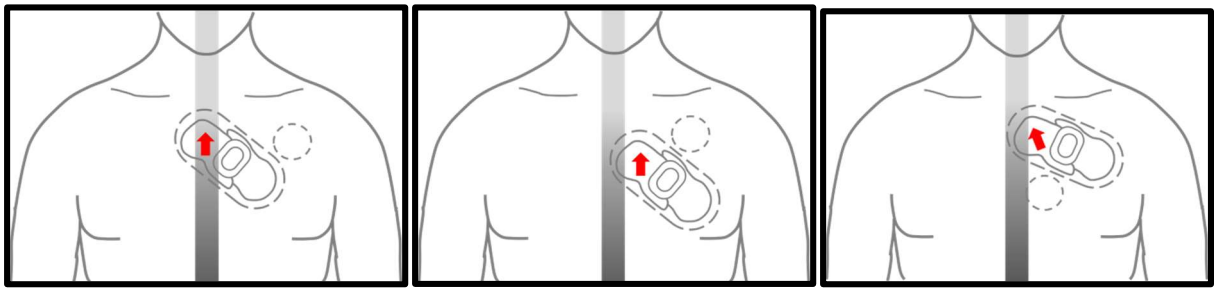


Once the patch is applied, turn on the device. Press and release the button.

The device is turned on when you see the green button flash 5 times. It is not turned on until/unless the green button flashes. If the device flashes orange, press across the wings of the device, and press the button again. If it still flashes orange or if there are no flashes, contact iRhythm for assistance (toll-free phone number provided at end of this MOP section). If the patch is still flashes orange or does not flash after iRhythm assistance, remove the patch using the adhesive remover wipe, clean the skin again with alcohol, register another patch and apply it to the participant's chest. Turn on that replacement device by pressing and releasing the button. Mark down the serial number of the defective Zio Patch (found on the outside of the box, beginning with an N), notify Dr. Susan Heckbert (see Contact Information) about the defective patch, and mail the defective patch back to iRhythm in the box provided. MESA will not be charged for the defective patch if you follow this procedure.

Applying the Zio Patch in a participant with a pacemaker or automatic implantable cardioverter defibrillator (AICD)

The Zio Patch can be applied in people with pacemakers or AICDs, but the location may need to be modified a bit. The placement that will work for each participant will depend upon exactly where their pacemaker/AICD is located and the shape and size of their chest. The Zio Patch should NOT be placed over the "lump" in the skin (where the pacemaker/AICD generator is located, shown as a dotted circle in the diagrams below) but instead, right above, below, or to the side of the "lump". The orientation of the arrow on the top label should be as close to "UP" as possible. A little tilting is OK but not much. Please see the diagrams below for suggested placement. If you cannot find a suitable location for the Zio Patch in a person with a pacemaker/AICD, please note this in the "Comments" section of the Atrial Fibrillation Study Completion Form.



3.8.4 Step-by-step instructions for applying the patch and what to tell the participant

The participant should be wearing a gown with the opening in the front.

Put on gloves.

> ***"I am going to apply the first patch in the clinic today. The battery in the patch allows it to record your heartbeat for a maximum of 14 days. The heartbeat information is stored on the patch, so it's very important for you to return the patch at the end of the monitoring period so we can get the heartbeat information from the patch. Please watch what I do so you will know how to apply the second patch yourself. Lots of other MESA participants have applied their own patch successfully."***
>
> ***First, I am going to decide where to place the patch on your chest.*** *Find the placement.*
>
> ***Next I am going to clean your skin really well so that the patch will really stick to the skin.*** *Use abrader and alcohol wipes.*

Remove your gloves.

> ***Now I'm going to remove the backing and apply the patch.*** *Remove clear backing from wings and place the patch on the chest. Press for two minutes.*
>
> ***Now, I'm going to remove these two white labels numbered 1 and 2.*** *Press for two more minutes.*
>
> ***Finally, I'm going to activate (turn on) the patch.*** *Show them where the green light flashes.*

3.8.4.1 Explain how to care for the Patch

> ***"We would like you to wear the patch for a full 14 days if possible. But if the patch comes off before that, it's OK and we'd still like you to return the patch in the box. The Zio Patch should be worn during all normal daily activities, including showering and sleeping. However, it should not be submerged under water, so you should not go in a swimming pool or hot tub. It is OK to take a bath but you must keep the patch above the water. Keep your showers brief, with your back to the flowing water if possible. Hold the patch down with your hand when you dry yourself after a shower and just pat it dry. It would be best if you don't take a shower today but wait until tomorrow to give the patch a chance to really stick to the skin.***
>
> ***Heavy sweating may cause the patch to come loose or fall off, so please try to avoid activity that causes heavy sweating. It is natural over time for the edges to lift slightly or loosen. If they do, push the edges back down. Call us if the patch falls off or if you have itching that is severe. A little itching is OK."***

3.8.4.2 Show them the Booklet and the Sleep/Wake Log

Front page

"If you have any questions about the heart monitoring patch, please call us at the number shown here."

FAQs

The booklet has information that you can read about how to care for your patch, on these pages."

Symptoms, Button Press Log

"If you have one of these symptoms while you are wearing the patch, push the button on the patch and then write down the symptom in this booklet. The patch will record the time that the button was pushed.

Take the participant's finger and show them how to press the button for a symptom. They will feel a "click." Show them the blank pages where they can write down their symptoms.

Sleep/Wake Log – show them the Log

"On this Sleep/Wake Log, write down the time you go to bed or to sleep and the time you wake up. I have already filled in the dates."

Removal and Return of the Patch (last 2 pages of booklet)

"At the end of the 14 days, you will use this adhesive remover in this packet to help you remove the patch."

Demonstrate using a demo patch on the table how to remove it.

"Tilt up the center of the patch and use the adhesive remover to sweep between the skin and the patch, peeling from the center out on one side and then on the other side."

"Then stick the patch on the last page of the booklet in the place shown here. It will stick by itself; no tape is needed. This blue tape is for you to tape the box closed. Put the booklet (with the patch attached) and the Sleep/Wake time log in the gray box. Seal it with the blue tape. Put the box in any US Postal Service blue mailbox, or give it to your postman. The postage is already pre-paid."

"Make sure you keep the booklet and the gray Zio Patch box, for returning the patch, booklet, and sleep/wake log at the end of the 14-day wear period."

Optional, if they ask about traveling by plane:

If it turns out that you need to travel by plane while you are wearing the patch, there is a statement in the booklet that you can show to the TSA/airport security people if they have questions (show page 8)."

3.8.4.3 Tell them about Patch #2

"About a week or two after you mail in the first Zio Patch, we will mail you a second Patch for you to apply to yourself, just as we are doing now in the clinic. The kit will be just like this one and will contain everything you need. You will need to determine the correct position, (shave the skin), abrade the skin, and clean the skin with the alcohol wipes provided."

Show them the Skin Prep and Placement Kit that came with Patch #1. Show them the instructions that tell how to apply the second patch. Tell them not to put their name on the Kit and that they don't need to Enroll online (areas circled on the diagram below), because you will take care of that.

You will wear this second patch again for 14 days (or as long as possible up to 14 days). You will again mail it back to us in the gray box provided. With this second patch, we will not be asking you to record your sleep and wake times – we will have enough information on this from the first patch."

3.8.4.4 Fill out the Atrial Fibrillation Study Completion Form

On the tablet, go to the Atrial Fibrillation Study Completion Form and record the fact that you have placed Patch #1. Enter the date and time Patch #1 was applied, and the serial number. Mark whether Patch #1 was applied by Field Center staff and enter your Tech ID (this will almost always be the case) or whether the participant applied it themselves (this should be very rare).

3.8.5 Clinic Staff Reminder Calls

1) Contact participant at 2-3 days to check in on how patch is going—record date of this call on the Atrial Fibrillation Study Completion Form.
2) Contact participant at 14 days to remind them of patch removal and confirm that they are mailing the patch in the booklet along with the Sleep/Wake time log—record date of this call on the Atrial Fibrillation Study Completion Form. Remind them that you will be mailing a second patch to them about 4 to 7 days after they mail in the first patch.
3) Contact participant 1 to 2 days after 2nd patch is mailed, provide encouragement, answer any questions, and offer to talk them through the applicaton of Patch #2 on the phone. Confirm that they turned the patch on. Record date of this call on Atrial Fibrillation Study Completion Form.
4) Contact participant at day 14 for 2nd patch, remind them of patch removal and to mail in the patch in the booklet (no sleep/wake time log for the 2nd patch) —record date of this call on Atrial Fibrillation Study Completion Form.

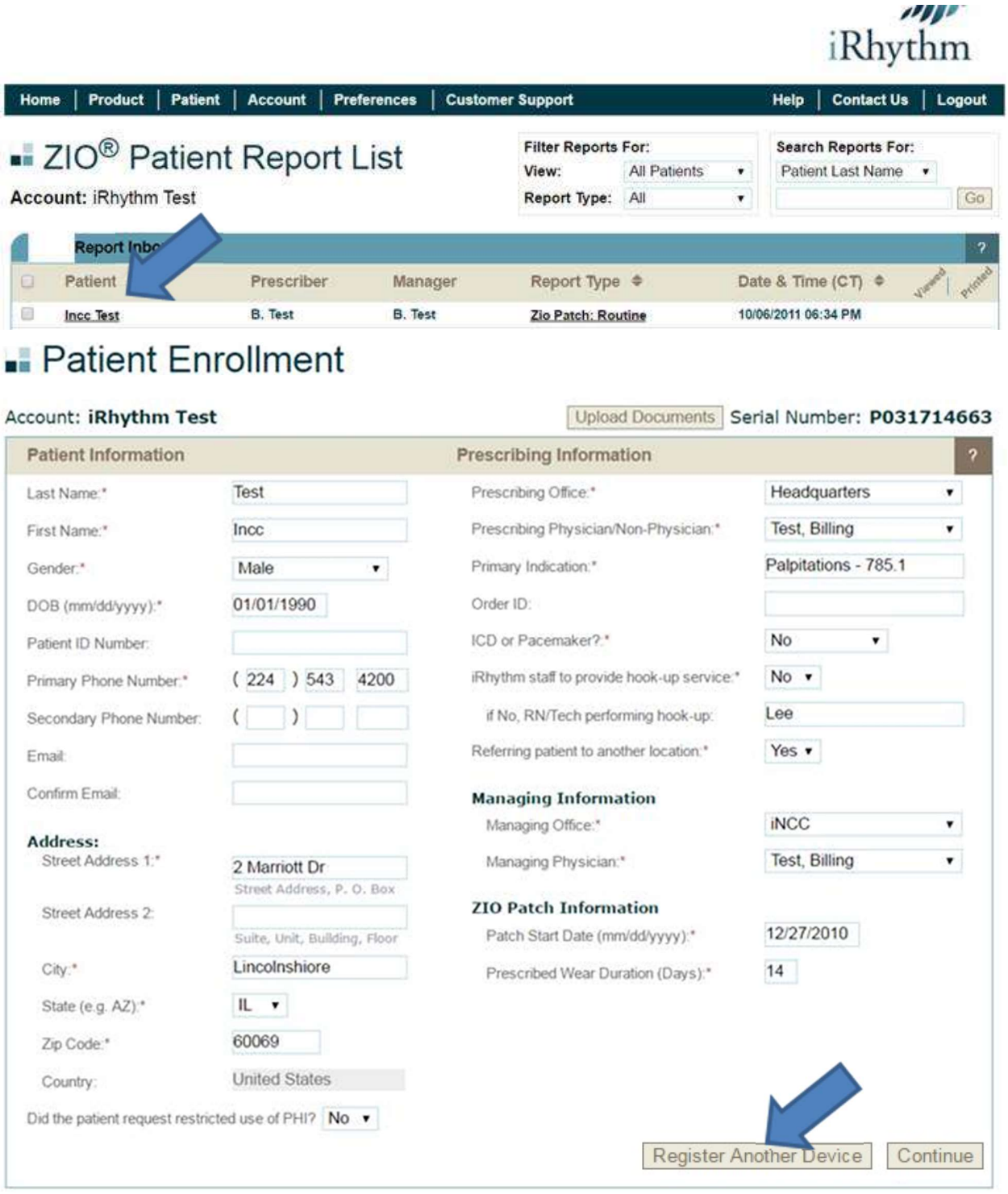
3.8.6 Prepare Zio Patch #2 for mailing to the participant

Supplies for Patch #2:

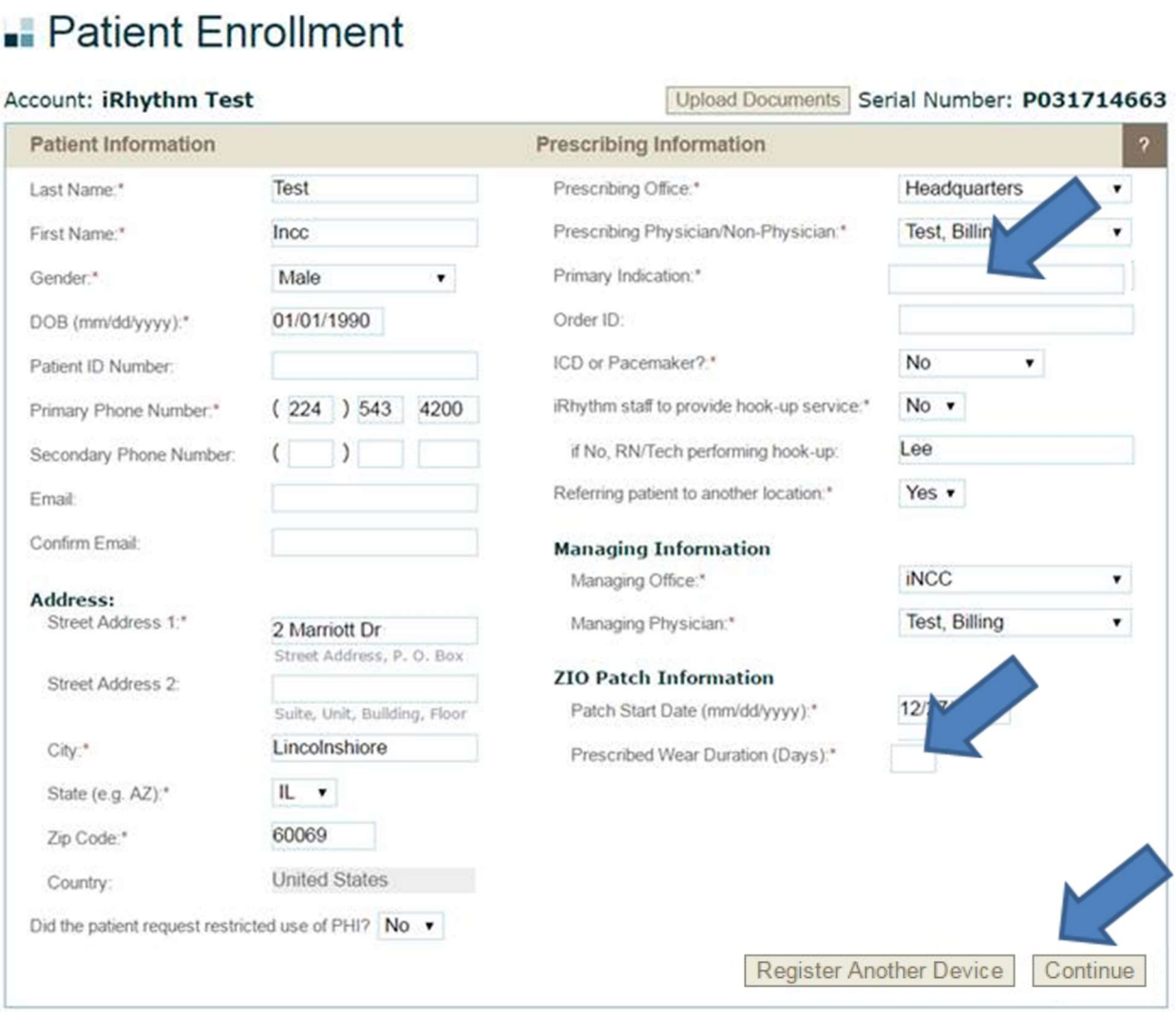
Zio Patch monitor kit
US Postal Service Priority Mail Small Flat Rate box
Booklet Page 1 Sticker
Booklet Page 1 Sticker in Spanish/Chinese, if appropriate for your participant

The CC will inform the FC staff when Patch #1 has been received from each participant and that it is time to mail Patch #2. Your FC will have a supply of Zio Patch kits that you can mail out. You will also need to have on hand at the FC a supply of US Postal Service Priority Mail Small Flat Rate boxes. These are available for free at your local US Post Office. The cost for mailing these Priority Mail Small Flat Rate boxes is $6.80 each. You budgeted for this in your FC budget. The USPS box should arrive at the participant's home 1 day after you mail it.

