

<p style="text-align: center;"><b>WOMEN'S INTERAGENCY HIV STUDY</b></p> <p style="text-align: center;"><b>SECTION 46: PULMONARY FUNCTION TESTING (PFT) PROTOCOL</b></p>
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**I. PULMONARY FUNCTION TESTING (SPIROMETRY ONLY)**

**A. BACKGROUND & STUDY PURPOSE**

There is evidence that HIV-infected persons have an increased incidence of chronic obstructive pulmonary disease (COPD), emphysema, and impaired pulmonary diffusing capacity compared to those without HIV infection. This study explores lung function in people with HIV to better understand how lung disease develops in persons with HIV and to identify targets for disease prevention and management. The aim is to improve the WIHS assessment of pulmonary health by including quality-assured, full pulmonary function testing (PFT) with standardized interpretation by a WIHS PFT Reading Center.

**B. SCIENTIFIC AIMS**

The scientific objectives are as follows:

- To identify and characterize HIV-associated pulmonary complications; and
- To evaluate hypotheses that could explain increases in COPD in those with HIV.

**C. STUDY DESIGN**

All WIHS women will participate in pulmonary function testing (PFT) during Visit 48. The PFT visit can take place at a core visit or at a separate visit from the core WIHS visit. PFT testing will be offered using the ndd Easy on-PC (nnd Medical Technologies, Andover, MA, USA) to study pulmonary function. This includes:

- Forced spirometry, also called pulmonary function testing (PFT) – Spirometry will be performed both pre- and post-bronchodilator administration.

All testing will be performed by trained study personnel per the American Thoracic Society (ATS) and the European Respiratory Society (ERS) guidelines (Miller MR et al. Eur Resp J. (2005) 26:153; Miller MR et al. Eur Resp J. (2005) 26:319; MacIntyre N et al. Eur Resp J (2005) 26:720). The ndd Easy on-PC uses ultrasonic transit time analysis to measure forced expiratory volume in one second (FEV1), forced vital capacity (FVC), and mid-expiratory flow rates (FEF25-75%).

In addition, two questionnaires with emphasis on smoking status, pulmonary symptoms, diagnoses, and medications will be administered:

- *St. George's Respiratory Questionnaire (SGRQ)* (self-administered between pre- and post-bronchodilation)
- *Modified Medical Research Council (MMRC)* (interviewer-administered between pre- and post-bronchodilation)

The flow of the PFT visit will be as follows:

- PFT participant consent

- Blood pressure and heart rate measurement(s)
- *PFT Screening Form (PFTSCR)*
- Pre-bronchodilation spirometry
- Albuterol administration
- Blood pressure and heart rate measurement(s)
- Administration of SGRQ and MMRC forms (if time allows)
- Post-bronchodilation spirometry
- *PFT Disposition Notification Form (PFTNOTI)*

The main outcomes variables will be:

- Pre- and post-bronchodilator forced expiratory volume in one second (FEV1) % predicted.
- Forced vital capacity (FVC) % predicted.
- FEV1/FVC ratio.
- Forced expiratory flow in the middle of expiration (FEF) 25-75%.

NHANES (Hankinson et al.) prediction equations will be used for predicted values for spirometry.

## **D. PARTICIPATING ORGANIZATIONS**

### **1. WIHS SITES**

- Bronx WIHS (PIs Kathryn Anastos and Anjali Sharma)
- Brooklyn WIHS (PIs Howard Minkoff and Deborah Gustafson)
- DC WIHS (PI Seble Kassaye)
- San Francisco WIHS (PIs Ruth Greenblatt, Phyllis Tien, and Bradley Aouizerat)
- Chicago WIHS (PIs Mardge Cohen and Audrey French)
- Chapel Hill WIHS (PI Adaora Adimora)
- Atlanta WIHS (PIs Igho Ofotokun and Gina Wingood)
- Miami WIHS (PIs Margaret Fischl and Lisa Metsch)
- UAB-MS WIHS (PIs Mirjam-Colette Kempf and Deborah Konkle-Parker)

### **2. DATA COORDINATING CENTER**

- WIHS Data Management and Analysis Center (WDMAC) (PIs Stephen Gange and Elizabeth Golub)