Register Patch #2 at www.Zioreports.com , similar to what you did for Patch #1. This time, go to "Patient Report List," and select the participant ID in the "Patient" column. You will be taken to the "Patient Enrollment" page where, in the bottom right hand corner, you will select "register another device." This will take you to the "Patient Registration" screen. Where it says "Register Device to:" you will select the participant ID—not NEW PATIENT—enter the device number and hit submit . You will be prompted with a "Warning" box. Confirm that you would like to register the device to the patient. This will bring you back to the Patient Enrollment page. Once there, you will need to enter "MESA" in the "Primary Indication" box and enter "14" in the "Prescribed Wear Duration (Days)" box. Once this is done, click "Continue" in the bottom right hand corner to complete the registration..


iRhythm
Home | Product | Patient | Account | Preferences | Customer Support | Help | Contact Us | Logout
ZIO® Patient Report List
Account: iRhythm Test
Filter Reports For:
View: All Patients
Report Type: All
Search Reports For:
Patient Last Name
Go
Report Inbo
Patient
Prescriber
Manager
Report Type
Date & Time (CT)
Viewed
Printed
Incc Test
B. Test
B. Test
Zio Patch: Routine
10/06/2011 06:34 PM
Patient Enrollment
Account: iRhythm Test
Upload Documents
Serial Number: P031714663
Patient Information
Prescribing Information
Last Name:* Test
First Name:* Incc
Gender:* Male
DOB (mm/dd/yyyy):* 01/01/1990
Patient ID Number:
Primary Phone Number:* (224) 543 4200
Secondary Phone Number: ( )
Email:
Confirm Email:
Address:
Street Address 1:* 2 Marriott Dr
Street Address, P. O. Box
Street Address 2:
Suite, Unit, Building, Floor
City:* Lincolnshiore
State (e.g. AZ):* IL
Zip Code:* 60069
Country: United States
Did the patient request restricted use of PHI? No
Prescribing Office:* Headquarters
Prescribing Physician/Non-Physician:* Test, Billing
Primary Indication:* Palpitations - 785.1
Order ID:
ICD or Pacemaker?:* No
iRhythm staff to provide hook-up service:* No
if No, RN/Tech performing hook-up: Lee
Referring patient to another location:* Yes
Managing Information
Managing Office:* iNCC
Managing Physician:* Test, Billing
ZIO Patch Information
Patch Start Date (mm/dd/yyyy):* 12/27/2010
Prescribed Wear Duration (Days):* 14
Register Another Device
Continue


Home | Product | Patient | Account | Preferences | Customer Support | Help | Contact Us | Logout
Patient Registration
Device Information
Register Device to:
Enter Device Number:
Submit
Warning
Are you sure you want to register device
" P031714663 " to Incc Test?
Confirm
Cancel


Patient Enrollment
Account: iRhythm Test
Upload Documents
Serial Number: P031714663
Patient Information
Prescribing Information
Last Name:*
Test
First Name:*
Incc
Gender:*
Male
DOB (mm/dd/yyyy):*
01/01/1990
Patient ID Number:
Primary Phone Number:*
(224) 543 4200
Secondary Phone Number:
Email:
Confirm Email:
Address:
Street Address 1:*
2 Marriott Dr
Street Address, P. O. Box
Street Address 2:
Suite, Unit, Building, Floor
City:*
Lincolnshiore
State (e.g. AZ):*
IL
Zip Code:*
60069
Country:
United States
Did the patient request restricted use of PHI?
No
Prescribing Office:*
Headquarters
Prescribing Physician/Non-Physician:*
Test, Billin
Primary Indication:*
Order ID:
ICD or Pacemaker?:*
No
iRhythm staff to provide hook-up service:*
No
if No, RN/Tech performing hook-up:
Lee
Referring patient to another location:*
Yes
Managing Information
Managing Office:*
iNCC
Managing Physician:*
Test, Billing
ZIO Patch Information
Patch Start Date (mm/dd/yyyy):*
Prescribed Wear Duration (Days):*
Register Another Device
Continue

On the tablet, go to the Atrial Fibrillation Study Completion Form. For Zio Patch #2, enter the Zio Patch serial number and the date it is mailed to the participant. Mark whether Patch #2 was applied by the participant or whether it was applied by Field Center staff. If FC staff, enter the Tech ID.

Open the box for Zio Patch #2 but do not open the sealed pouch. On a Booklet Page 1 Sticker, record the MESA participant ID and the Field Center phone number. Apply a serial number sticker to the bottom right of Booklet Page 1 Sticker. Save the other two serial number stickers in the participant's paper chart at the Field Center, in case you need them later. Stick the corner of the sticker onto the outside of the pouch and put both into the gray Zio Patch mailing box. Place the gray Zio Patch mailing box inside a US Postal Service Priority Mail Small Flat Rate box, and address it to the participant. Mail the box to the participant.

3.8.7 Spanish or Chinese language materials

The Coordinating Center has prepared Spanish and Chinese language versions of all printed materials needed for the heart rhythm monitoring, and will mail them to the appropriate Field Centers.

Patch #1:
If the participant is a Spanish or Chinese-speaker, for Patch #1, remove the English-language Booklet and replace it with a Spanish or Chinese Booklet. Fill out the front page of the Booklet. Also, include a Spanish or Chinese version of the Sleep/Wake Log, which you should fold into quarters with the print showing. Make sure you send the participant home with the gray box, Booklet, and Sleep/Wake log in the appropriate language.

Patch #2:
For a Spanish or Chinese-speaker, get a Booklet in the appropriate language, fill out the front page with the participant's MESA ID, the start date and time, and the target removal date and time. Get a Start Guide in the appropriate language and fold it into quarters with the print showing. Put the Booklet and the Start Guide into the box along with the unopened pouch. You do not need to stick on a Booklet Page 1 sticker, because you have written this information directly on the Spanish/Chinese-language booklet. Follow the other instructions for Patch #2, above.

3.8.8 Troubleshooting

The Patch comes off after less than 48 hours
If the participant calls to tell you (or you learn) that a patch (either Patch #1 or Patch #2) has come off less than 48 hours after activation, and if the participant is willing to try again, ask him/her to mail the patch that has come off to iRhythm in the gray box. Re-register the participant on the iRhythm website for a new patch, prepare a new patch for mailing, and send him/her the replacement patch in the mail. Record that you have sent a Replacement Patch on the Atrial Fibrillation Study Completion Form. Please notify Dr. Susan Heckbert (see Contact Information) of the patient ID and the serial # of the Patch that came off whenever you send a replacement patch so that she can advise iRhythm to expect a "short recording" on the patch that came off, and so that the study will not be charged for the patch that came off.

The participant loses Sleep/Wake Log or the booklet or the Zio Patch box
If the participant loses the Sleep/Wake Log, that is of minimal importance and they should be encouraged to go ahead without it, complete the 14-day wear time, and return the Patch in the prepaid mailing box as instructed. If they lose the booklet, they should get a piece of paper and stick the Zio Patch to it, and go

ahead and mail it in to iRhythm using the prepaid mailing box. If they lose the box, they should bring the patch in to the Field Center, and the FC staff can mail the patch in for them. Alternatively, if the participant prefers, they can mail the patch to the FC. The FC will have extra "demo" kits on hand, and FC staff can use a box from a demo device to mail the patch to iRhythm (remove or black out the "Demo" sticker, black out or cover the incorrect serial number in 3 places on the gray box, and affix a correct serial number sticker for that participant's device to the front of the box).

Participant loses the adhesive removal packet
If the participant loses the adhesive removal packet used to help remove the patch at the end of the monitoring period, they can use a little baby oil or Dawn dishwashing liquid on a piece of paper towel to help remove it.

Participant loses the blue tape used to seal the prepaid mailer
If the participant loses the blue tape, they can just use any tape to seal the prepaid mailer.

Participant refuses to complete a second Zio Patch
If the participant refuses to apply or wear a second Zio Patch, it is still of value to the study to have the data from their first patch, so they should be encouraged to wear the first patch for as much of the 14 days as possible. They can still participate in the brain MRI later even if they wear only one patch.

Documenting participant reported concerns
Please note any problems or concerns reported by the participant (such as adhesive/skin reaction, patch falling off, etc.) on the "Comments" section of the Atrial Fibrillation Study Completion form.

3.8.9 Participant Alerts and Results Reporting

For each ECG monitor received, a written report and selected ECG tracings are placed by the iRhythm technician on the iRhythm HIPAA-compliant server. The EPICARE ECG Reading Center staff members are notified by iRhythm staff within 24 hours if an Alert condition (listed below) is detected by the iRhythm technician. For participants both with and without Alert conditions, the EPICARE reader downloads the iRhythm report and selected ECG tracings from the iRhythm server to an EPICARE server and conducts a physician over-read of the results. The EPICARE reader then fills out a MESA form on the MESA Intranet classifying the report as one with Alert conditions, with other non-urgent findings, or as within normal limits. If there is an Alert condition, the EPICARE reader notifies the Field Center principal investigator and at least one other Field Center staff member by email. The Field Center personnel then obtains information on the EPICARE classification, the iRhythm report, and the rhythm strips from the MESA Intranet and communicates these results to the participant, and with permission, to his or her physician. For all participants, a results letter is mailed to the participant from the Field Center within a few weeks after both monitoring episodes are concluded, summarizing the results.

3.8.10 Technician Certification

Field Center technicians will complete the following to become certified in applying the heart rhythm monitor:

1. Attend the phone call/webinar with Martha Livingston, the representative from the iRhythm company, on July 19, 2016. For those who missed the webinar, go over the webinar slide set with the lead technician at their site.

2. Attend MESA Central Training in Chicago in July 2016 and attend Martha Livingston's presentation on the Zio Patch. Successfully complete the registration of a participant at the iRhythm website, apply a demo Zio Patch on a volunteer, and provide all the participant information as directed in the MOP. For those who miss the Central Training session, complete the registration of a participant on the iRhythm website and complete the application of a demo Zio Patch on a volunteer, providing all the information as directed in the MOP, with the lead technician at their site. A completed certification checklist for every tech should be sent to the CC for each technician who will be applying the heart monitor patch. This must be overseen/administered by the lead technician at each site.

3. Demonstrate the preparation of a Zio Patch #2 for mailing to a participant, including registering the participant at the iRhythm website, preparing the mailed kit, putting the gray Zio Patch mailing box inside a US Postal Service Priority Mail Small Flat Rate box, and addressing it to the participant.

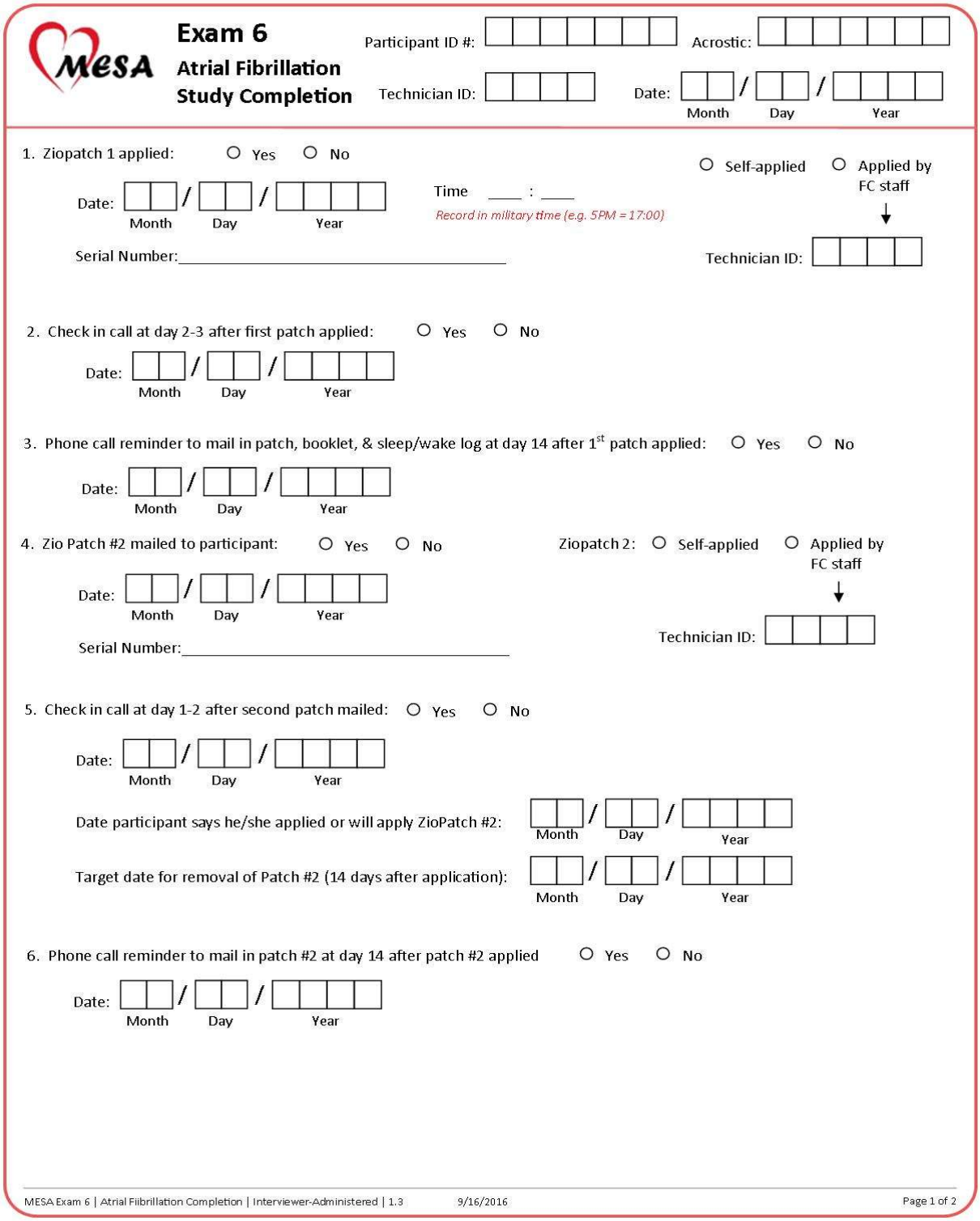
3.8.11 Contact information

Call iRhythm for questions about the Zio Patch
Toll-free number, 7 days a week, 24 hours a day -- for study staff, not for MESA participants
1-888-693-2401

Susan R. Heckbert, MD, PhD (MESA Atrial Fibrillation PI)
University of Washington
1730 Minor Ave, Suite 1360
Seattle, WA 98101
Phone: 206-221-7775
Email: heckbert@uw.edu

Elsayed Z. Soliman, MD, MSc, MS (EPICARE ECG Reading Center PI)
Wake Forest School of Medicine
Medical Center Blvd
Winston Salem, NC 27157
Phone: 336-716-8632
Email: esoliman@wakehealth.edu

3.8.12 Atrial Fibrillation Study Completion Form



Exam 6
Atrial Fibrillation Study Completion

Participant ID #: ☐☐☐☐☐☐☐ Acrostic: ☐☐☐☐☐☐☐

Technician ID: ☐☐☐☐ Date: ☐☐ / ☐☐ / ☐☐☐☐ (Month / Day / Year)

1. Ziopatch 1 applied: ○ Yes ○ No

Date: ☐☐ / ☐☐ / ☐☐☐☐ (Month / Day / Year)

Time ____ : ____ *Record in military time (e.g. 5PM = 17:00)*

○ Self-applied ○ Applied by FC staff ↓

Serial Number:_____

Technician ID: ☐☐☐☐

2. Check in call at day 2-3 after first patch applied: ○ Yes ○ No

Date: ☐☐ / ☐☐ / ☐☐☐☐ (Month / Day / Year)