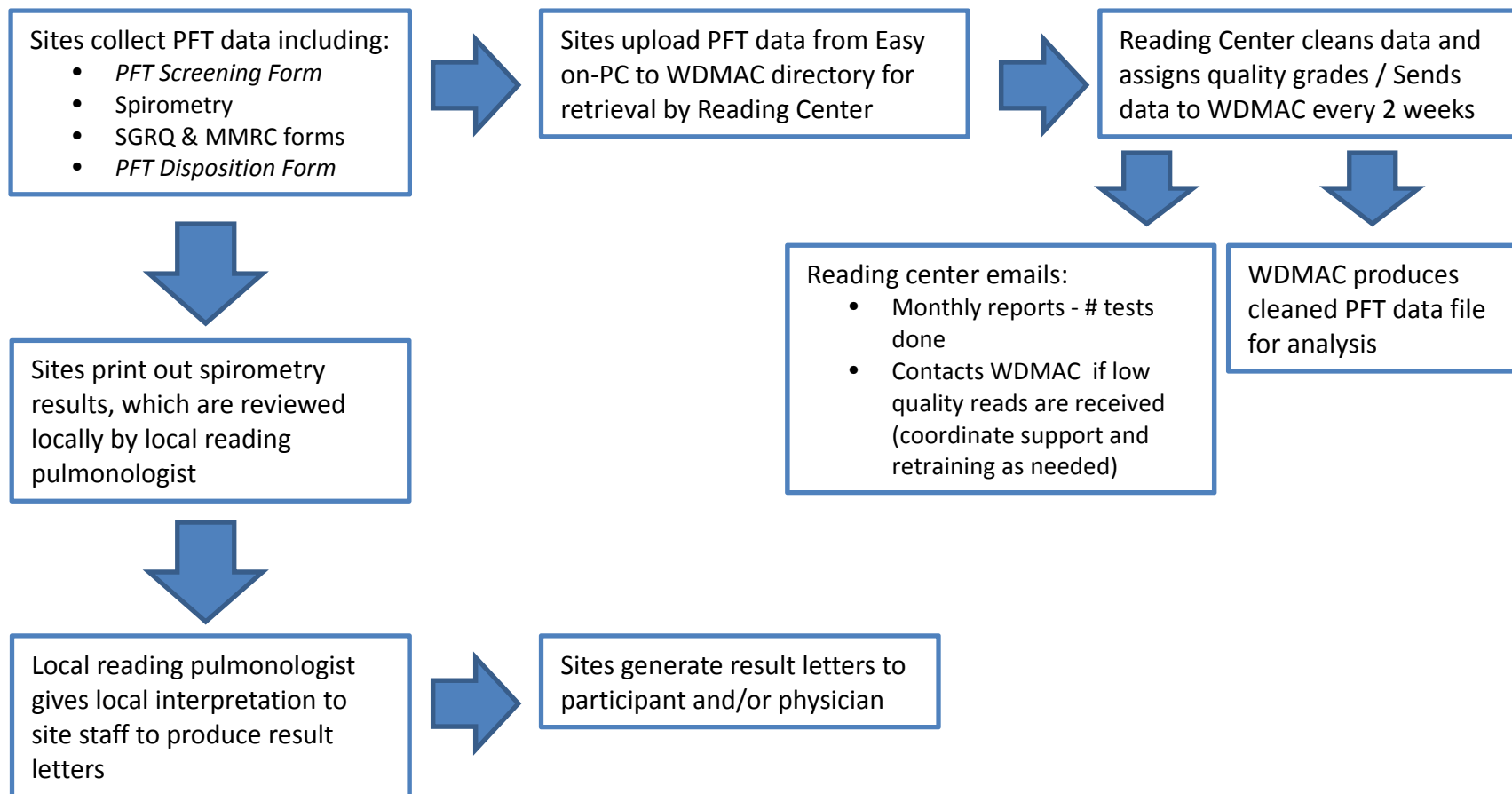
### 3. READING CENTER

- University of Utah (Robert Jensen)

**Figure 1: Participating Organizations Core Roles - Overview**

Partner	Role in PFT
WIHS Site Staff	<ol style="list-style-type: none"> <li>1. Administer PFTs and questionnaires to participants.</li> <li>2. Complete <i>PFT Screening Form</i> and <i>PFT Disposition Form</i>.</li> <li>3. Upload PFT results to WDMAC directory.</li> <li>4. Send hardcopy or electronic file of PFT results to the local reading pulmonologist for review.</li> <li>5. Receive result findings from local reading pulmonologist.</li> <li>6. Write and mail result letters to the participant and/or her physician.</li> </ol>
Local Reading Pulmonologist	<ol style="list-style-type: none"> <li>1. Review hardcopy or electronic file of PFT results.</li> <li>2. Indicate result findings on PFT hardcopy or send electronically to site.</li> </ol>
WDMAC	<ol style="list-style-type: none"> <li>1. Obtain clean data from PFT reading center.</li> <li>2. Generate cleaned PFT data file for analysis.</li> </ol>
Reading Center	<ol style="list-style-type: none"> <li>1. Make decisions on examiner certification through review of certification PFT files.</li> <li>2. Monitor data quality of site examiner testing results throughout visit.</li> <li>3. Communicate with sites about certification decisions and examiner data quality monitoring (send reports to sites).</li> <li>4. Communicate with WDMAC about certification decisions and ongoing PFT data quality issues (send reports to WDMAC).</li> <li>5. Clean spirometry data and send to WDMAC.</li> </ol>

**Figure 2: Participating Organizations Core Roles - Overview**



## E. PRE-VISIT PREPARATION

To prepare for the PFT study visit, site staff will need to:

1. Submit PFT protocol materials to local IRB.
2. Review pulmonary questionnaires to be administered.
3. Send staff to centralized training for instruction on how to perform PFT testing.
4. Assign a clinician to each study clinic in case of clinical concerns.
5. Identify local pulmonologist to review PFT results and decide on final interpretation to be included in results letter.
6. Prepare IT and staff personnel to provide Easy on-PC PFT results to Reading Center on a daily basis.
7. Assign pulmonologist to represent the site to provide research expertise in pulmonary function and disease, HIV exposure, and ART to address the research goals.

## F. TRAINING OF STAFF IN PFT (SPIROMETRY)

Site staff will receive centralized training over a one-day period and will return to their sites for the submission of training PFTs to be reviewed by the Reading Center for certification consideration.

Site staff who do not participate in the centralized training will be trained at their site using the train the trainer method, which will include hands on practice and the submission of training PFTs to be reviewed by the Reading Center for PFT certification consideration.

It is strongly recommended that all site staff review the following training videos prior to the in-person training session:

- [https://www.youtube.com/watch?v=eJbpu\\_kJypA](https://www.youtube.com/watch?v=eJbpu_kJypA)
- <https://www.youtube.com/watch?v=s89QaJ1X6C0>
- <https://www.youtube.com/watch?v=B-rbEBZLYy4>
- <https://www.youtube.com/watch?v=142hkjtav80>

## G. CERTIFICATION OF STAFF PERFORMING PFT (SPIROMETRY)

Prior to administering PFTs on participants, each staff person (examiner) must become certified by performing and submitting 10 PFT sets of sufficient quality on at least 10 different participants. Training PFTs can be done on staff members, friends, or volunteers.

- **Examiners should not administer albuterol during these practice tests.**
- Examiners may not use the same person multiple times for the 10 certification PFTs.
- Examiners should perform a minimum of 1-2 PFTs per week until the study start date to maintain proficiency.

See **Section M** for information on how to submit data to the Reading Center for certification.

Following the Reading Center review of certification tests, certification results will be sent to each site.

- Examiners will receive certification reports along with comments from the Reading Center for each individual test performed.
- Examiners will need to show PFT testing proficiency in order to be initially certified, and will need to maintain proficiency throughout the study to ensure that they will be allowed to continue administering PFTs.
- Decisions about each Examiner's PFT testing proficiency will be at the discretion of the Reading Center, and will be based on the quality of the PFTs produced by the examiner.
- Testing proficiency is best represented by the grades assigned to each PFT test by the Easy on-PC system:
  - A-grade data is the most representative data of an individual's lungs (the most accurate).
  - B-grade data is slightly downgraded, but due to the sensitivity of the Easy on-PC's sensor, is still usually highly accurate, though it may contain some artifact (i.e., coughs).
  - As quality grades are further downgraded, there is not as much reproducibility and less confidence in the data.

#### **H. MATERIALS AND EQUIPMENT**

- Easy on-PC<sup>®</sup> Device
  - Standard two-year warranty
- Case of 200 Spirettes<sup>®</sup>
  - Single patient use only
- Nose clips, 25 count
  - Single patient use only
- HP OfficeJet 6100E for Pro/LAB (suggested printer) or Windows compatible printer
- 3-Liter Calibration Syringe and Calibration Adapter
- Calibration Adapter
- Portable 5-Wheel Rolling Cart (optional)
  - Includes: Swivel and tilt mounting plate, easy grip handle, tray for disposables, printer clamp, small (E) cylinder tank holder, and 4-outlet power strip

- Albuterol and Spacers (purchased by sites locally)
- Laptop, PC, or Tablet
  - Compatible with Windows XP SP3, Windows Vista, Windows 7, and Windows 8 (32 and 64 bit)

#### **I. DISTRIBUTION OF MACHINES TO SITE**

Machines will be shipped individually as requested by each site. Please communicate with Kevin Hodgdon at ndd (919-480-3616, [khodgdon@nddmed.com](mailto:khodgdon@nddmed.com)), or the appropriate ndd representative for your region, for any shipping questions or machine ordering.

#### **J. ALBUTEROL AND SPACERS**

Albuterol MDI (metered-dose inhaler):

- Should be purchased locally from a pharmacy
- Should be stored at room temperature; has an expiration date
- Delivers a specific number of puffs, depending on the size ordered (e.g., 200 puffs per canister is the most common); the number of puffs left in the inhaler can be tracked by counting each puff used
- Can be tested to verify if there is medicine remaining before administering the 4 puffs to each participant; Do this by dispensing one puff into the air and listening for the sound of aerosolized medicine being released

Calculation of puffs: If the MDI has 200 puffs, then 1 test puff into the air, plus delivery of 4 puffs, would be:

- 1 test puff + 4 delivered puffs = 5 puffs per participant
- 200 puffs per MDI/5 puffs per participant = approximately 40 participants for each 200-puff MDI

It is recommended to keep two albuterol MDIs on site at all times in case of malfunction, or if the albuterol MDI runs out unexpectedly.

Spacer – One “valved spacer” is required for each participant:

- Dispose of spacer after one use
- Allows accurate delivery of albuterol; Ensures that each subject gets the same amount of albuterol
- Avoids mouth contact with the albuterol MDI
- May have a whistle which will sound if the participant is inhaling too fast, indicating that less albuterol is getting into the lungs

The price of spacers varies (e.g., \$6, \$10, \$30) so you should shop around. If you are able to buy in bulk (e.g., through a medical center purchasing department), you may get a better price.

## K. ELIGIBILITY AND QUESTIONNAIRES

### 1. INCLUSION CRITERIA

All WIHS participants seen at Visit 48 are eligible for this study.

### 2. EXCLUSION CRITERIA

See *PFT Screening Form* (PFTSCR) in **Appendix A** for definitions of the conditions below:

- Inability to complete study procedures
- Recent pneumothorax, myocardial infarction, or heart condition
- Recent surgery on eyes, chest, or abdomen
- Active TB
- Current retinal detachment
- Uncontrolled hypertension
- Current respiratory infection
- Currently pregnant

Site staff should complete the *PFT Screening Form* (PFTSCR) (**Appendix A**) to determine participant eligibility. If the participant responds “Yes” to any of Questions A6-A14 on the form, then the participant is not eligible for spirometry.

If the participant is currently pregnant she is not eligible for spirometry. If the participant is currently breastfeeding she should not be given Albuterol and her results will be recorded as pre-bronchodilation only.

If the participant is excluded due to having uncontrolled hypertension, she may return after blood pressure is controlled.

### 3. QUESTIONNAIRE ADMINISTRATION

Two questionnaires that ask about respiratory symptoms and related health and behavior will be administered to each participant. Questionnaires should be completed on paper or in Apollo, as appropriate, and will take up to 30 minutes to complete (these forms can be completed on paper and entered into Apollo at a later time). Timing of each questionnaire is as follows:

- *Modified Medical Research Council* (MMRC), 1-5 minutes, interviewer-administered via paper form or DDE (**Appendix B**)
- *St. George’s Respiratory Questionnaire* (SGRQ), 20-25 minutes, self-administered via paper form (**Appendix C**)

There is a 15-minute wait time after the albuterol is administered and before the post-bronchodilation test. During this time, the site may administer the MMRC and/or the SGRQ. If a participant is approaching 30 minutes on the SGRQ, stop, do the post-bronchodilation test, and then continue with the questionnaire after testing is done.



All participants completing the SGRQ and MMRC must be consented before answering the questions.

Site staff should complete the *PFT Disposition Notification Form* (PFTNOTI) (**Appendix D**) regardless of whether the PFT was performed or not. Answers should be based on the results of the exam and questionnaire completion.

## L. TESTING PROCEDURES

### 1. PFT TESTING

The ndd Easy on-PC testing system measures lung function with the flow-volume loop recorded, before and after bronchodilator administration.

When starting a new spirometry exam, follow the steps outlined below. Most participants will have two sets of spirometry maneuvers performed, one before bronchodilation and one after.

If participant reports recent bronchodilator use (see below), then only one set of spirometry maneuvers is collected, which will be considered “post-bronchodilator testing.” Please note, the Easy on-PC refers to the first spirometry done on each participant as the “Pre-bronchodilator spirometry” and this cannot be changed, even when the participant is already bronchodilated.

### 2. PRE- VS POST-BRONCHODILATION TESTING

As part of the screening process, staff should take a blood pressure and heart rate measurement from the participant. If the participant’s systolic blood pressure is > 180 mm HG or her diastolic blood pressure is > 100 mm HG, ask the participant to rest for 5 minutes. After 5 minutes, repeat the blood pressure measurement. If the average of the two systolic blood pressure readings is still > 180 mm HG or the average of her diastolic blood pressure readings is > 100 mm HG, the participant is not eligible for PFT testing. The examiner will note this on Question A13 on the *PFT Screening Form* (PFTSCR).

During screening, staff will ask whether the participant has used a short acting bronchodilator within the last 4 hours and/or a long-acting bronchodilator in the last 12-24 hours and record this information on the *PFT Screening Form* (PFTSCR) (**Appendix A**). If participant answers “Yes” to any of Questions A15-A17, record the time taken, and then proceed with post-bronchodilator spirometry only. If the participant answers “No” to all three questions, staff will proceed with pre-bronchodilator testing.

If the screening form indicates that the participant’s medication is still effective and the participant is already bronchodilated, then only one spirometry test should be performed, which will be considered post-bronchodilator spirometry.

- a) Pre-bronchodilator testing: Perform spirometry to ATS/ERS standards and as outlined below (**Pre-Bronchodilation Spirometry**).
- b) Post-bronchodilator testing: Repeat spirometry 15 minutes after inhalation of 4 puffs of albuterol delivered by a metered dose inhaler (MDI) with spacer. See **Post-Bronchodilation** below for details.