3. Phone call reminder to mail in patch, booklet, & sleep/wake log at day 14 after 1st patch applied: ○ Yes ○ No

Date: ☐☐ / ☐☐ / ☐☐☐☐ (Month / Day / Year)

4. Zio Patch #2 mailed to participant: ○ Yes ○ No

Ziopatch 2: ○ Self-applied ○ Applied by FC staff ↓

Date: ☐☐ / ☐☐ / ☐☐☐☐ (Month / Day / Year)

Technician ID: ☐☐☐☐

Serial Number:_____

5. Check in call at day 1-2 after second patch mailed: ○ Yes ○ No

Date: ☐☐ / ☐☐ / ☐☐☐☐ (Month / Day / Year)

Date participant says he/she applied or will apply ZioPatch #2: ☐☐ / ☐☐ / ☐☐☐☐ (Month / Day / Year)

Target date for removal of Patch #2 (14 days after application): ☐☐ / ☐☐ / ☐☐☐☐ (Month / Day / Year)

6. Phone call reminder to mail in patch #2 at day 14 after patch #2 applied ○ Yes ○ No

Date: ☐☐ / ☐☐ / ☐☐☐☐ (Month / Day / Year)

MESA Exam 6 | Atrial Fiibrillation Completion | Interviewer-Administered | 1.3 9/16/2016 Page 1 of 2

Exam 6
Atrial Fibrillation
Study Completion

7. If a replacement patch is needed due to wear time less than 48 hours:

Replacement Zio Patch mailed to participant:

Date mailed: ☐☐ / ☐☐ / ☐☐☐☐ (Month / Day / Year)

○ Patch 1 ○ Patch 2

○ Self-applied ○ Applied by FC staff

Serial Number:_____

Technician ID: ☐☐☐☐

Comments:

8. Brain MRI scheduling call: ☐☐ / ☐☐ / ☐☐☐☐ (Month / Day / Year)

MRI scheduled: ☐☐ / ☐☐ / ☐☐☐☐ (Month / Day / Year)

Time ____ : ____
Record in military time (e.g. 5PM = 17:00)

MRI completed: ☐☐ / ☐☐ / ☐☐☐☐ (Month / Day / Year) (imported from MRI completion)

3.9 Six Minute Walk Test

3.9.1 Background

There are several modalities available for the objective evaluation of functional exercise capacity. The most popular clinical exercise tests in order of increasing complexity are stair climbing, a 6MWT, a shuttle-walk test, detection of exercise-induced asthma, a cardiac stress test (e.g., Bruce protocol), and a cardiopulmonary exercise test. THE 6MWT is easy to administer, better tolerated, and more reflective of activities of daily living than the other walk tests.

The 6MWT is a practical simple test that requires a 70-ft hallway but no exercise equipment or advanced training for technicians. Walking is an activity performed daily by all but the most severely impaired patients. This test measures the distance that a patient can quickly walk on a flat, hard surface in a period of 6 minutes (the 6MWD). It evaluates the global and integrated responses of all the systems involved during exercise, including the pulmonary and cardiovascular systems, systemic circulation, peripheral circulation, blood, neuromuscular units, and muscle metabolism. It does not provide specific information on the function of each of the different organs and systems involved in exercise or the mechanism of exercise limitation, as is possible with maximal cardiopulmonary exercise testing. The self-paced 6MWT assesses the submaximal level of functional capacity. Most patients do not achieve maximal exercise capacity during the 6MWT; instead, they choose their own intensity of exercise and are allowed to stop and rest during the test. However, because most activities of daily living are performed at submaximal levels of exertion, the 6MWD may better reflect the functional exercise level for daily physical activities.

3.9.2 Contraindications

Absolute contraindications for the 6MWT include the following:

- Unstable angina (chest pain) during the previous month , or new or worsening symptoms of chest pain, shortening of breath, or fainting in past 8 weeks
- Use of a wheelchair, crutches or walker (cane is OK for 6MW test).

Relative contraindications include the following:

- Resting heart rate of less than 50 or more than 110 at rest
- Systolic blood pressure of more than 180 mm Hg
- Diastolic blood pressure of more than 110 mm Hg

These are assessed during the anthropometry portion of the visit, or inquired about at the beginning of the testing period and are documented on Item 1 of the 6MWT Completion Form.

3.9.3 Safety Issues

Testing will occur in be performed in a location where a rapid, appropriate response to an emergency is possible. Although adverse events are rare and we are excluding participants with absolute contraindications, it is helpful to have medical supplies (e.g., albuterol, aspirin, oxygen available in the case of an emergency). Physicians are not required to be present during tests; however, it is helpful if testing occurs in a setting in which medical professionals (e.g., RNs) are available in the case of an emergency. If a patient is on chronic oxygen therapy, oxygen should be given at their standard rate as discussed below.

Reasons for immediately stopping a 6MWT include the following:

1 chest pain
2 intolerable dyspnea

3 leg cramps
4 staggering
5 diaphoresis
6 pale or ashen appearance

Technicians must be trained to recognize these problems and the appropriate responses. If a test is stopped for any of these reasons, the patient should sit or lie supine as appropriate depending on the severity or the event and the technician's assessment of the severity of the event and the risk of syncope. The following should be obtained based on the judgment of the technician: blood pressure, pulse rate, oxygen saturation, and a physician evaluation. Oxygen should be administered as appropriate.

3.9.4 Technical Aspects of the 6MWT

The 6MWT should be performed indoors, along a long, flat, straight, enclosed corridor with a hard surface that is seldom traveled.. The walking course must be 20 meters in length. A n approximately 70-ft hallway is, therefore, required. The length of the corridor should be marked every 2 meters. The turnaround points should be marked with a cone (such as an orange traffic cone). A starting line, which marks the beginning and end of each 40-m lap, should be marked on the floor using brightly colored tape.

3.9.5 Required Equipment

1. Countdown timer (or stopwatch) (as back up) OR Notebook Computer with timer tool
2. Mechanical lap counter
3. Two small cones to mark the turnaround points
4. A chair that can be easily moved along the walking course
5. Worksheets on a clipboard
6. A source of oxygen
7. Sphygmomanometer
8. Telephone
9. Automated electronic defibrillator (on site)
10. Pulse oximeter - Devon Medical Handheld Pulse Oximeter PC-66

3.9.6 Patient Preparation

1. Comfortable clothing should be worn.
2. Appropriate shoes for walking should be worn.
3. Patients should use their usual walking aids during the test (cane, walker, etc.).
4. The patient's usual medical regimen should be continued.
5. A light meal is acceptable before early morning or early afternoon tests.
6. Patients should not have exercised vigorously within 2 hours of beginning the test.

3.9.7 Testing

1. Testing should be performed about the same time of day to minimize intraday variability.

2. A "warm-up" period before the test should **not** be performed.

3. The patient should sit at rest in a chair, located near the starting position, for at least 10 minutes before the test starts. During this time, check for contraindications (Item 1 on the 6MWT Completion Form), evaluate for and record supplemental oxygen to be used during the test (Item 2), and make sure that clothing and shoes are appropriate.

4. Measure and record the baseline heart rate(Item 3) and baseline oxygen saturation (SpO2) (Item 4) on the 6MWT Completion Form.

5. Have the patient stand and rate their baseline dyspnea and overall fatigue using the Borg scale. Show the 6MW Borg Scale Form to the patient and ask the patient this:

"Please grade your level of shortness of breath using this scale."

Then ask this: *"Please grade your level of fatigue using this scale."*

Record the responses on the 6MWT Borg Scale Form, Item 5, Pre-test.

6. Set the lap counter to zero and the timer to 6 minutes. Assemble all necessary equipment (lap counter, timer, clipboard, Borg Scale, worksheet) and move to the starting point.

7. Instruct the participant using the script provided (page 6) including doing a demonstration of turning around the cone briskly.

8. Position the participant at the starting line. You should also stand near the starting line during the test. Do not walk with the patient (unless you have to hold the oxygen tank). As soon as the patient starts to walk, start the timer (and record Start time, item 6)

9. Do not talk to anyone during the walk. Use an even tone of voice when using the standard phrases of encouragement. Watch the patient. Do not get distracted and lose count of the laps. Each time the participant returns to the starting line, click the lap counter once (or mark the lap on the worksheet). Let the participant see you do it. Exaggerate the click using body language, like using a stopwatch at a race.

During the walk, give the participant the remaining time in the test every minute, using the script on page 6. Do not use other words of encouragement (or body language to speed up).

If the patient stops walking during the test and needs a rest, say this: *"You can lean against the wall if you would like; then continue walking whenever you feel able."* Do not stop the timer.

If the patient stops before the 6 minutes are up **and refuses to continue** (or you decide that they should not continue), wheel the chair over for the patient to sit on, discontinue the walk, and note on the worksheet the distance, the time stopped (Item 7) and the reason for stopping prematurely (item 8)

When the timer is 15 seconds from completion, say this: *"In a moment I'm going to tell you to stop. When I do, just stop right where you are and I will come to you."*

When the timer rings (or buzzes), say this**: *"Stop!"***
Walk over to the patient. Consider taking the chair if they look exhausted. Mark the spot where they stopped by placing a bean bag or a piece of tape on the floor.

10. Post-test: Record the stop time (item 7), then the postwalk Borg dyspnea and fatigue levels (item 12)..

At the end of the 6-minute exercise, show the 6MW Borg Scale Form to the patient again and ask the patient this: *"Please grade your level of shortness of breath using this scale."* Then ask this: *"Please grade your level of fatigue using this scale"* after reminding them of their grades before the exercise.

11. Measure oximetry and pulse rate from the pulse oximeter on the 6MWT Completion Form

12. Record any symptoms of discomfort at the end of the test on the 6MWT Completion Form (item 13)

13. Record the number of complete laps from the counter on the 6MWT Completion Form (Item 9A). One lap around is twice 20 meters, or 40 meters.

14. Record the additional distance covered (the number of meters in the final partial lap) using the markers on the wall as distance guides.(Item 9B). Calculate the total distance walked, rounding to the nearest meter, and record it on the worksheet.

*Example: 10 complete laps, then walked to the 8th tape marking and stopped: 10*40=400 +8*2 (16) meters. OR, 12 complete laps, then walked to the end, and stopped at the 2nd tape marking: 12*40= 480, +18*2 (36) meters.*

15. Congratulate the patient on good effort and offer a drink of water.

16. If paper formed used for data collection, transfer information to the computerized system.

3.9.8 Supplemental Oxygen

If the participant usually uses oxygen supplementation, then continue it for the 6MWT. If they use it only for exercise, do not use it for the 6MWT. If the patient uses oxygen for the walk, the technician should walk behind the patient carrying the oxygen source. Measurements of pulse oximetry should be made after waiting at least 10 minutes after any change in oxygen delivery.

3.9.9 Script

"The object of this test is to walk as far as possible for 6 minutes. You will walk back and forth in this hallway. Six minutes is a long time to walk, so you will be exerting yourself. You will probably get out of breath or become exhausted. You are permitted to slow down, to stop, and to rest as necessary. You may lean against the wall while resting, but resume walking as soon as you are able. You will be walking back and forth around the cones. You should pivot briskly around the cones and continue back the other way without hesitation. Now I'm going to show you. Please watch the way I turn without hesitation."

"Are you ready to do that? I am going to use this counter to keep track of the number of laps you complete. I will click it each time you turn around at this starting line. Remember that the object is to walk AS FAR AS POSSIBLE for 6 minutes, but don't run or jog. Start now, or whenever you are ready."

When the timer shows 5 minutes, tell the participant the following (in even tones):
"You are doing well. You have 5 minutes to go."

When the timer shows 4 minutes remaining, tell the participant the following:
"Keep up the good work. You have 4 minutes to go."

When the timer shows 3 minutes remaining, tell the participant the following:
"You are doing well. You are halfway done."

When the timer shows 2 minutes remaining, tell the participant the following:
"Keep up the good work. You have only 2 minutes left."

When the timer shows only 1 minute remaining, tell the participant:
"You are doing well. You have only 1 minute to go."

Do not use other words of encouragement (or body language to speed up).

If the participant stops walking during the test and needs a rest, say this:
"You can lean against the wall if you would like; then continue walking whenever you feel able." Do not stop the timer.

If the participant stops before the 6 minutes are up **and refuses to continue** (or you decide that they should not continue), wheel the chair over for the patient to sit on, discontinue the walk, and note on the worksheet the distance, the time stopped (Item 7) and the reason for stopping prematurely (item 8)

When the timer is 15 seconds from completion, say this:
"In a moment I'm going to tell you to stop. When I do, just stop right where you are and I will come to you."
When the timer rings (or buzzes), say this: ***"Stop!"***

Laps

4 ALERTS

I. PURPOSE

The purpose of defining medical alerts is to make sure that the participant and his/her physician are aware of any significant medical findings that arise as a result of the MESA clinic exam.

II. DEFINITIONS

Alert: Any of the medical findings listed in Table 1 that may have adverse health consequences to the participant if untreated.
Immediate Referrals: Medical emergencies, which require immediate notification of both the participant and his/her primary physician. Participants receiving immediate referrals should be considered as those who would go directly from the Field Center clinic to their physician or hospital. Immediate notification of the participant should occur during the clinic visit. Immediate notification of the participant's physician should be accomplished by telephone, to be completed before the participant leaves the clinic. A follow-up letter documenting information discussed by phone should also be sent to the participant's physician for findings included in the initial report, or immediately upon receipt from the central agency for findings on the later reports.
Urgent Referrals: Urgent referrals are made for abnormalities detected, which require medical attention, but not on an emergency basis. Urgent notification of the participant should occur before the participant leaves the clinic (for findings included in the initial participant report), or immediately upon receipt from the central laboratory (for findings on later reports). Urgent notification of the participant's physician should be sent within the week.

III. METHODS

1. General Instructions

Whenever one of the alerts listed above is identified for a participant, the actions defined under Immediate or Urgent Referrals, above, must be completed.

4.1 MESA Alerts and Alert Levels

Finding	Alert Level
Systolic BP > 210	Immediate
Diastolic BP > 120	Immediate
180 < Systolic BP < 211	Urgent
110 < Diastolic BP < 121	Urgent
Oxygen Saturation (resting) <88%	Urgent
Heart rhythm monitor: Wide QRS tachycardia >120 bpm and sustained for >30 seconds	Urgent
Heart rhythm monitor: Complete AV block	Urgent
Heart rhythm monitor: 2nd degree AV Block, Mobitz II	Urgent

Heart rhythm monitor: Pause >6 seconds	Urgent
Heart rhythm monitor: Bradycardia <40 bpm and sustained for >30 seconds	Urgent
Heart rhythm monitor: Atrial fibrillation/atrial flutter with average heart rate <40 bpm or >180 bpm and sustained for 60 seconds	Urgent
Heart rhythm monitor: Atrial fibrillation that is sustained for more than 6 minutes	Urgent
Heart rhythm monitor: Narrow QRS tachycardia >180bpm and sustained for 60 seconds	Urgent
Heart rhythm monitor: Other abnormalities deemed important by the ECG center readers	Urgent
Brain MRI: Acute subdural or epidural hematoma	Immediate
Brain MRI: Subarachnoid hemorrhage	Immediate
Brain MRI: Acute intraparenchymal hematoma	Immediate
Brain MRI: Acute infarct	Immediate
Brain MRI: Abscess	Immediate
Brain MRI: Suspected tumor with significant mass effect	Immediate
Brain MRI: Tumor without significant mass effect	Urgent
Brain MRI: Subacute infarct	Urgent
Brain MRI: Arteriovenous malformation	Urgent
Brain MRI: Aneurysm	Urgent
Brain MRI: Obstructive hydrocephalus	Urgent
ECHO: Suspected tamponade	Immediate
ECHO: Aortic aneurysm (measuring >5.0 cm) or dissection	Immediate
ECHO: Intracardiac abscess or obvious vegetation	Immediate
ECHO: Intracardiac thrombus or mass	Immediate
ECHO: Pseudoaneurysm	Immediate
ECHO: Significant arrhythmia (eg atrial fibrillation with heart rate > 110 bpm, sustained ventricular arrhythmias, or NSVT > 10 beats)	Immediate
ECHO: Severe left ventricular or right ventricular enlargement	Urgent
ECHO: Severe regurgitation of any valve	Urgent
ECHO: Severe stenosis of any valve	Urgent

ECHO: Moderate or greater pericardial effusion without evidence of tamponade	Urgent
Carotid US: carotid artery dissection	Immediate
Carotid US: atherosclerotic plaque visually >70% occlusive	Urgent (Immediate if symptoms)
Carotid US: occluded carotid artery or color Doppler "String sign"	Urgent (Immediate if symptoms)
Carotid US: thyroid pathology (nodule > 1.0 cm or severe enlargement)	Urgent
Carotid US: mass > 1.0 cm	Urgent
Carotid US: jugular vein thrombosis	Immediate
Carotid US: systolic BP >210 mmHg, or diastolic BP >120 mmHg or heart rate exceeds 130 beats/minute	Immediate
Carotid US: systolic BP between 160-210 mmHg or the diastolic BP between 110-120 mmHg	Urgent
PET MRI: >70% stenosis of the carotid on MRI	Urgent
Total cholesterol > 360 mg/dL	Urgent
Triglyceride > 1000 mg/dL	Urgent
Calculated LDL cholesterol > 260 mg/dL	Urgent
Fasting glucose < 50 mg/dL or > 400 mg/dL	Urgent
Creatinine > 2.0 mg/dL	Urgent
Any abnormalities identified by CT tech	Urgent
Any abnormalities identified by ECHO tech	Urgent
ECG Reading Center (RC) Alert	Urgent
CT RC Alert	Urgent
ECHO RC Alert	Urgent
Sodium MRI: soft tissue mass	Urgent
Sodium MRI: bone mass	Urgent

4.2 Heart Rhythm Monitor Alerts

Clinic Alerts
None.