To determine if the participant is eligible for post-bronchodilator testing only, follow the prompts on the *PFT Screening Form* (PFTSCR). This decision is based on the participant reporting the use of an inhaler in the last 4, 12, or 24 hours in Questions A15-A17.

If the participant reports an allergy to albuterol or levalbuterol, no bronchodilator will be given. Results will be recorded as pre-bronchodilator testing.

### 3. PREPARATIONS

If possible (e.g., in a visit reminder letter or phone call), ask the participant not to smoke the day of their WIHS PFT visit, as it can interfere with the breathing tests. However, this is not required.

During the testing, the participant should be relaxed and should not wear tight clothing. It is recommended that the participant sit in a chair with arms. Watch the participant closely in the event that she becomes dizzy or lightheaded during the test.

For the duration of the breathing exercises, the participant should not take a break to smoke.

Spirometry and bronchodilator testing require active participation from the participant, so it is very important to explain and demonstrate all test maneuvers and leave time for participant questions. Explain the purpose of the testing thoroughly (Appendix E).

### 4. SETTING UP THE NDD EASY ON-PC DEVICE

See **Section 2** of the **Easy on-PC Manual** for details on how to set up the device. Once the device has been set up and all software has been installed, the flow sensor will connect to the PC/laptop/tablet by means of a USB cable. You will need to connect the printer via USB port as well.

### 5. PREPARE EQUIPMENT: START-UP AND CALIBRATION

1. Open the Easy on-PC application.
2. The machine should display a **Login** screen, followed by **Startup** screen. Be sure to log in and out after each use so that the correct Examiner ID is attached to each pulmonary function test.
3. Using the calibration adaptor, connect the sensor to the syringe. The piston must be fully inserted and at the stop position.
4. In the **Utilities** menu, click **Check Calibration**, then select **Multiflow**.
5. Wait until baseline has been set. Then execute one full inspiratory pump stroke followed by one full expiratory pump stroke.
6. Three trials each at different flow rates are required for the **Multiflow** calibration check.
7. You should see **“Accuracy Confirmed”** on the device along with the % deviation and the average flow velocity of the pump stroke. You should reach +/-3.5 % accuracy.

8. The equipment should be checked once daily, before first use. Value must be within calibration limits ( $\pm 3.5\%$ ). Calibration checks only need to be done on days the device is used for testing. The site should maintain documentation of repairs, computer software or hardware updates or changes. If the equipment is altered or relocated, document calibration checks and quality-control procedures on equipment before further participant testing.

#### 6. ENTERING PARTICIPANT DEMOGRAPHICS

1. From the Main Menu, click **Patients** and add a new participant by selecting **New** in the bottom left corner of the **Patients** Screen.
2. You will be required to enter the following information to create a new Patient ID:
  - a. Patient ID (use WIHSID)
  - b. Last name (use WIHSID)
  - c. First name (use WIHSID)
  - d. Gender
  - e. Ethnicity
  - f. Year of Birth
  - g. Height
  - h. Weight
3. Once demographic information is entered, press **OK** to return to the participant list and select the correct participant. If data is entered incorrectly, it can be edited at a later date.

#### 7. EXAMINERS: COACHING AND PROVIDING FEEDBACK

Examiners are encouraged to do the following when testing participants:

1. Demonstration by examiner of the FVC maneuver before participant's first attempt.
2. Vigorously coach to obtain a full inspiration followed by a "blast" at outset of maneuver.
3. Provide encouragement of complete exhalation by saying "squeeze everything out."
4. Observe participant throughout the maneuver.
5. Offer enthusiastic feedback to encourage maximal efforts.

The Easy on-PC provides an integrated feedback system to the examiner during maneuvers; they receive an immediate score: "A / B" grade meets the most stringent 2005 ATS/ERS spirometry quality criteria, "C" meets less stringent 1994 ATS criteria, and "D / F" are not acceptable. In addition to a grade, the device also provides feedback

suggestions after each maneuver, such as “Blow out longer” or “Take a deeper breath,” thus helping examiners troubleshoot at the point of care.

#### 8. PRE-BRONCHODILATION SPIROMETRY

1. Connect the handheld sensor in order to perform the test.
2. Insert the spirette so that the upwards pointing arrow on the spirette matches the arrow on the sensor. Be sure to leave plastic wrapper around mouthpiece of the spirette to avoid flow during initialization of the test.
3. Once you have entered the participant’s demographic information, click on her Patient ID, followed by the “**Test.**” You will see a screen with various tests available. To select a spirometry test, select **FVL (ex/in)**.
4. Confirm the environmental measurements (Body Temperature & Pressure Saturated (BTPS)) on the screen. Please note that the machine will also direct you to block the spirette (keep packaging on) until prompted. This is for the first trial only. It is to ensure baseline has been set.
5. Explain the purpose of the test as well as the test maneuver, as it is important for the participant to understand and participate fully. Because this will likely be the participant’s first time using the Easy on-PC to perform a spirometry test, it is important to explain the instructions fully and allow time for participant questions. It is important for the participant to maintain an upright position for the duration of the testing with her head upright (no leaning forward, bending head forward, etc.). A general description of the procedure for spirometry is below; see **Appendix E** for coaching tips and techniques:
  - a. Participant will need to breathe normally initially, then fill lungs fully, inhaling completely.
  - b. They will have a minimal pause (<1 second) with full lungs briefly, then exhale as forcefully and quickly as possible (within the first second), continuing to blow out until lungs are completely empty, maintaining an upright posture.
  - c. Once empty, participant will again inhale completely and rapidly and the examiner will manually stop the test.
  - d. This test will need to be completed successfully at least three times to ensure accuracy.
    - i. ATS/ERS spirometry guidelines for high-quality spirometry require 3 acceptable (defined below) and 2 reproducible tests. If such criteria cannot be obtained within 8 attempts, further testing will not be productive, and may be terminated at the judgment of the examiner. Inability to perform spirometry should be reported on the *PFT Disposition Notification Form* (PFTNOTI) because it may affect participation in the study.

6. Instruct the participant to put on the nose clip and sit upright, with both feet planted firmly on the floor. Once the trial starts, the monitor will display **“Setting Baseline, Avoid Flow”**.
  7. When **“Start Test”** displays on the monitor, instruct the participant to remove the plastic wrap around the mouthpiece and place her teeth firmly around the mouthpiece. Ask her to place the spirette on top of her tongue and seal her lips around it to avoid leaks, making sure not to block the opening or bite down excessively.
  8. The participant will perform the procedure as outlined above. Provide the participant with motivating feedback and remind her that this test has to be repeated successfully at least two more times.
    - a. For each additional trial, click **“Add Trial”** to start the process over again until three successful trials have been completed. Please note that trials can only be added for same-day testing. If a participant needs a break, she must complete the remaining trials during this same day.
  9. After the third acceptable spirometry trial, the machine will display the message **“Session Complete.”** Let the participant know this part of the testing is over. They should be instructed to breathe normally and relax.
  10. After bronchodilation, when you return to the spirometry (FVL) test, click **“Add Post”** rather than **“Add Trial.”**
9. ACCEPTABILITY OF PFT TEST
1. During testing, a quality grade and variability information will be displayed. This will indicate the session quality and session interpretation.
  2. After each trial, the screen will display a quality grade and system interpretation. Session comments can be added in the **Comment** section next to **Test Information**. The examiner should add comments here if a participant attempted to perform a trial but was unsuccessful, or refused to participate in any of the trials. This should also be noted on the *PFT Disposition Notification Form* (PFTNOTI) (**Appendix D**) at the end of testing.
  3. The session will be graded with A, B, C, D, or F. Acceptable trials have the following characteristics:
    - a. Good start of test (sharp upward peak on flow-volume curve indicating deep, quick inhale).
    - b. Good end of test (plateau on volume-time graph indicating no more air is being exhaled).
    - c. Artifact free (no coughs, dips on flow-volume curve that indicate stopping exhalation prematurely).

4. An acceptable session is 3 acceptable trials with the 2 best having a FEV1 and FVC that is repeatable within 150 mL. Do not worry about these numbers, the machine will let you know when you have achieved this. At this time, a session complete message will be displayed.

#### 10. ALBUTEROL ADMINISTRATION

1. Use albuterol (90 µg x 4 doses) via MDI with new spacer.
2. Shake MDI well.
3. Activate inhaler in air to check for adequate operation.
4. Attach spacer to MDI.
5. Instruct participant to blow out any remaining air in lungs and then insert the spacer mouthpiece into participant's mouth.
6. Instruct participant to inhale slowly; examiner activates inhaler during inspiration and delivers 1 puff of albuterol.
7. Have participant hold breath for 10 seconds before exhaling after each puff.
8. Wait 10-30 seconds and repeat process 3 more times, for a total delivery of 4 puffs of albuterol.
9. Wait at least 15 minutes after last inhalation before beginning the post-bronchodilator spirometry testing.
10. Use the **Albuterol Administration Checklist** in **Appendix E** for tips on this procedure.
11. While you are waiting to perform the post-bronchodilation spirometry (FVL) test, you may elect to administer the MMRC and/or SGRQ questionnaires.
12. If participant identifies a concern about side effects because of her health history (e.g., heart rate, tremor, history of arrhythmias), albuterol will not be used (i.e., only pre-bronchodilator set of spirometry maneuvers will be obtained), but this should be logged in the comments section of the Easy on-PC and on the *PFT Screening Form* (PFTSCR).

After albuterol administration, the examiner should take another heart rate and blood pressure measurement from the participant. If the participant's systolic blood pressure is > 180 mm HG or her diastolic blood pressure is > 100 mm HG or her heart rate is > 100 beats per minute, the testing should be stopped. Discretion should be used to determine if the increase in blood pressure/heart rate is due to the albuterol and should be considered an adverse event or not. For example, if the participant's initial heart rate was 95 beats per minute and increases to 101 beats per minute post albuterol administration, this is likely not a drug reaction. Testing should still be stopped, however. If the participant's initial heart rate was 60 beats per minute and increases to 101 beats per minute post albuterol administration, it is more likely due to a drug

reaction and testing should stop. The examiner will then fill out the *PFT Adverse Event Form* (PFTAER).

#### 11. POST-BRONCHODILATION FOLLOWING PRE-BRONCHODILATION SPIROMETRY

Administer four puffs of albuterol by a metered dose inhaler (MDI) attached to a spacer (see above). Then repeat spirometry between 15-30 minutes after the albuterol inhalation was completed (15 minutes is preferred).

1. On the Main Screen, click **“Patients”** and select the appropriate participant. Before performing Bronchodilation testing (post-test), forced spirometry (pre-test) should already be measured, unless the participant is only eligible for Post-Bronchodilation Spirometry, so you will not need to add participant information for this test again. In the event that the participant is not eligible for albuterol administration, you will have to select a new patient as outlined above and note in the session comments section that the test is a “Post-only” test.
2. Once you have selected the appropriate participant, select the **“FVL Test”** as you did for forced spirometry testing earlier. In this case, you will select **“Add Post”** rather than **“Add Trial”** in the bottom right-hand corner of the screen since you are adding a new trial post-bronchodilation with albuterol. You will be able to see all of the **“Pre-Tests”** performed earlier.
3. Conduct the test as outlined in the **Pre-Bronchodilation Spirometry** section of this manual above and use the **Coaching Tips/ Techniques** in **Appendix E** as a resource. An acceptable session is 3 acceptable trials with the 2 best having a FEV1 and FVC that is repeatable within 150 mL. Do not worry about these numbers, the machine will let you know when you have achieved this. At this time, a session complete message will be displayed.

#### 12. POST-BRONCHODILATION WITHOUT PRE-BRONCHODILATION SPIROMETRY

In the event that a participant is not eligible for bronchodilation per the *PFT Screening Form* (PFTSCR) (**Appendix A**), examiners will need to select **“Add Trial”** and perform the Pre-Bronchodilation Spirometry as outlined above. Examiners will need to note in the Easy on-PC session comments section that the participant was not eligible for pre-bronchodilation spirometry and the session reflects post-bronchodilation spirometry. They will also note this on the *PFT Disposition Notification Form* (PFTNOTI) after all testing is complete (**Appendix D**).

#### 13. EVALUATION AND REPORTING OF SPIROMETRY

1. Acceptability (within maneuver evaluation): Three acceptable tests are required for an adequate spirometry maneuver. Examples of acceptability criteria are listed below, along with suggested criteria for implementing computerized checks.
  - a. Slow start of test: Participant did not begin her initial peak flow early enough; repeat, coaching for a more forceful and abrupt start (“BLAST it

out"). This error occurs when volume at the back extrapolated zero-time is more than 5% of the FVC or greater than 150 ml.