Reading Center Alerts &/or Incidental Findings
The ECG patch monitor will be applied at the Exam 6 visit. After 14 days of ambulatory ECG monitoring, the participant will mail the patch to the iRhythm company for analysis. If the iRhythm technologist sees a concerning ECG finding, they will contact the EPICARE center. Dr. Soliman will evaluate the finding and, if he confirms the finding, will contact the FC PI. EPICARE staff will also review each report received from iRhythm, conduct a cardiologist over-read of the findings, transmit any alert findings to the FC PIs, and prepare a results report for participants. A second ECG patch monitor will be mailed to the participant, applied by the participant, and returned to the company for analysis in the same manner as the first. Any concerning ECG findings on the second monitor will be handled in the same manner as for the first monitor. The ECG monitor alerts are as shown in Table 1.

4.3 Chest CT Alerts (with or without contrast)

Significant Alerts
Alerts of potential and established significance are aortic aneurysms, dense aortic valve calcifications (aortic stenosis), lung masses (> 3 cm), pneumonia, pneumothorax and large pericardial effusions. These will be communicated to Field Center PIs, or designee, directly.

a. Aortic diameter > 45 mm – aortic aneurysm screening is the only cardiovascular imaging modality ever shown to improve outcomes.[i]
b. lung masses (>30 mm)
c. lobar pneumonia,
d. pneumothorax and
e. large pericardial or pleural effusions, along with unusual findings deemed significant by the reading center.
f. Large perfusion defects in the absence of obvious cause (e.g., emphysema).

Other Findings
Other findings of potential significance that may require follow-up include pulmonary nodules and hepatic or splenic lesions. These will be communicated to via the high-tech results letter.

g. Nodules (non-calcified densities in the lung < 30 mm). In December 2013, the U.S. Health U.S. Preventative Services Task Force issued a Grade B recommendation for lung cancer screening **for individuals at increased risk of lung cancer** (criteria below).[1] Based on this recommendation, participants meeting these criteria ("high-risk individuals") with lung nodules will receive an alert in accordance with the LungRADS™ assessment categories.[2-4]

For low-risk individuals (those not meeting the USPSTF criteria), there is no current data to suggest that intervention on small nodules provides benefit, and some data that there may be harm reporting asymptomatic nodules (cost, anxiety, follow up tests, morbidity and mortality). Consistent with prior MESA Exams, a nodule size threshold of 8 mm will be used. Scans with nodules ≥8mm in size will prompt an evaluation of older scans for comparison. Nodules will not be reported if unchanged from prior MESA scans (if available), as these are considered benign. Only solid nodules will be considered. Nodule size was collected systematically in Exam 1 and all nodules (including 1-2 mm)

were reported. The prevalence of reported nodules among low-risk individuals is expected to be <10%.

h. Dense (non-cystic) lesions in the liver and spleen will be reported. These are rare.

Radiologist Review Chest CT scans with or without contrast will be reviewed for pulmonary alerts and other findings that may require clinical follow-up either locally by a board-certified radiologist at the Field Center or centrally by Dr. John Austin, a board-certified thoracic radiologist and member of the Fleischner Society, who has extensive experience in lung imaging or locally. If Dr Austin is not available, another board-certified thoracic radiologist will perform the read. Central reads will occur for the University of Minnesota and UCLA. Local reads will take place at: Wake Forest University, Columbia University, Johns Hopkins University, and Northwestern University.

For local reads, the local radiologist will perform either a safety read for alerts and other findings, as defined above, or a full clinical read, according to local practice, and complete the CT Safety Reading form. If a safety read is performed, a report will be generated only in the event of an alert or other finding; if a full clinical read is performed, the result will be returned to the participant along with a cover letter explaining the significance of the report in lay language.

For central reads, Dr. Austin will perform a safety read and complete the CT Safety Reading form. For alerts and other findings, he will provide the clinic and participant with a report on letterhead documenting the potential issue in clear language with a recommended next action. In addition to the reports, the CT reading center is ready to help participants obtain copies of their images upon request if this proves difficult from the primary source, the site where the CT exam is performed.

Drs. Austin, Barr and Smith will also consult and discuss cases with FC local radiologists, physicians and PIs as requested and have done this in the past on several occasions.

The table below describes a summary of findings and the appropriate action

Finding	**Action**
Alert: aortic aneurysms, dense aortic valve calcifications, lung masses (≥ 3 cm), pneumonia, large pericardial,pleural effusions or large perfusion defect	If the radiologist feels that an alert is warranted, he/she will write a report and this will be transmitted immediately to the field site PI, coordinator and a copy sent to the coordinating center. The participant will receive a letter that describes the finding and suggests that the participant share the letter with their physician. The PI will contact the participant directly.
Other findings: Lung nodules (<3 cm) in participants who meet US Preventative Task Force eligibility criteria for lung cancer screening CT[1] (Adults ages 55 to 80 years who have a 30 pack-year smoking history AND who currently smoke OR have quit within the past 15 years).	The radiologist will write a report in accordance with the LungRADS™ assessment categories.[2-4] The participant will receive a letter that describes the finding and suggests that the participant share the letter with their physician. For findings requiring follow-up in 6 months or less, the PI will contact the participant directly.
Other findings: Lung nodules (<3 cm) in participants who do NOT meet US Preventative Task Force eligibility criteria for lung cancer screening CT[1] (Participants over age 80 years OR who have a less than 30 pack-year smoking history OR who have not smoked	The radiologist will write a report for non-calcified lung nodules ≥8 mm, unless they are stable and have not increased compared to a prior CT scan. The participant will receive a letter that describes the finding and suggests that the

cigarettes for more than 15 years).	participant share the letter with their physician. For findings requiring follow-up in 6 months or less, the PI will contact the participant directly.
Other Findings: non-water density lesions of the liver or spleen, etc	The radiologist will write a report and this will be transmitted to the field site for inclusion in the high-tech results letter. The participant and their physician, if approved, will receive this letter that describes the finding
Routine: Emphysema Extent.	The participant will receive a letter that provides these results and suggests that the participant share the letter with their physician.

4.4 ECHO Alerts

In addition to the electronic transmission of echo images using WebPAX, the site sonographer is responsible for filling out an Echo Transmittal Form to accompany each study echocardiogram sent to the NUECL. This form is used to record basic physiologic information about each patient and also gives the site sonographer the opportunity to comment on any echo findings or problems with image acquisition. A copy of this form should be filled out, signed, and emailed to the technical director of the NUECL (lauren.nelson@northwestern.edu) each time an echo is submitted.

For routine studies, a qualitative echo report will be provided within 6-8 weeks of study receipt. The report will be emailed to the site PI and site study coordinator, who are responsible for supplying it to the participant. The echocardiographic protocol for MESA is a limited research protocol and is not intended to provide a comprehensive evaluation of cardiac structure and function. In addition, these studies are not clinically indicated and will be reviewed in the absence of any clinical information. Qualitative reporting of the echocardiographic findings is provided as a courtesy to MESA participants, and is not intended as a substitute for a full echocardiographic assessment.

Because routine studies may not be fully analyzed for 6-8 weeks, it is important that the site sonographer note any abnormalities at the time of the echo, report them to the site PI and/or cardiologist, and generate a medical alert for the study as outlined below. The NUECL has created a list of abnormalities that will qualify as medical alerts for this study. The purpose of defining these alerts is to make sure that the participant and his/her physician are aware of any significant medical findings that arise as a result of the MESA clinic exam. If any of the qualifying abnormalities are noted, the sonographer should acquire additional echo images as needed and notify the site PI or cardiologist at the time of the echocardiogram. Each site is responsible for coordinating local echo review and follow up for any patient with a clinical alert or other abnormal finding noted on the echo. *The NUECL is not responsible for detecting or reporting abnormal echo findings.*

IMMEDIATE REFERRALS

Immediate referrals are medical emergencies which require immediate notification of both the participant and his or her primary physician. Participants receiving immediate referrals are those who would go directly from the Field Center clinic to their physician's office or hospital. If a potentially serious or life-threatening abnormality is detected that may require urgent medical evaluation, the sonographer is expected to **immediately** notify both the site PI and the NUECL (by phone or email). The site PI will then review the images, verify the study findings, and determine whether emergent medical care is required. The site PI is also responsible for communicating the results to the participant and his/her personal physician **at the time of the clinic visit**. An immediate referral is indicated by the sonographer on the Echo Transmittal Form, accompanied by a description of the findings. The study is then

transmitted to the NUECL for rapid review and verification by the NUECL readers and physicians. A detailed echocardiographic report will be generated and e-mailed to the site within 24-48 hours. Abnormalities that should be classified as immediate referrals include:

- Suspected tamponade
- Aortic aneurysm (measuring ≥5.0 cm) or dissection
- Intracardiac abscess or obvious vegetation
- Intracardiac thrombus or mass
- Pseudoaneurysm
- Significant arrhythmia (eg atrial fibrillation with heart rate > 110 bpm, sustained ventricular arrhythmias, or NSVT > 10 beats)

URGENT REFERRALS

Urgent referrals are made when abnormalities are detected which may require medical attention, but not on an emergency basis. The site sonographer is expected to notify the site PI at the time of the echocardiogram. The site PI will review the images and verify the study findings, then communicate the results to the participant at the time of the clinic visit**.** The site PI is also responsible for providing notification of the participant's physician within one week of the clinic visit. An urgent referral is indicated by the sonographer on the Echo Transmittal Form, accompanied by a description of the findings. The study is then transmitted to the NUECL and a detailed echocardiographic report will be generated and e-mailed to the site within 48-96 hours.
Abnormalities that should be classified as urgent referrals include:

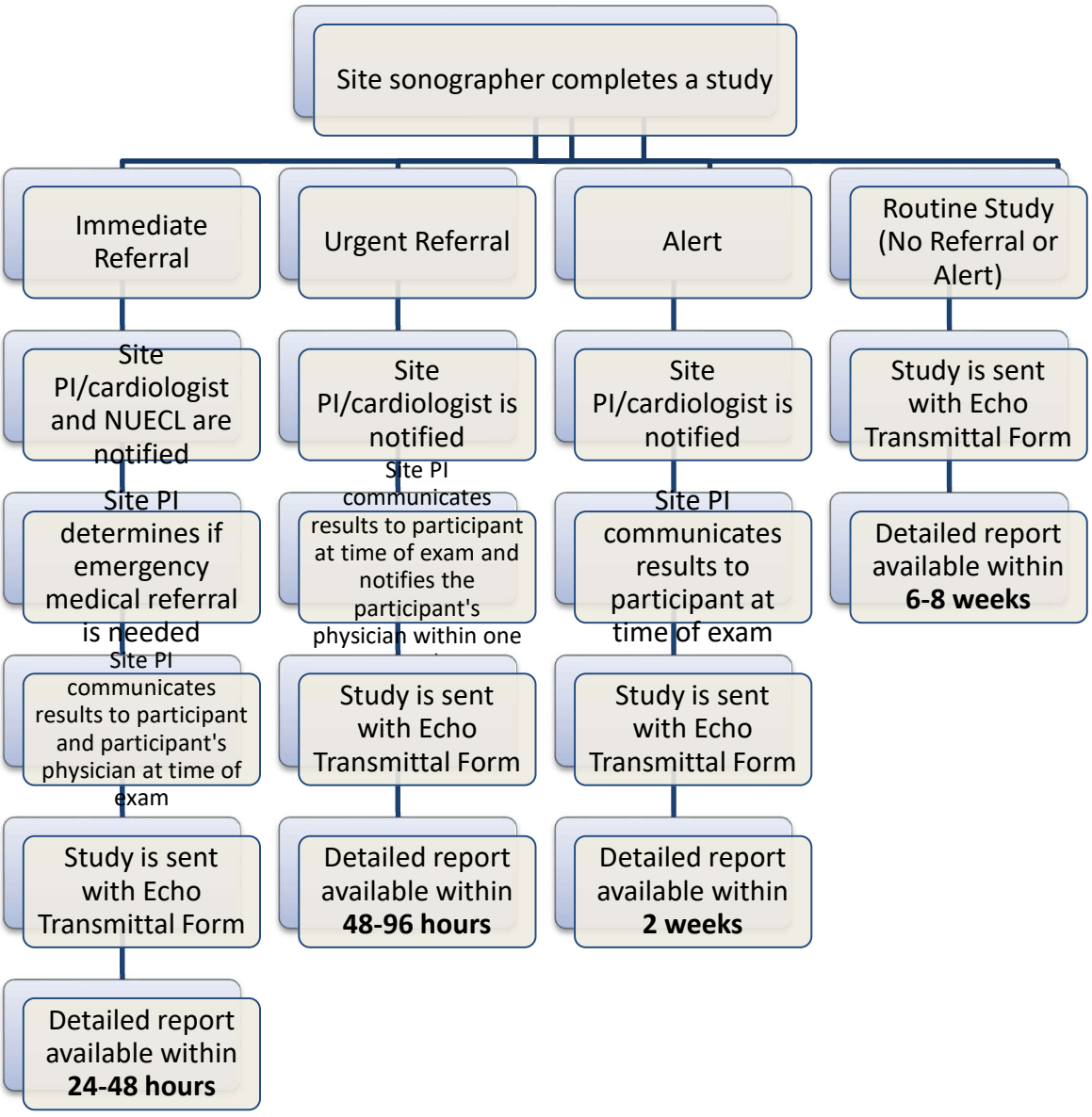
- Severe left ventricular or right ventricular enlargement
- Severe stenosis of any valve
- Severe regurgitation of any valve
- Moderate or greater pericardial effusion without evidence of tamponade

ALERTS

Alerts are medical findings that may have adverse health consequences to the participant if left untreated. In the case of an alert, the site sonographer is expected to notify the site PI at the time of the echocardiogram. The site PI will review the images and verify the study findings, then communicate the results to the participant at the time of the clinic visit. An alert is indicated by the sonographer on the Echo Transmittal Form, accompanied by a description of the findings. The study is then transmitted to the NUECL and an echocardiographic report will be generated and e-mailed to the site within two weeks.

Abnormalities that should be classified as alerts include:

- Mild or moderate stenosis of any valve
- Moderate mitral or aortic regurgitation
- Moderate or greater dynamic LVOT obstruction (gradient at rest or with Valsalva ≥40 mmHg)
- Intra-cardiac shunt
- Moderate to severe pulmonary hypertension (RVSP>45 mmHg)
- Evidence of RV pressure or volume overload
- Low ejection fraction (≤40%) or wall motion abnormality


Site sonographer completes a study
Immediate Referral
Urgent Referral
Alert
Routine Study (No Referral or Alert)
Site PI/cardiologist and NUECL are notified
Site PI/cardiologist is notified
Site PI/cardiologist is notified
Study is sent with Echo Transmittal Form
Site PI determines if emergency medical referral is needed
Site PI communicates results to participant at time of exam and notifies the participant's physician within one
Site PI communicates results to participant at time of exam
Detailed report available within **6-8 weeks**
Site PI communicates results to participant and participant's physician at time of exam
Study is sent with Echo Transmittal Form
Study is sent with Echo Transmittal Form
Study is sent with Echo Transmittal Form
Detailed report available within **48-96 hours**
Detailed report available within **2 weeks**
Detailed report available within **24-48 hours**

4.5 Brain MRI Alerts

For MESA Memory, clinic reads will be performed centrally by Wake Forest and study reads will be performed by Nick Bryan.