- b. Cough: This causes abrupt irregularities in flow, and is a reason to reject the test when it occurs during the first second of the effort. Coach the participant to make the effort without coughing.
  - c. Abrupt end of test: At the end of exhalation, the participant stopped blowing out too abruptly, ending her effort too soon. Coach the participant to maintain her expiratory effort to the very end until told to stop by the examiner.
  - d. Short expiratory time: Participant did not continue her expiration for at least 6 seconds or did not reach a volume plateau. In participants with severe COPD, the expiration often does not reach a plateau in reasonable time. In this case, 6 seconds of effort is the minimal duration of effort but 10 to 12 seconds of effort is reasonable.
  - e. Low peak flow: The participant did not achieve an adequately forceful blast. Repeat the effort, coaching to blow harder and faster if possible.
2. Reproducibility (between maneuver evaluations): Reproducibility criteria are used to determine when more than 3 acceptable FVC maneuvers are needed. The nnd Easy on-PC will indicate if the results do not meet reproducibility quality.
  3. Abnormal Spirometry Review: A pulmonologist at each site will review printed results at regular intervals. If any abnormal results are discovered during this review, a member of the research team will notify the participant or the participant's primary care physician, who will assess the need to provide additional evaluation.

#### 14. ADVERSE EVENT

- Definition: An "Adverse Event" is a significant medical event that is felt to be at least possibly related to the research study.
- Example: Shortness of breath that causes the participant to be unable to continue the PFT testing.
- Describe the adverse event in the *Adverse Event Form* (PFTAER) (**Appendix F**) if the participant reports an adverse event while participating in the PFT procedure.

#### 15. PFT DISPOSITION FORM (**Appendix D**)

- Complete this form following the PFT.
- Indicate whether the testing was performed successfully (Pre-Bronchodilation, Post-Bronchodilation).
- Indicate the participant's preference for having PFT result letters sent to herself and/or her doctor.



## M. PROCEDURE AFTER VISIT

### 1. PFT DATA TRANSFER

#### a. Timing

Each site is expected to upload their Easy on-PC data file at the end of each day. There is no need for sites to select individual tests; all tests in the Easy on-PC database will be sent to the Reading Center for cleaning and quality control.

#### b. Site Responsibilities

Sites should upload all PFT testing results to their remote site directory (altwihs, bkwihs, bxwihs, chwihs, dcwihs, miawihs, mswihs, sfwihs, uabwihs, and uncwihs) for Reading Center review. See more detailed information below.

#### c. Reading Center Responsibilities

- Retrieve the PFT data uploaded to each site's remote directory
- Process and clean the testing results data to ensure quality control
- Send cleaned data to WDMAC via a clinic-specific ACCESS database
- Create reports for each site examiner based on quality of PFT testing results

#### d. WDMAC Responsibilities

- Provide Reading Center access to all site results (via PFT folder in remote site directories) and email Reading Center on a daily basis regarding new database uploads by sites
- Receive the cleaned PFT data from the Reading Center and generate data edits
- Communicate with sites and Reading Center regarding data edits and generate data file once complete
- Compare number of participants reported to have PFT testing done to the actual data received by the Reading Center (inform sites and Reading Center of any discrepancies)
- Generate monthly progress reports of PFT progress for the Pulmonary Working Group (PWG)

#### e. Steps for Data Transfer to WDMAC

1. The full PFT database should be uploaded at the end of each day (i.e., cumulative transmission). On the home screen, select **Utilities** → **Export Data** → **Patient Data** (uncheck everything else) → **Export**. Select the location on your computer where you want to save the database and hit **OK**. You will receive a message that the export was completed successfully. This version should be maintained at the site and not uploaded to WDMAC.

2. Make a copy of the full PFT database. This version will be uploaded to WDMAC. Use the following naming convention:

a. **Site#\_DATE(YYYYMMDD)\_WIHS** (e.g., 10\_20180221\_WIHS)

b. Use the following site numbers:

i. 10 = Bronx

ii. 20 = Brooklyn

iii. 30 = Washington, DC – Georgetown

iv. 31 = Washington, DC – Inova

v. 32 = Washington, DC – Montgomery County

vi. 50 = UCSF – Scott Street

vii. 51 = UCSF - EBAC

viii. 60 = Chicago - Main

ix. 61 = Chicago - Rush

x. 80 = UNC – Raleigh

xi. 81 = UNC – Durham

xii. 82 = Emory

xiii. 83 = Miami

xiv. 84 = UAB

xv. 85 = Jackson

3. Upload the full PFT database to WDMAC using FTP client software such as “SSH Secure File Transfer” or “FileZilla FTP Client.” Securely log in to WDMAC’s FTP server using the username and password assigned to your site. Use the host name **statepi5.jhsph.edu** and the port **22**.

4. After you log in, you should see a list of directories and files on the computer you are using in the left pane, as well as a list of directories on WDMAC’s server in the right pane. On the WDMAC server (right pane), navigate to the directory called **PFT**. Click and drag the file you want to transfer from the left pane into **PFT**.

#### **f. Bloodwork Data and Results**

Carboxyhemoglobin must be collected on the same date as the PFT testing. Hemoglobin from the WIHS visit can be used as long as it was collected within 60 days of the PFT data and no hospitalization or serious illness/conditions have occurred in the interim. If the hemoglobin result from the WIHS visit cannot be used, hemoglobin will need to be collected on the date of the PFT testing.

Sites will enter data from the PFT29 into Apollo in real time on the day of the PFT testing. Lab results will be entered into Apollo on the PFTLAB form as they are received at the sites. It is necessary for these results to be entered in a timely manner as the data is required for the Reading Center to properly calculate values.

WDMAC will download the lab results (PFTLAB) at least every two weeks to provide to the Reading Center.

**g. Questionnaire Data**

Sites will enter questionnaire data in Apollo, which will be downloaded by WDMAC as needed.

**h. Data Transfer for PFT Certification**

Sites will transfer their certification data from the Easy on-PC at the end of each day for Reading Center review and certification following the instructions listed above. Examiners are required to submit 10 PFT sets of sufficient quality on at least 10 different people. The naming convention for the file will be:

**999\_xxx\_EXID**

'xxx' are sequential, 3-place digits, beginning with a 001 and increasing by 1 each time the examiner starts a new set of certification test sets (10 sets required).

'EXID' is the unique examiner ID assigned and distributed by WDMAC.

Example: 999\_002\_142

**i. Clean PFT Data**

The cleaned PFT data will be transferred back to WDMAC and a data file will be created to store this information. From the cleaned data, reports for the data received/expected will be generated for all sites and provided to each site and the Reading Center.

**2. PROCEDURE FOR PRODUCING RESULTS AND RESULTS LETTERS**

Sites will be able to print reports for local pulmonologist review, or alternatively export and send the pdf electronically. There are several layouts available for the Easy on-PC display (1-2 page summaries), and sites will need to decide locally with their pulmonologist which is the best for their interpretation of the results. (See **Appendix G** for a recommended Easy on-PC Report format.)

At regular intervals (weekly suggested), sites will:

- Collect PFT hard copies.
- Send hardcopy or electronic report to local reading pulmonologist for reading.
- Record-keeping as per site (example: count, date sent, person sending).

#### Reading Pulmonologist Procedure (NOTE: Centers may tailor procedures)

- Receive regular delivery of PFT hard copies or electronic copies (recommended weekly).
- Handwrite, send electronically, or use another method to indicate the type of result letter that should be produced; confirm with signature or other method.
  - Suggest establishing deadlines for turnaround times by the pulmonologists.
- Return printout to site or send electronic indication of final interpretation to be used for result letter.
- Sites coordinate with their local pulmonologist for clinical interpretation of the research test results.
- Use pulmonologists' final interpretation to generate result letters.

#### Site Procedure

- Receive delivery of PFT hard copies or electronic version of reading pulmonologist signature.
- Use Final Interpretation Notes to produce results letter (**Appendix I**).
  - Suggest establishing deadlines.
  - Site may select to include more specific findings in participant results letter by using terms written on the PFT printout along with the description of these terms (see **Appendix H**: Glossary of PFT Terms).

Participant Result Letter: Each site will create a customized participant letter using the Participant Letter Templates (**Appendix I**).

Doctor Result Letter: Each site will create a customized doctor's letter using the Doctor Letter Templates, which will include findings per local pulmonologist (**Appendix I**).

Sites will be given the option to opt out of sending normal results letters to participants and doctors. If the site chooses not to send normal results letters, the participant must be told that she will be notified, by either phone or letter, if the local pulmonologist reports any abnormal findings.

## II. PULMONARY FUNCTION TESTING (SPIROMETRY AND DLCO)

### A. BACKGROUND & STUDY PURPOSE

There is evidence that HIV-infected persons have an increased incidence of chronic obstructive pulmonary disease (COPD), emphysema, and impaired pulmonary diffusing capacity compared to those without HIV infection. This study explores lung function in people with HIV to better understand how lung disease develops in persons with HIV and to identify targets for disease prevention and management. The aim is to improve the WIHS assessment of pulmonary health by including quality-assured, full pulmonary function testing (PFT) with standardized interpretation by a WIHS PFT Reading Center.

### B. SCIENTIFIC AIMS

The scientific objectives are as follows:

- To identify and characterize HIV-associated pulmonary complications; and
- To evaluate hypotheses that could explain increases in COPD in those with HIV.

### C. STUDY DESIGN

All WIHS women at the UCSF, UNC, and Atlanta sites will participate in pulmonary function testing (PFT), including spirometry and DLCO, during Visit 48. The PFT visit can take place at either a core visit or at a separate visit from the core WIHS visit. PFT testing will be offered using the ndd EasyOne Pro (nnd Medical Technologies, Andover, MA, USA) to study pulmonary function. This includes:

- Forced spirometry, also called pulmonary function testing (PFT) – Spirometry will be performed both pre- and post-bronchodilator administration.
- Diffusing capacity (DLCO).

All testing will be performed by trained study personnel per the American Thoracic Society (ATS) and the European Respiratory Society (ERS) guidelines (Miller MR et al. Eur Resp J. (2005) 26:153; Miller MR et al. Eur Resp J. (2005) 26:319; MacIntyre N et al. Eur Resp J (2005) 26:720). The ndd EasyOne Pro uses ultrasonic transit time analysis to measure forced expiratory volume in one second (FEV1), forced vital capacity (FVC), and mid-expiratory flow rates (FEF25-75%). The device also measures single-breath diffusing capacity of carbon monoxide (DLCO) using the automated single-breath procedure of the integrated testing system, which conforms to ATS standards.

In addition, two questionnaires with emphasis on smoking status, pulmonary symptoms, diagnoses, and medications will be administered:

- *St. George's Respiratory Questionnaire* (SGRQ) (self-administered between pre- and post-bronchodilation)
- *Modified Medical Research Council* (MMRC) (interviewer-administered between pre- and post-bronchodilation)

The flow of the PFT visit will be as follows:

- PFT participant consent
- Blood pressure and heart rate measurement(s)
- *PFT Screening Form* (PFTSCR)
- Blood draw (PFT29)
- Pre-bronchodilation spirometry
- Albuterol administration
- Blood pressure and heart rate measurement(s)
- MMRC and SGRQ (if time allows)
- Post-bronchodilation spirometry
- DLCO
- *PFT Disposition Notification Form* (PFTNOTI)

The main outcomes variables will be:

- Pre- and post-bronchodilator forced expiratory volume in one second (FEV1) % predicted.
- Forced vital capacity (FVC) % predicted.
- FEV1/FVC ratio.
- Forced expiratory flow in the middle of expiration (FEF) 25-75%.
- Diffusing capacity of the lung for carbon monoxide (DLCO) % predicted.

NHANES (Hankinson et al.) and Neas et al. prediction equations will be used for predicted values for spirometry and DLCO, respectively, with DLCO adjusted for hemoglobin and carboxyhemoglobin.

#### **D. PARTICIPATING ORGANIZATIONS**

##### **1. WIHS SITES**

- San Francisco WIHS (PIs Ruth Greenblatt, Phyllis Tien, and Bradley Aouizerat)
- Chapel Hill WIHS (PI Adaora Adimora)
- Atlanta WIHS (PIs Igho Ofotokun and Gina Wingood)

##### **2. DATA COORDINATING CENTER**

- WIHS Data Management and Analysis Center (WDMAC) (PIs Stephen Gange and Elizabeth Golub)