For MESA Atrial Fibrillation, clinic reads will be performed locally at Columbia, Northwestern and Johns Hopkins and by Nick Bryan for Wake Forest, Minnesota, and UCLA. Nick Bryan will perform all study reads.

References

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2. McKee BJ, Regis SM, McKee AB, et al. Performance of ACR Lung-RADS in a clinical CT lung screening program. JACR 2105; 12(3): 273-276.

3. Pinsky PF, Gierada DS, Black W, Munden R, et al. Performance of Lung-RADS in the national lung screening trial: a retrospective assessment. Ann Int Med 2015; 162(7):485-491.

4. Lung-RADS™ Version 1.0 Assessment Categories Release date: April 28, 2014. Accessed March 30, 2016: http://www.acr.org/~/media/ACR/Documents/PDF/QualitySafety/Resources/LungRADS/AssessmentCategories.pdf

4.6 Sodium MRI Alerts

MRI technologists at Northwestern University will be performing the sodium MRI scans on Chicago, IL field center participants. The technologists will transmit the sodium MRI scans electronically in a de-identified, secure, encrypted electronic format to the Vanderbilt Sodium MRI reading center. The MRI technologists at Northwestern will also complete a tracking form for the sodium MRI that will contain the MESA study ID, date of scan, and technical details regarding the image acquisition and transmission. Any notable findings identified by the MRI technologist should be recorded on this tracking form. A copy of this form should be transmitted to the Vanderbilt sodium MRI reading center via email to d.gupta@vanderbilt.edu or fax (615-322-3837, attention Deepak Gupta) each time a sodium MRI scan is performed. The sodium MRI scans may not be analyzed immediately upon receipt at the Vanderbilt sodium MRI reading center (could be 8-12 weeks). Therefore, it is important for the Northwestern MRI technologist performing the sodium MRI scan to note on the tracking form whether any unexpected findings were seen during image acquisition.

The sodium MR imaging sequences are for research only and not a clinical standard. The images are utilized and optimized for visualization of sodium, rather than clinical musculoskeletal imaging. Therefore, the likelihood of ancillary findings of clinical relevance, for example, unexpected musculoskeletal findings, such as soft tissue or bone masses, is very low. Nevertheless, all images will be reviewed by an analyst and over-read by a radiologist as appropriate. If unexpected findings of potential clinical relevance are identified on the MRI, the MRI reading center at Vanderbilt will contact the field center (Northwestern PI, coordinator, or their designees) to convey the unexpected findings via a written report. The Northwestern University MESA field center will then be responsible for contacting participants and/or their primary physician. *In the absence of alert findings, a report will not be generated for the purposes of conveying information about the sodium MRI to the participant or his/her physician because these are research sequences not considered as part of clinical standard of care. The Vanderbilt sodium MRI reading center is not responsible for detecting or reporting abnormal findings from the sodium MRI scans.*

5 REPORTING PARTICIPANTS' RESULTS

I. METHODS

1. Reporting Participants' Results

Participants receive three results reports.

- The Exit Report
- The lab results report contains the results of the blood values. This letter informs the participant if any of the results are abnormal. In addition, a letter is sent to the participant's physician, along with a page of reference ranges and the participant's lab results.
- The "high-tech" results report contains the results of the MRI, and CT scans and informs the participant of any abnormal finding. A letter containing a more detailed report of the scan results is also sent to the physician.

- All results letters should be carefully reviewed before they are sent to participants and physicians.

6 DATA ENTRY

6.1 Microsoft Surface Pro 4 Basics

Terminology

- **Touch –** A gentle press and release with your finger (corresponds to a mouse click)
- **Swipe –** Touch the screen and move finger in the indicated direction
- **Sleep mode –** Power conservation state for the Surface. Press the power button once to enter or exit sleep mode.
- **Charge –** Amount of battery power available. Make sure the tablet has sufficient charge before seeing patients
- **Kickstand –** Built-in stand for use on flat surfaces

Logging in

When you turn on the device or return from sleep mode you can log in using facial recognition by looking into the front facing camera.

Setting up Facial Recognition

These are Microsoft's instructions for setting up the facial recognition.

Step 1: Go to Start , and select **Settings** > **Accounts** > **Sign-in options**.

Step 2: Under **Windows Hello**, locate the infrared (IR) camera or fingerprint setup option. Select **Set Up** > **Get Started**.

Step 3: You may be asked to set up your account with a PIN. If so, follow the on-screen instructions.

Step 4: Follow the on-screen instructions to scan your face using the IR camera built into your Surface or to scan your finger using the fingerprint reader on Surface Pro 4 Type Cover with Fingerprint ID until Windows notifies you that the setup process is complete.

Step 5: Select **Finish**.

Connecting to Wi-Fi

Touch the [ ] icon in the bottom right corner of the screen. In the menu that appears, make sure airplane mode is turned off and Wi-Fi is turned on. Select your network from the list, touch Connect, and enter the network password.

> *You can check the 'Connect automatically' box when choosing a network if you plan to use it again.*

Using this manual

Important sections of screenshots are highlighted with blue boxes.

Additional tips are listed in *italics.*

Please send any additional questions about the Microsoft Surface Pro 4 tablet or the MESA data entry program to Kayleen Williams (kmfw@uw.edu), or Jerry Watson (jerryw@uw.edu)

Power button

If the device is turned off, hold this button for 1-2 seconds to turn it on.

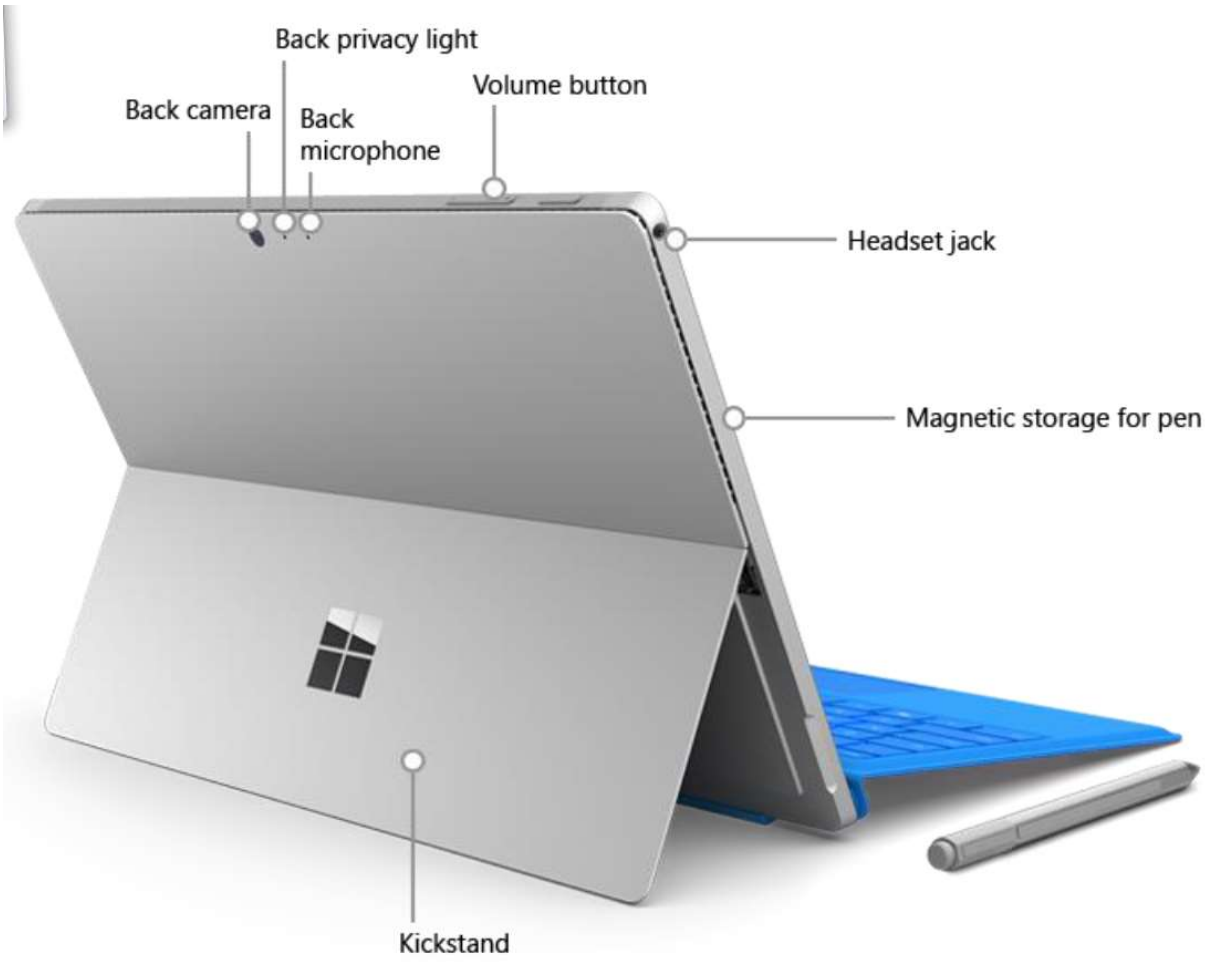
If the device is on, press the power button once or close the keyboard to enter sleep mode (conserves battery).

The device will enter sleep mode automatically after 2 minutes of inactivity to conserve power. Your data will be saved. Press the power button once to return from sleep mode and continue where you left off.

If the device is asleep, press the power button once to turn it back on. Swipe the screen upwards, then enter your username and password if prompted.

Swiping downwards instead of upwards will enter Camera Mode. Press the 'Unlock' icon in the bottom left corner to exit this mode.

To turn the device off, hold the power button until the screen changes, then release the button and follow the on-screen prompt. The device is designed to stay on, so this is usually not necessary unless it will not be used for a long period of time.



Kickstand

Pull out from the bottom edge of the device to use the Surface on a desk.

USB 3.0 port

If desired, a USB mouse can be plugged into the port. All functionality is available with touch or mouse controls.

Micro USB charging port

Plug in the charging cable here. Charging takes between 2-4 hours. **Please ensure the device is charged before a visit.** The battery meter in the right-hand corner of the screen will show you how much power is left.

Charge your Surface Pro 4

1. Connect the two parts of the power cord
2. Connect the power cord securely to the charging port.
3. Plug the power supply into an electrical outlet.

Connect the Type Cover

Snap the type cover into place and open the kickstand.

Keyboard and Touchpad

With the keyboard connected, you can enter data in form fields.

- Press Tab to move to the next field (or select the field using the touchpad)
- Press Shift+Tab to go back to the previous field

Use the touchpad to navigate the forms if you do not want to use the screen's touch feature.

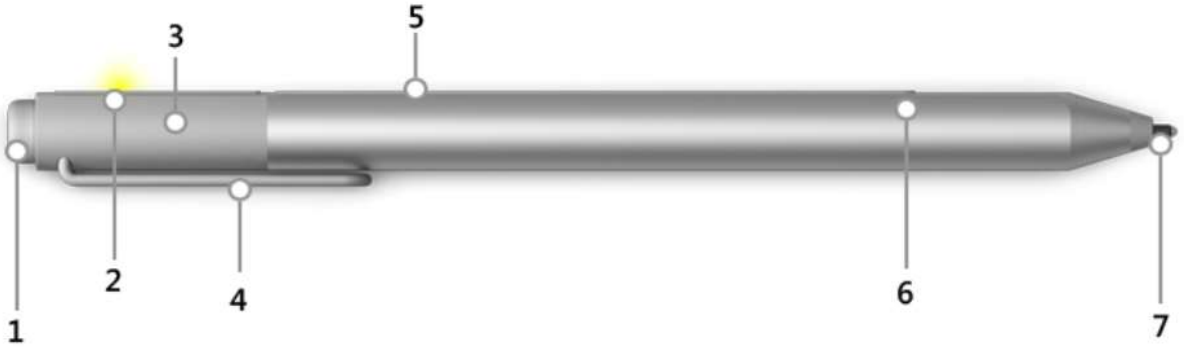
- Move your finger across the touchpad to move the on-screen mouse
- Touch the pad once to select objects, similar to a mouse click
- Double-touch to open apps, including the Exam 6 program
- Push on the bottom left or right of the pad to physically click like a mouse button

The keyboard can be removed by pulling it out from the bottom of the tablet. To put it back on, align the silver connector pins with the bottom of the tablet.

On-screen Keyboard

To activate the on-screen keyboard, touch the keyboard icon [] in the bottom right corner of the screen. The keyboard will block part of the screen, but can be repositioned by touching and dragging the top of the keyboard. Touch the '&123' key to type numbers and symbols.

Surface Pen



1 – Top button: To erase, flip the pen over and use the top as an eraser
2 – LED: When the pen is in pairing mode, the LED glows white. When the battery is low, the LED glows red.
3 – Cap
4 – Clip
5 – Magnet: Use the magnet on the flat side of the cap to attach your Surface Pen to the edge of your Surface Pro 4.
6 – Right-click button: the tip end of the raised area on the flat side of the pen works as a right-click button.
7 – Tip

Battery Status

Battery status appears on the right side of the taskbar.

Other tips

To change the screen brightness, swipe from the right edge of the screen to the left, then touch Settings, then hold your finger on the Screen icon and move it up or down. Touch an area outside the Settings menu to exit.

> *Other settings can also be viewed by swiping to the left.*

To switch between full screen and window mode, touch the bar labeled 'MESA Exam 6' at the top of the screen and drag it toward (full screen) or away from (windowed) the top.

The Exam 6 program is also accessible from the Start menu. Press the Windows button, then swipe your finger to the left until it is visible.

You can enter data using the stylus to select a response, or by writing the numbers and letters into the text box. You can also tap the box where you want to type data and use the keyboard to type your response.

Care and cleaning

To minimize wear and tear, fold the keyboard cover over the Surface screen when not in use.

To clean the screen, wipe it with a soft cloth (dampened slightly with water or eyeglass cleaner if desired). **Do not use any other cleaning products on the screen.** They keyboard can be cleaned with a cloth dampened in soapy water. Stains on the cover can be treated with small amounts of rubbing alcohol.

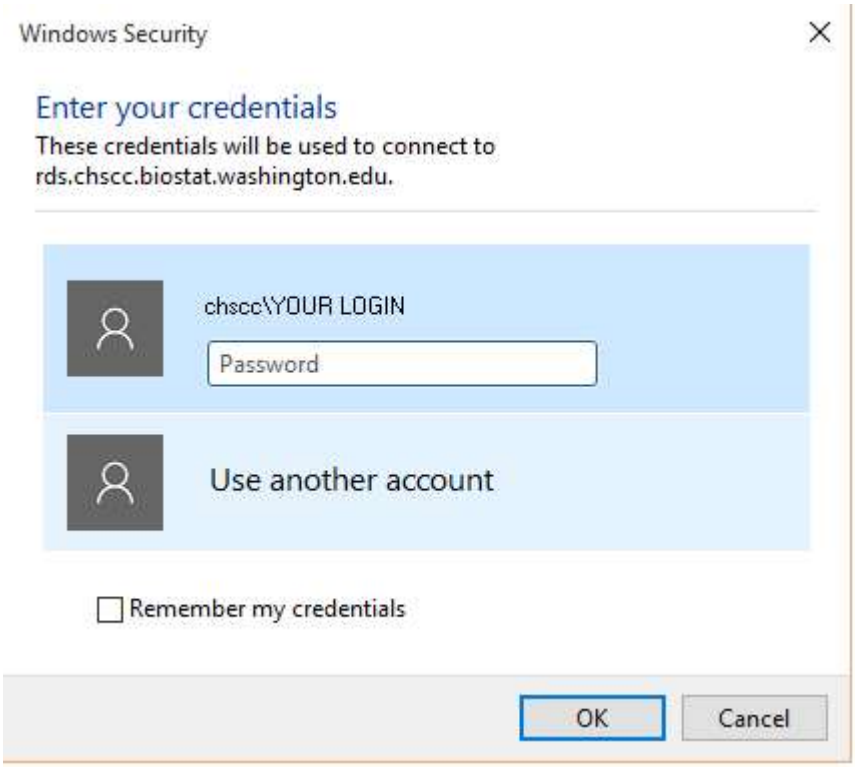
To sanitize the tablet, Microsoft makes the following suggestions:

> *"Healthcare customers can sanitize Microsoft Surface Pro 4 devices using one of our recommended solutions—PDI Sani-Cloth Plus, CaviWipes, Covidien Alcohol Prep Pads, any similar wipes with IPA (Isopropyl Alcohol) solution under 70%, Total Solutions Full Spectrum Disinfectant Wipes, or Clorox Healthcare Bleach Germicidal Wipes--without risk of damaging the device.*
>
> *The alcohol-based solutions can also be used to clean the entire Surface Type Cover 3 without damage. Total Solutions Wipes may leave cotton fibers on the bottom side of the Type Cover 3, but these can be removed by hand. Clorox Healthcare Bleach Germicidal Wipes may discolour the bottom surface of the Type Cover with prolonged use, and therefore are not recommended to sanitize the Type Cover .*
>
> *Users should not douse the items with solution, but rather use pre-moistened wipes or apply IPA to application cloth and use the cloth on the unit."*

6.2 MESA Exam 6 Software Instructions

Starting the software

The Exam 6 program is hosted on our RemoteApp server. To start the Exam 6 program, the user clicks the Remote Desktop Protocol (.RDP) file on the desktop and then enters login information.

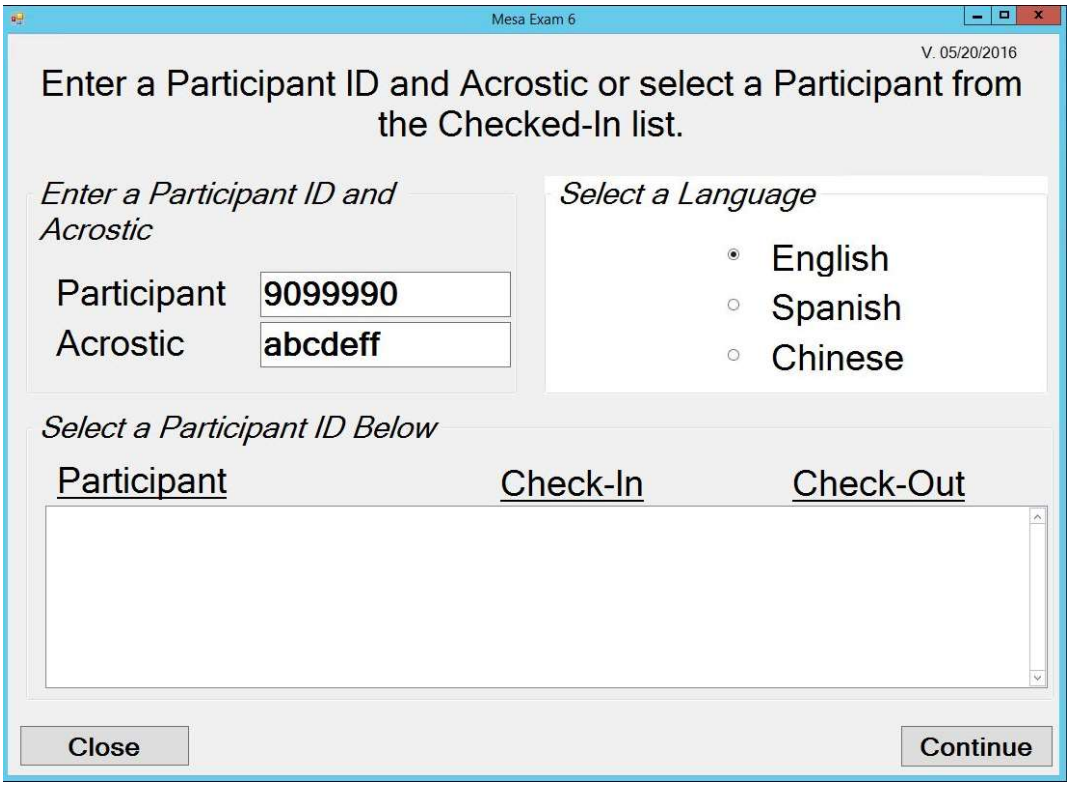


The main menu screen will display:

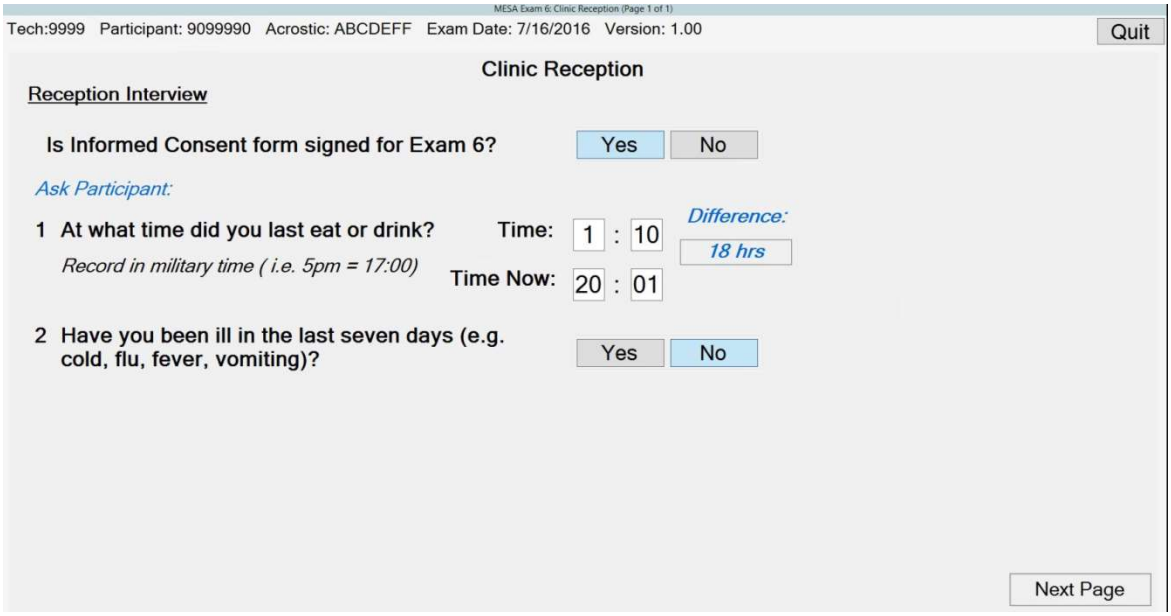
Enter your MESA Tech ID and password.

Entering data

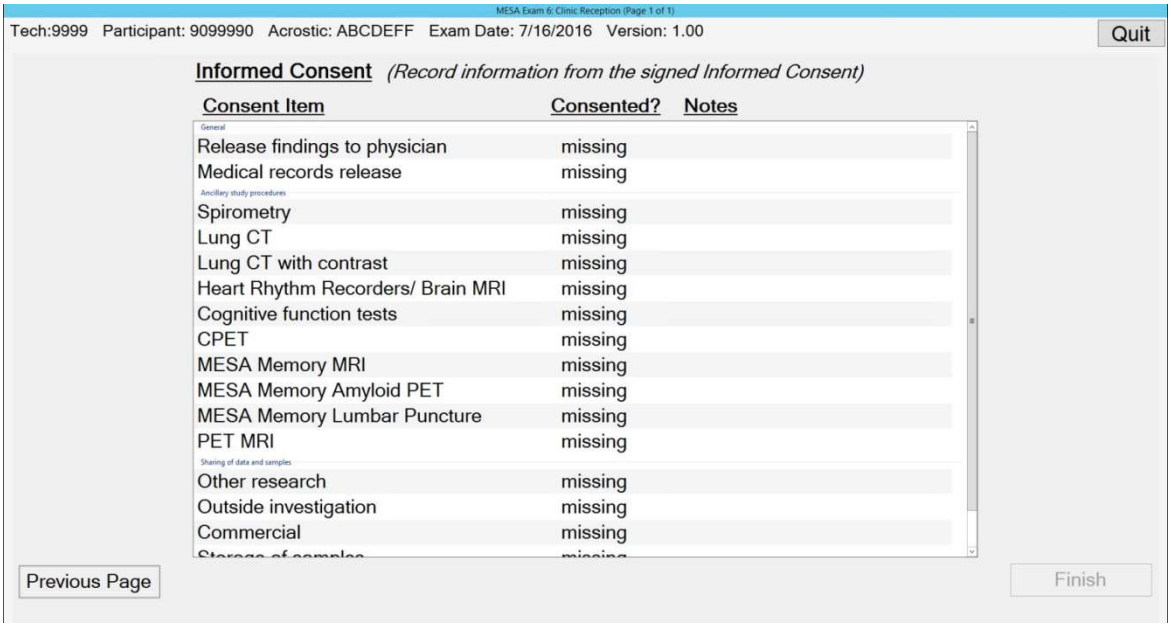
After logging into the program, enter the participant ID and acrostic for the scheduled participant. The language that the participant used at previous exams will be indicated in the "Select a Language" section. The language can be updated by selecting another language that the participant prefers to use. Then click "continue" to go to the Clinic Reception form.



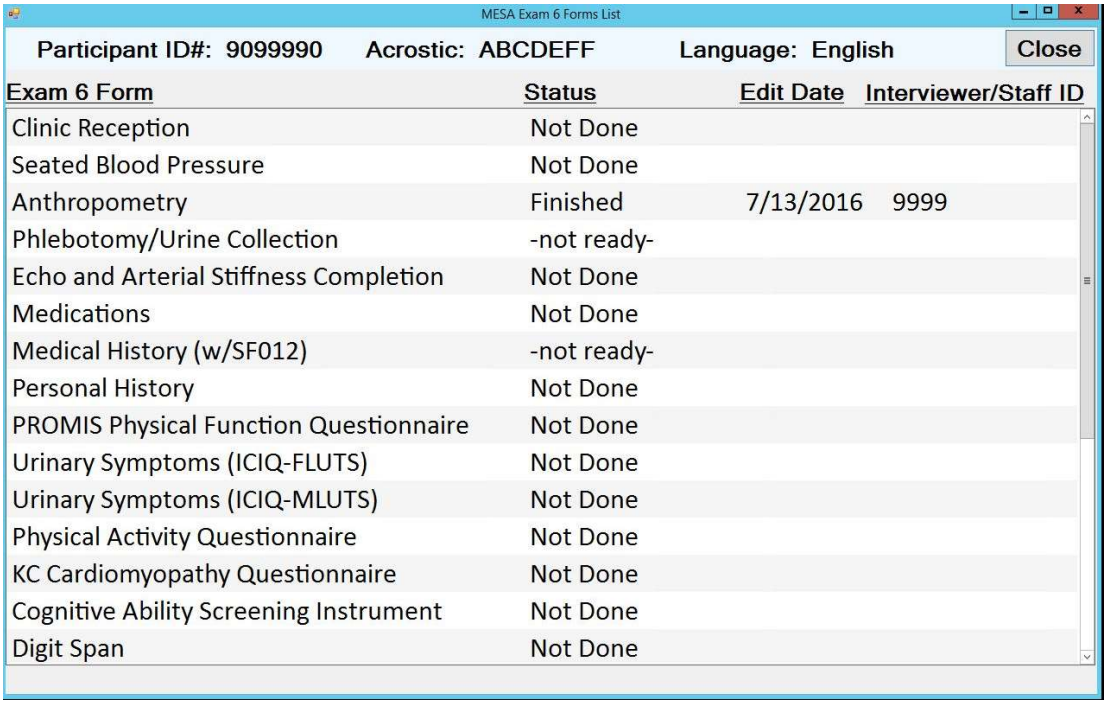
Before moving forward to the individual consent items for Exam 6, you must confirm that the Exam 6 consent form was signed, that the participant has not eaten or drank for more than 8 hours, and that the participant has not been sick in the past 7 days. If these criteria are met, click "Next page,"



Consent status must be entered for each Exam 6 procedure for which the participant is selected.



After consent status for each procedure is entered, a forms list will be generated for the participant. Click on the name of each form to enter data. After completing a form, the status in the Forms List screen will be updated form “Not Done” to “Finished.”

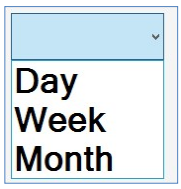


Filling out forms

- Questions are organized on multiple pages.
- Select 'Next Page' to continue the form, or 'Previous page' to go back.
- Select 'Quit' to save your responses and return to the menu.
- When you reach the end of a form, click '**Finish**' to return to the forms list

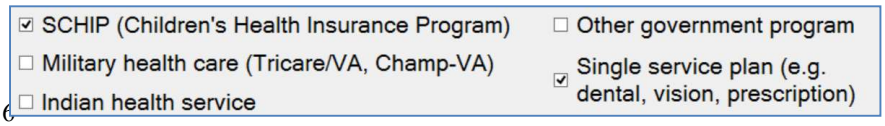
Question Types

Dropdown: Touch to select a response from the list.



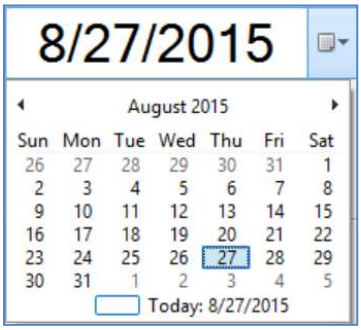
Yes/No: Select either 'Yes' or 'No'. 

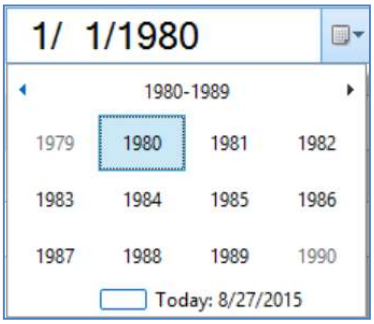
Checkbox: Touch a box to select it.



Text box: Touch the box, then enter data using the keyboard. The system will prompt you if an entry does not fit within an expected range.

Calendars: Touch the relevant date. To zoom out and pick an earlier/later date, touch the month/year at the top of the calendar. Touch a date range to zoom back in, then use the arrows on the left and right of the calendar to fine-tune.





Scales: Touch one option within the given range.

Troubleshooting Connectivity Issues

Upload issues are likely indicative of a weak or spotty connection to the internet. The tablet may be able to connect sometimes, but drops the signal, or the signal isn't strong enough to upload the data.

Check the strength of your connection by opening the Networks menu (see instructions on page 1). It will show you if the tablet is connected to a network, what the name of the network is, and how strong the signal is. The network strength is indicated by how many of the five bars in the network symbol are shaded. If only a couple bars in the symbol are shaded, the signal may be weak. You can also get an idea of the strength of your signal by opening a web browser and checking how slow or fast webpages load.

If the signal is weak, you can try connecting to another network. You can also try moving around--there might be areas in the center where the signal is much stronger.

Software Updates

The CC will periodically release software updates. These will push automatically to the tablet, and are detected when the software launches and establishes a connection with the remote database. For this reason, it is important that you do not keep the software continually running in the background. *Please*

make a habit of exiting the program' after data entry is complete, and re-launching the program when you are ready to use it again.

If an update is available, the program will open and display a pop-up message that prompts you to click 'OK'. The program will then close. When you re-launch the program, the new version will be installed. The version number is displayed in the upper left side of the main menu.

Data Upload

Data is automatically saved as the user moves from page to page, or form to form.

7 EVENTS SURVEILANCE

7.1 Purpose

MESA's official, scheduled "Follow-up Phone Calls" serve several purposes:

- To update participants' tracking data, including their address, phone number, and contact information
- To update participants' vital status
- To obtain information regarding participants' general health and health care treatment.
- To obtain detailed information about specific medical conditions diagnosed by a physician that the participants report have had since their last MESA Follow-up phone interview
- To obtain detailed information about any procedures or hospitalizations participants have had since their last MESA Follow-up phone interview
- To schedule the participant for an upcoming Exam Clinic Visit appointment, when necessary, including MESA CT/MRI appointments, when necessary.

7.2 Follow-up Call

The "Follow-up Call" is a telephone interview conducted with each participant. Calls are scheduled every twelve months. The eighteenth follow-up call should be linked to Exam 6, and is designed to allow for the scheduling of the exam during this call.

If the Exam staff needs to contact a participant (e.g., to schedule an Exam Visit after the Follow-up Call did not succeed in scheduling the Exam Visit), the Exam staff should be aware of the participant's usual schedule of official Follow-up Calls. Unscheduled contact is not the same as a scheduled Follow-up Call used to collect data. If, during an unscheduled contact, the participant tells the Exam staff member about a condition, procedure, or hospital stay, the staff member should alert the Events Coordinator so that full information about the potential event can be collected.

7.3 Continuing Participant Surveillance

If, during an Exam visit, a participant tells the Exam staff member about a condition, procedure, or hospital stay, the staff member should alert the Events Coordinator so that full information about the potential event can be collected.

At the end of the Exam, each participant is asked to notify the clinic should any changes occur in his/her health, especially involving a hospitalization, nursing home admission, or diagnosis of myocardial infarction (heart attack), angina (chest pain), heart failure (CHF), peripheral vascular disease (PVD), stroke, or transient ischemic attack (TIA).

Clinic staff should inform the participant s/he will be later be contacted for his/her scheduled Follow-up Call, which may include the scheduling of the next Exam Visit.

Let the participant know that we are attempting to keep the record as updated as possible to learn all that we can.

All Follow-up forms are interviewer-administered to MESA participants over the telephone. If the participant prefers to relay this information in person or, for some reason, is unable to complete the interview by phone, a home or clinic visit may be scheduled.

7.4 Use of Proxy

If a participant is not able to do the interview (e.g., due to a medical problem), a proxy may be used. A "proxy" is a relative or other knowledgeable contact. If the participant has died, the proxy may complete the questionnaire for the period between the last Follow-up Call and the date of death.

The proxy may or may not be someone previously designated as a contact by the participant. For example, the participant may have designated his/her spouse as a primary contact, but the participant's son or daughter actually ends up being the person to complete the questionnaire. This is fine, as long as the new person is knowledgeable regarding the participant's medical condition, procedures of interest, etc.

7.5 Administering and Processing Follow-up Forms

Please refer to the Events Manual of Operation for detailed information regarding the administration and processing of follow-up forms

8 CERTIFICATION

8.1 Summary of Certification Requirements

Exam 6 Certification Requirements for new and returning technicians are outlined in the following table.

In addition to the detailed requirements listed in the table by examination component, the following certification requirements apply to all components:

- Trainees must thoroughly read the relevant section in the MOP.
- Appropriate supporting documents (e.g. checklists and tests) must be completed when required.
- All certification documentation should be sent to the CC and to designated RCs when specified.
- A copy of the supporting certification documents should be retained at the FC for local records in a designated binder.

	Exam Component	Requirements	Certification Details
1.	**Interviewer-Administered Questionnaires** (Medical History, Medications, KCCQ-12)	1. Read the interviewing protocol in the Exam 6 MOP (Section 3.4) 2. Practice the questionnaire at least 5 times or as much as possible. 3. Conduct and audiotape 3 sets of interviews with 3 different volunteers. 4. Send all 3* sets of completed forms and tapes to the study certifier for review. *Exam 5 certified interviewers submit 1 set of interviews.	Certified Field Center staff may train additional staff. Certification performed by Coordinating Center

	Exam Component	Requirements	Certification Details
2.	Anthropometry	1. Read Section in the Exam 6 MOP and practice the procedure according to the MOP on volunteers as many times as necessary depending on previous experience. 2. Practice the procedures on at least 5 volunteers. 3. For Certification, obtain height, weight, hip and waist, and bioelectric impedance measurements on 5* volunteers in accordance with the MESA Anthropometry Certification / Supervisor Checklist. The readings must not differ from the trainer's by more than the following: ± 1 cm for height, ± 0.5 pounds for weight (balance beam), and ± 1 cm for hip and waist girth. 4. Send Anthropometry checklists, completed by the trainer technician, to the CC. Include the test ID used to enter data in the Exam 6 software. *Exam 5 certified techs submit data for 2 volunteer.	Certified Field Center staff may train and certify additional staff.
3.	**Seated Blood Pressure**	1. Read the blood pressure protocol in the Exam 6 MOP. 2. Practice the procedure according to the MOP as many times as necessary depending on previous experience. 3. Perform 5* blood pressure measurements in accordance with certification checklist under supervision of the lead staff person in the clinic. 5. Send Seated Blood Pressure checklists, completed by the trainer technician, to the CC. Include the test ID used to enter data in the Exam 6 software. *Exam 5 certified techs submit data for 2 volunteer.	Certified Field Center staff may train and certify additional staff.

	Exam Component	Requirements	Certification Details
4.	**Oximetry**	1. Read and understand the Oximetry Protocol in the Exam 6 MOP. 2. Practice the procedure on at least 5 volunteers or as often as needed to become comfortable with the procedure. 3. Perform 5 oximetry measurements in accordance with certification checklist. 4. Send checklists, completed by the trainer technician, to the CC. Include the test ID used to enter data in the Exam 6 software. *Exam 5 certified techs submit data for 2 volunteer.	Certified Field Center staff may train and certify additional staff.
5.	**Phlebotomy**	1. Read MESA's Laboratory MOP and section of the Exam 6 MOP. 2. Observe the process performed by a certified technician. 3. Successfully perform 1 phlebotomy on a volunteer as described in the protocol and in accordance with certification checklist under supervision of the lead person in the clinic. 4. Pass written examination prepared by CBAL. 5. Send exams and checklists to CBAL and CC.	Certified Field Center staff may train additional staff. Certification performed by Central Lab
6.	**Blood Processing**	1. Read MESA's Laboratory MOP and section of the Exam 6 MOP. 2. Observe the process performed by a certified technician. 3. Successfully process blood samples from 1 volunteer as described in the protocol and in accordance with the certification checklist under supervision of the lead person. 4. Pass written examination prepared by LCBR. 5. Send exams and checklists to LCBR and CC.	Certified Field Center staff may train additional staff. Certification performed by Central Lab

	Exam Component	Requirements	Certification Details
7.	**Cognitive Function**	1. Read and understand the Cognitive Function protocol in the Exam 6 MOP. 2. Practice each of the three cognitive assessment components (CASI, DSST, and Digit Span) on at least 5 volunteers with script, with lead tech performing supervision checklist. 3. Perform and audio tape 1 cognitive battery (CASI, DSST, and Digit Span) if did not attend central training session. 4. Send completed forms (and tape if applicable) to the Coordinating Center along with the completed supervisor checklists.	Certified Field Center staff may train additional staff. Certification performed by Coordinating Center
8.	**Heart Monitor Patch**	1. Read the Heart Monitor Patch Application section of the Exam 6 MOP. 2. Participate in the webinar with the iRhythm representative, or go over the slide set from that webinar with the lead person in the clinic. 3. Observe the process performed by a certified technician. 4. Successfully perform 1 patch application on a volunteer as described in the protocol. If this was not done at central training, application must be videotaped and final applied patch photographed and these should be transmitted to the CC. 5. Successfully perform patch application procedures as described in the protocol and in accordance with certification checklist under supervision of the lead person in the clinic. 6. Send checklist to CC.	Certified Field Center staff may train and certify additional staff.

	Exam Component	Requirements	Certification Details
9.	**Arterial Stiffness**	1. Participate in central training 2. Read and review the Arterial Pulse Wave Manual of Operations, and contact the NUECL with any questions before performing the certification arterial stiffness recording 3. Perform the certification recording on a non-study participant, making sure to include all required information 4. Copy the study directly from VaSera device to the Northwestern Box MESA Exam 6 folder (each site will receive a site-specific link). 5. Wait for confirmation of certification from the NUECL before submitting any arterial stiffness recordings performed on study participants	For questions, contact Lauren Nelson: lauren.nelson@ Northwestern.edu
10.	**Echocardiography**	1. Participate in central echocardiography training 2. Read and review the Echo Manual of Operations, and contact the NUECL with any questions before performing the certification echo 3. Perform the certification echo on a non-study patient, making sure to include all required protocol views 4. Copy the study directly from the echo machine to CD in modified DICOM format, then use WebPAX to transmit to the NUECL 5. Wait for confirmation of certification from the NUECL before submitting any echocardiograms performed on study patients.	For questions, contact Lauren Nelson: lauren.nelson@ Northwestern.edu
11.	**Six Minute Walk Test**	1. Review Six Minute Walk Central Training slides (available on the MESA Website). 2. Set up the 6MW course using tape and cones. 3. Explain the procedure to the participant 4. Use stop watch and lap counter to count the laps and record the data in the 6MW completion form. 5. Send completed paper 6MW Completion form and Certification Check list to Lenore Crago at lcrago@wakehealth.edu.	For questions, contact Lenore Crago: lcrago@wakehealth.edu.

	Exam Component	Requirements	Certification Details
13.	**Spirometry**	1. Read and understand the Spirometry Protocol in the Spirometry MOP. 2. Practice the procedure (including albuterol inhalation) on at least 5 volunteers or as often as needed to become comfortable with the procedure. 3. Review web training. 4. Complete on-line test 5. Perform and transmit 10 good quality tests (as determined by Spirometry RC staff. If any are of poor quality, additional practice and transmission of 5 additional tests will be required. Note: techs that have performed MESA-related spirometry in the past 6 months may skip steps 3 and 4.	For questions, contact Graham Barr at rgb9@ cumc.columbia.edu
14.	**Brain MRI**	1. Read and understand the MRI protocol in the MRI MOP. 2. Perform 5 scans of excellent (E) quality (as determined by MRI RC staff following the certification checklist. (transmission required). 3. For non-centrally trained technicians, send checklists to MRI RC.	
15.	**Lung CT**	1. Read and understand the CT protocol in the CT MOP 2. Perform and transmit 5 scans of excellent (E) quality (as determined by CT RC staff or by the local physician investigator responsible for CT performance at their FC) following the protocols as described in the CT MOPs.	

8.2 Summary of Requirements for Maintaining Certification

	Exam Component	Requirements
1.	**Interviewer-Administered Questionnaires**	1. Administer questionnaires to at least 6 MESA participants every 2 months. 2. Be observed and evaluated by FC supervisor according to the supervisor checklist monthly quarterly. 3. Audiotape all sessions. Study coordinator (or FC interviewer supervisor) reviews 1 randomly selected taped session monthly. 4. Repeat certification process prior to each new examination cycle.
2.	**Anthropometry**	1. Perform all anthropometric measurements on at least 6 MESA participants every 2 months. 2. Be observed and evaluated by FC supervisor according to the supervisor checklist monthly for the first 2 months, then quarterly. 3. Repeat certification process prior to each new examination cycle.
3.	**Seated Blood Pressure**	1. Perform seated blood pressure measurements on at least 6 MESA participants every 2 months. 2. Be observed and evaluated by FC supervisor according to the supervisor checklist monthly for the first 2 months, then quarterly. 3. Repeat certification process prior to each new examination cycle.
4.	**Phlebotomy**	1. Perform Phlebotomy procedure on at least 6 MESA participants every 2 months. 2. Be observed and evaluated by FC supervisor according to the supervisor checklist monthly for the first 2 months, then quarterly. 3. Repeat certification process prior to each new examination cycle.
5.	**Blood Processing**	1. Perform Blood Processing on at least 6 MESA participants every 2 months. 2. Be observed and evaluated by FC supervisor according to the supervisor checklist monthly for the first 2 months, then quarterly. 3. Repeat certification process prior to each new examination cycle.
6.	**Cognitive Assessment**	1. Administer questionnaires to at least 6 MESA participants every 2 months. 2. Be observed and evaluated by FC supervisor according to the supervisor checklist monthly quarterly. 3. Audiotape all sessions. Study coordinator (or FC interviewer supervisor) reviews 1 randomly selected taped session monthly. 4. Repeat certification process prior to each new examination cycle.

	Exam Component	Requirements
7.	**MRI**	1. Perform MRI procedures of acceptable quality on at least 6 MESA participants every 2 months. 2. Be observed and evaluated by the physician/ investigator responsible for MRI acquisitions at the FC according to the supervisor checklist quarterly. 3. Repeat certification process as needed if data quality is not acceptable based on MRI RC review.
11.	**CT**	1. Perform CT procedures of acceptable quality on at least 6 MESA participants every 2 months. 2. Be observed and evaluated by the physician/ investigator responsible for CT acquisitions at the FC according to the supervisor checklist quarterly. 3. Repeat certification process as needed if data quality is not acceptable based on CT RC review.
16.	**Spirometry**	1. Perform Spirometry tests of acceptable quality on at least 6 MESA participants every 2 months. 2. Be observed and evaluated by the Spirometry Supervisor according to the supervisor checklist quarterly 3. Repeat certification process as needed if data quality is not acceptable based on Spirometry RC review.
17.	**Oximetry**	1. Perform oximetry measurements on at least 6 MESA participants every 2 months. 2. Be observed and evaluated by FC supervisor according to the supervisor checklist monthly for the first 2 months, then quarterly. 3. Repeat certification process prior to each new examination cycle.

- All certification documentation should be sent to the CC and to designated RCs when specified.
- A copy of the supporting certification documents should be retained at the FC for local records in a designated binder.

8.3 Certification/QC Checklists

MESA Oximetry Certification / Supervisor / Site Visit Checklist

DATE: ☐ ☐ ☐ (mo day year) **Field Center:** _____

Technician name/ID: _____

Supervisor: _____

Purpose of Evaluation:

Certification ☐ **Supervisor QC Check** ☐ **Site Visit** ☐

Please check the appropriate box if technician performance is satisfactory for each line item. Please note any comments or remedial action taken in 'Comments' section if performance was not satisfactory.

Steps in Exam:

1. ☐ ☐ Places probe correctly.
2. ☐ ☐ Confirms good signal (pulse) is obtained
3. ☐ ☐ Observes for one minute
4. ☐ ☐ Accurately estimates apparent median value (+/- 1%)
5. ☐ ☐ Records value on form or computer screen

Comments/Corrective Actions: _____

_____

_____

Supervisor /Site Visitor Signature _____

FOR QC ACTIVITY, MAKE SURE TO COMPLETE THE WEB-BASED QC PROCEDURES/ACTIVITIES FORM

MESA Interviewer-Administered Questionnaire Supervisor Checklist

DATE: ☐ ☐ ☐ (mo day year) **Field Center:** _____

Interviewer: Name/ID _____

Interview/form reviewed: **Supervisor:** _____

Medical History ☐ **KCCQ-12** ☐ **Medications** ☐ ☐ ☐

Purpose of Evaluation:

Certification ☐ **Supervisor QC Check** ☐ **Site Visit** ☐

Using the scale key below, evaluate the interviewer's performance based on each of the following criteria. Write any comments in the space provided at the bottom of the page. If rating is below 3 OR above 3, please explain in comment area. (Refer to appendix #.)

Answers respondent's questions and concerns.	*N/A*	*1*	*2*	*3*	*4*	*5*
Speaks slowly and distinctly reading the questions at neutral (but expressive) and even pace	*N/A*	*1*	*2*	*3*	*4*	*5*
Maintains the focus of the interview but allows participant to express thoughts.	*N/A*	*1*	*2*	*3*	*4*	*5*
Follows instructions/reads questions as written.	*N/A*	*1*	*2*	*3*	*4*	*5*
Initiates (where needed) appropriate, nonleading questions	*N/A*	*1*	*2*	*3*	*4*	*5*
Records/codes answers correctly (follows skip patterns as needed).	*N/A*	*1*	*2*	*3*	*4*	*5*
General Overall Rating	*N/A*	*1*	*2*	*3*	*4*	*5*

Key: *N/A – Not applicable*
1 – Unsatisfactory (failed to meet standards)
2 – Below expectation (did not meet some standards)
3 – At expectations (met standards)
4 – Above expectation (met all standards and in some cases exceeded them
5 – Outstanding (distinguished consistently exceeded all standards)

Comments: _____

_____

_____

_____

Corrective Action Taken: _____

_____

_____

_____

Supervisor Signature _____

WHEN CERTIFYING NEW INTERVIEWER - SEND COPY TO CC
FOR QC, COMPLETE THE WEB-BASED FORM ONLY!!!

MESA Anthropometry Certification / Supervisor / Site Visit Checklist

DATE: ☐ ☐ ☐ **Field Center:**
mo day year

Technician: Name/ID

Supervisor:

Purpose of Evaluation:

Certification ☐ **Supervisor QC Check** ☐ **Site Visit** ☐

Please check the appropriate box if technician performance is satisfactory for each line item. Please note any comments or remedial action taken in 'Comments' section if performance was not satisfactory.

	S	U	
1.	☐	☐	Thoroughly explains the procedure to the participant.
2.	☐	☐	Insures the participant is wearing light gowns or scrubs.
3.	☐	☐	Gives instruction for the proper position to measure height.
4.	☐	☐	Reads and records the height measurement to the nearest 0.1 cm.
5.	☐	☐	Gives instruction to measure the weight.
6.	☐	☐	Reads and records the weight measurement to the nearest 0.5 lb.
7.	☐	☐	Locates the exact marking for the waist measurement.
8.	☐	☐	Reads and records the waist measurement to the nearest 0.1 cm.
9.	☐	☐	Locates the exact marking for the hip measurement.
10.	☐	☐	Reads and records the hip measurement to the nearest 0.1 cm.
11.	☐	☐	Gives instructions to stand on body comp scale and grip handles.
12.	☐	☐	Correctly enters participant height, gender, and age into scale.
13.	☐	☐	Prints report from body comp scale (BCS).
14.	☐	☐	Records values from printed BCS report.

Comments: _____

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Corrective Action Taken: _____

_____

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_____

Supervisor / Site Visitor Signature _____

WHEN CERTIFYING NEW TECHNICIAN - SEND COPY TO CC

FOR QC, COMPLETE THE WEB-BASED FORM ONLY!!!

MESA Seated Blood Pressure Certification / Supervisor / Site Visit Checklist

DATE: ☐ ☐ ☐ (mo day year) **Field Center:** _____

Technician name/ID: _____

Supervisor: _____

Purpose of Evaluation:

Certification ☐ **Supervisor QC Check** ☐ **Site Visit** ☐

Please check the appropriate box if technician performance is satisfactory for each line item. Please note any comments or remedial action taken in 'Comments' section if performance was not satisfactory.

Throughout Exam:

	S	U	
1.	☐	☐	Keeps participant warm, relaxed, and comfortable.
2.	☐	☐	Discourages participant from talking, except to voice discomfort or confusion about instructions.

Steps in Exam:

3.	☐	☐	Greets the subject and communicates appropriately with participant regarding purpose, time requirement, and process of blood pressure measurement.
4.	☐	☐	Seats participant in proper position.
5.	☐	☐	Insures that participant was not chewing gum.
6.	☐	☐	Places right arm on table in proper position.
7.	☐	☐	Bares participant arm to above point of shoulder.
8.	☐	☐	Measures and records arm circumference according to protocol.
9.	☐	☐	Selects proper size cuff using table in protocol.
10.	☐	☐	Palpates brachial artery.
11.	☐	☐	Places cuff directly on skin (no sleeve or rolled-up), with center of bladder over brachial art.
12.	☐	☐	Places cuff at level of participant's heart.
13.	☐	☐	Asks if participant was relaxed and helped subject to relax if needed.
14.	☐	☐	Instructs participant on posture.
15.	☐	☐	Times 5 minutes of relaxed sitting.
16.	☐	☐	Obtains 3 blood pressure measures with 1-minute intervals between end and restart.
17.	☐	☐	Records all three blood pressures correctly.
18.	☐	☐	Correctly identifies and records blood pressure for participant.
19.	☐	☐	Communicates appropriately with participant regarding an alert level blood pressure.
20.	☐	☐	Communicates appropriately with participant regarding a normal blood pressure.
21.	☐	☐	Communicates appropriately with participant regarding completion of blood pressure procedure.

Comments/Corrective Actions: _____

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_____

Supervisor /Site Visitor Signature _____

MESA Classic Exam 6 Phlebotomy - Supervisor Checklist

DATE: ☐☐ Mo ☐☐ Day ☐☐ Year

Field Center: _____

Technician Name/ID: _____

Supervisor: _____

Please check the appropriate box if technician performance is satisfactory for each line item. Please note any comments or remedial action taken in 'Comments' section if performance was not satisfactory.

Preparation:

1. ☐ Phlebotomy area properly prepared and stocked with supplies (tube rocker, ice bucket, extra draw tubes & labels, etc.).
2. ☐ Checked Phlebotomy Form is labeled with the participant's assigned MESA ID, and if applicable lists ancillary study draw tubes based on participant's eligibility and consent.
3. ☐ Checked draw tubes labeled with correct MESA ID, and in correct order for the blood draw.
4. ☐ Questions on Phlebotomy Form asked and answers recorded.

Venipuncture:

5. ☐ Personal protective equipment in use (non-permeable lab coat, gloves, eye/face protection).
6. ☐ Correct preparation of venipuncture site
7. ☐ Applied tourniquet and immediately started timer.
8. ☐ Venipuncture smoothly executed.
9. ☐ Tubes filled in correct draw tube priority order.
10. ☐ Any replacement tubes correctly labeled.
11. ☐ Tourniquet released within 2 minutes (tourniquet may be reapplied if necessary).
12. ☐ Proper appropriate care of venipuncture site after needle is removed.
13. ☐ Needle & tubing disposed of appropriately.

Handling of filled draw tubes:

14. ☐ Correct mixing and handling of filled draw tubes as specified in the study protocols.
15. ☐ Filled tubes placed in the correct racks – on ice or at room temperature – ASAP per protocol.
16. ☐ MESA Classic EDTA or Serum tubes < ½ full discarded.

P/P Form:

17. ☐ Venipuncture start and end times legibly recorded on the Phlebotomy form.
18. ☐ Elapsed tourniquet time(s) recorded (if reapplied, additional elapsed tourniquet times noted).
19. ☐ All sections on Phlebotomy Form completely filled out.
20. ☐ Comments pertaining to the phlebotomy or urine collection noted in the Comments section.

Urine:

21. ☐ Check urine collection container is labeled with correct MESA ID and urine section on Phlebotomy Form completed.

Comments: _____

_____

_____

Supervisor Signature _____

MESA Cognitive Assessment Supervisor Checklist

DATE: ☐☐ mo ☐☐ day ☐☐ year **Field Center:** _____

Interviewer: Name/ID _____

Interview/form reviewed: **Supervisor:** _____

CASI ☐ **Digit Span** ☐ **Digit Symbol** ☐ ☐ ☐ ☐

Purpose of Evaluation:

Certification ☐ **Supervisor QC Check** ☐ **Site Visit** ☐

Using the scale key below, evaluate the interviewer's performance based on each of the following criteria. Write any comments in the space provided at the bottom of the page. If rating is below 3 OR above 3, please explain in comment area. (Refer to appendix #.)

Answers respondent's questions and concerns.	*N/A*	*1*	*2*	*3*	*4*	*5*
Speaks slowly and distinctly reading the questions at neutral (but expressive) and even pace	*N/A*	*1*	*2*	*3*	*4*	*5*
Maintains the focus of the interview.	*N/A*	*1*	*2*	*3*	*4*	*5*
Follows instructions/reads questions as written.	*N/A*	*1*	*2*	*3*	*4*	*5*
Initiates appropriate, nonleading questions only where permitted	*N/A*	*1*	*2*	*3*	*4*	*5*
Records/codes answers correctly.	*N/A*	*1*	*2*	*3*	*4*	*5*
Completes the scoring process where appropriate.	*N/A*	*1*	*2*	*3*	*4*	*5*
General Overall Rating	*N/A*	*1*	*2*	*3*	*4*	*5*

Key: *N/A – Not applicable*
1 – Unsatisfactory (failed to meet standards)
2 – Below expectation (did not meet some standards)
3 – At expectations (met standards)
4 – Above expectation (met all standards and in some cases exceeded them
5 – Outstanding (distinguished consistently exceeded all standards)

Comments: _____

_____

_____

_____

Corrective Action Taken: _____

_____

_____

Supervisor Signature _____

WHEN CERTIFYING NEW INTERVIEWER - SEND COPY TO CC
FOR QC, COMPLETE THE WEB-BASED FORM ONLY!!!

Field Center MRI Technologist Training Checklist

DATE: ☐ ☐ ☐ **mo** **day** **year**

Field Center:

Technologist: Name/ID

FC MR Physician or Principal Investigator:

A check indicates yes to the questions below:

1. The technologist meets the requirements as specified in the FC MOP: ☐
   Completion of a two-year AMA approved program and two to three years MRI experience
2. Reviewed the overall MESA Protocol and Study Design: ☐
3. Reviewed the MESA MRI protocol Lecture: ☐
4. Presented the Cardiac Anatomy Lecture: ☐
5. Presented the Cardiac Gating Lecture: ☐
6. Presented the Physics Lecture: ☐
7. Reviewed the FC MOP: ☐
8. Reviewed the procedure for Alerts: ☐
9. The technologist completed the written examination under direct supervision: ☐
10. The technologist completed an examination under my direction and demonstrated all items listed on the MESA MRI Certification/ Supervisor Checklist: ☐

FC MR Physician or Principal Investigator Signature:

SEND COPY TO MRC (WHEN NEW TECHNOLOGIST IS CERTIFIED)

MESA CT Certification / Supervisor / Site Visit Checklist

DATE: ☐ ☐ ☐ (mo day year) **Field Center:** _____

Technician Name/ID: _____

Supervisor: _____

Purpose of Evaluation:

Certification ☐ **Supervisor QC Check** ☐ **Site Visit** ☐

Please check the appropriate box if technician performance is satisfactory for each line item. Please note any comments or remedial action taken in 'Comments' section if performance was not satisfactory.

During examination:

1. ☐ Greets participant professionally.
2. ☐ Places calibration pad phantom correctly.
3. ☐ Teaches participant breath-holding technique (at end-inspiration).
4. ☐ Checks that participant is centered prior to the scan.
5. ☐ Selects correct field of view (35 cm) including the phantom.
6. ☐ Selects appropriate ECG triggering (80% per protocol).
7. ☐ Scans entire heart (at least 35 slices per scan, preferably 40).
8. ☐ Instructs participant to relax between scans.
9. ☐ Assesses the adequacy of positioning, ECG gating, and lack of respiratory motion.

Data transmission and quality control:

11. ☐ Transmits images successfully via Internet.
12. ☐ Uses proper MESA ID labeling on study form.
13. ☐ Demonstrates understanding of QA procedure and frequency of CT calibration using the Calibration and Torso phantoms.
14 ☐ Documents any problems (if they occurred) in obtaining either scan.

Comments: _____

_____

Corrective Action Taken: _____

_____

_____

Supervisor / Site Visitor Signature _____

COMPLETE THE WEB-BASED QC ACTIVITIES/PROCEDURES FORM

MESA Heart Patch Certification/Supervisor/Site Visit Checklist

DATE: ☐ ☐ ☐ (mo day year) Field Center: ☐

Technician name/ID ☐

Supervisor ☐

Purpose of Evaluation:
Certification ☐ Supervisor QC Check ☐ Site Visit ☐

Please check the appropriate box if the technician performance is satisfactory (S) for each line item. Please note any comments or remedial action taken in Comments section if performance was not satisfactory (U).

Throughout Exam:

	S	U	
1.	☐	☐	Keeps participant warm, relaxed, comfortable
2.	☐	☐	Answers participants questions and concerns.

Steps in Exam:

	S	U	
3.	☐	☐	Successfully registers patch #1 online at www.zioreports.com
4.	☐	☐	Prepares booklet and sleep/wake log for patch #1.
	☐	☐	Determines appropriate placement for patch #1
	☐	☐	Appropriately and thoroughly preps (shave/abrade/alcohol wipe) skin for patch #1
	☐	☐	Apply Zio patch to correct location, pressing for two minutes
	☐	☐	Remove two top labels, pressing for an additional two minutes
	☐	☐	Turns on device
	☐	☐	Explain and describe the device and procedures as described in the MOP (4.7.8)
	☐	☐	Show Sleep/Wake log, answer questions
	☐	☐	Demonstrate with demo patch removal of patch
	☐	☐	Discuss patch #2, timing, show participant kit
	☐	☐	Complete Atrial Fibrillation Study Completion form, patch #1
	☐	☐	Demonstrates timing and completion of reminder calls at 2/3 and 14 days
	☐	☐	Complete Atrial Fibrillation Study Completion form, reminder calls for patch 1
	☐	☐	Prepares patch #2 for mailing, including online registration of second patch
	☐	☐	Demonstrates timing and completion of reminder calls at 2/3 and 14 days
	☐	☐	Complete Atrial Fibrillation Study Completion form, reminder calls for patch 2

Comments/Corrective Actions: _____

_____

Supervisor/Site Visitor Signature_____

MESA Spirometry Certification / Supervisor / Site Visit Checklist

DATE: ☐ ☐ ☐ (mo day year) **Field Center:** ☐

Technician name/ID: ☐

Supervisor: ☐

Purpose of Evaluation:

Certification ☐ **Supervisor QC Check** ☐ **Site Visit** ☐

Please check the appropriate box if technician performance is satisfactory for each line item. Please note any comments or remedial action taken in 'Comments' section if performance was not satisfactory.

Steps in Exam:

1. ☐ ☐ Greets the subject and communicates appropriately with participant regarding purpose, time requirement, and process of spirometry measurement.
2. ☐ ☐ Completes questions 1-4 on the Spirometry Completion Form before starting the procedure.
3. ☐ ☐ Insures that participant is wearing loose clothing, has removed objects from the mouth including unsecured dentures, and has used the restroom prior to spirometry exam.
4. ☐ ☐ Opens spirometry software and locates the correct participant
5. ☐ ☐ Follows scripted instructions
6. ☐ ☐ Asks participant to sit straight up with head up during the examination (standing is OK if more comfortable for the participant).
7. ☐ ☐ Places nose clips on the nose
8. ☐ ☐ With a new mouth piece, has the participant do a trial exhalation and appropriately corrects any problems.
9. ☐ ☐ Attaches mouthpiece to spirometry hose/machine and conducts the examination
10. ☐ ☐ Demonstrates and properly coaches the participant during the procedure
11. ☐ ☐ Coaches participant until both "6 second" and "Plateau Achieved" messages are displayed
12. ☐ ☐ Appropriately uses curves on the screen to coach and provide feedback
13. ☐ ☐ Indicates testing position and impression of test quality.
14. ☐ ☐ Only rejects curves that are completely unusable and achieves three acceptable maneuvers from participant (in 8 attempts or fewer).
15. ☐ ☐ Monitors participant for headache, dizziness, lightheadedness, fainting, shortness of breath, or significant cough.
16. ☐ ☐ Correctly administers albuterol where appropriate.
17. ☐ ☐ Records appropriate comments.
18. ☐ ☐ Prints a hard copy of the spirometry report
19. ☐ ☐ Transmits data to Spirometry Reading Center

Comments/Corrective Actions: _____

_____

_____

Supervisor /Site Visitor Signature _____

FOR QC ACTIVITY, MAKE SURE TO COMPLETE THE WEB-BASED QC PROCEDURES/ACTIVITIES FORM

MESA 6 Minute Walk Certification / Supervisor / Site Visit Checklist

DATE: ☐ ☐ ☐ **Field Center:**
mo day year

Technician name/ID:

Supervisor:

Purpose of Evaluation:

Certification ☐ **Supervisor QC Check** ☐ **Site Visit** ☐

Please check the appropriate box if technician performance is satisfactory for each line item. Please note any comments or remedial action taken in 'Comments' section if performance was not satisfactory.

Steps in Exam:

1. ☐ ☐ Accurately sets up the 6MW course (using cones and tape).
2. ☐ ☐ Uses stop watch and lap timer to record laps.
3. ☐ ☐ Provides instructions to the participant.
4. ☐ ☐ Uses appropriate coaching/scripts
5. ☐ ☐ Accurately records data in the 6MW completion form.
6. ☐ ☐ Records value on form or computer screen

Comments/Corrective Actions: _____

_____

_____

Supervisor /Site Visitor Signature _____