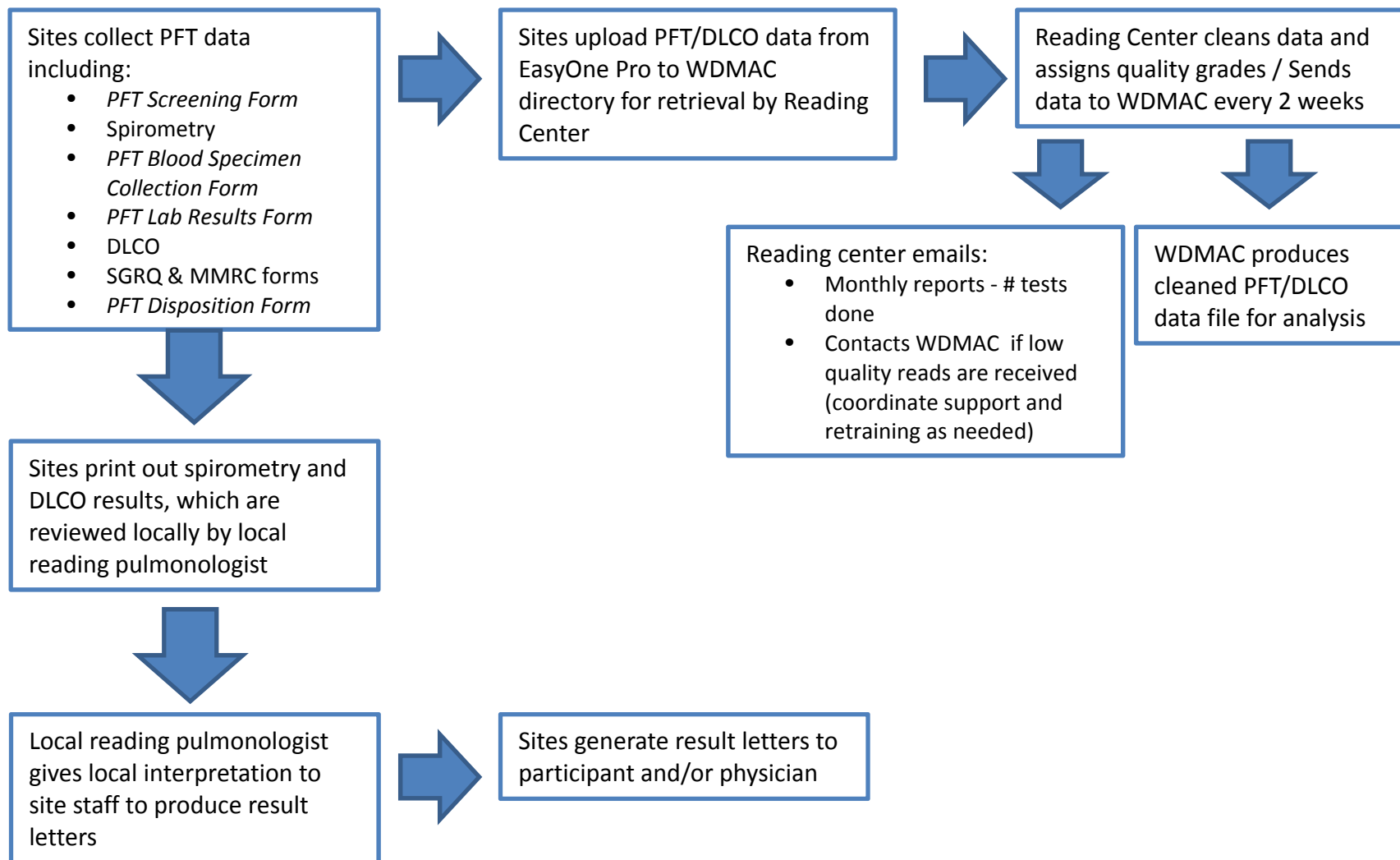
##### **3. READING CENTER**

- University of Utah (Robert Jensen)

**Figure 3: Participating Organizations Core Roles - Overview**

Partner	Role in PFT
WIHS Site Staff	<ol style="list-style-type: none"> <li>1. Administer PFTs and questionnaires to participants.</li> <li>2. Complete <i>PFT Screening Form (PFTSCR)</i>, <i>PFT Disposition Notification Form (PFTNOTI)</i>, <i>PFT Blood Specimen Collection Form (PFT29)</i>, and the <i>PFT Lab Results Form (PFTLAB)</i>.</li> <li>3. Upload PFT results to WDMAC directory.</li> <li>4. Send hardcopy or electronic file of PFT results to the local reading pulmonologist for review.</li> <li>5. Receive result findings from local reading pulmonologist.</li> <li>6. Write and mail result letters to the participant and/or her physician.</li> </ol>
Local Reading Pulmonologist	<ol style="list-style-type: none"> <li>1. Review hardcopy or electronic file of PFT results.</li> <li>2. Indicate result findings on PFT hardcopy or send electronically to site.</li> </ol>
WDMAC	<ol style="list-style-type: none"> <li>1. Obtain clean data from PFT reading center.</li> <li>2. Generate cleaned PFT data file for analysis.</li> </ol>
Reading Center	<ol style="list-style-type: none"> <li>1. Make decisions on examiner certification through review of certification PFT files.</li> <li>2. Monitor data quality of site examiner testing results throughout visit.</li> <li>3. Communicate with sites about certification decisions and examiner data quality monitoring (send reports to sites).</li> <li>4. Communicate with WDMAC about certification decisions and ongoing PFT data quality issues (send reports to WDMAC).</li> <li>5. Clean spirometry and DLCO data and send to WDMAC.</li> </ol>

**Figure 4: Participating Organizations Core Roles - Overview**





## E. PRE-VISIT PREPARATION

To prepare for the PFT study visit, site staff will need to:

1. Submit PFT protocol materials to local IRB.
2. Review pulmonary questionnaires to be administered.
3. Send staff to centralized training for instruction on how to perform PFT testing.
4. Assign a clinician to each study clinic in case of clinical concerns.
5. Identify local pulmonologist to review PFT results and decide on final interpretation to be included in results letter.
6. Prepare IT and staff personnel to provide EasyOne Pro PFT results to Reading Center on a daily basis.
7. Assign pulmonologist to represent the site to provide research expertise in pulmonary function and disease, HIV exposure, and ART to address the research goals.

## F. TRAINING OF STAFF IN PFT (SPIROMETRY AND DLCO)

Site staff will receive centralized training over a one and one half day period and will return to their sites for the submission of training PFTs to be reviewed by the Reading Center for certification consideration.

Site staff who do not participate in the centralized training will be trained at their site using the train the trainer method, which will include hands on practice and the submission of training PFTs to be reviewed by the Reading Center for PFT certification consideration.

It is strongly recommended that all site staff review the following training videos prior to attending in-person training session:

- [https://www.youtube.com/watch?v=eJbpu\\_kJypA](https://www.youtube.com/watch?v=eJbpu_kJypA)
- <https://www.youtube.com/watch?v=s89QaJ1X6C0>
- <https://www.youtube.com/watch?v=B-rbEBZLYy4>
- <https://www.youtube.com/watch?v=142hkitav80>

## G. CERTIFICATION OF STAFF PERFORMING PFT

Prior to administering PFTs on participants, each staff person (examiner) must become certified by performing and submitting 10 PFT sets of sufficient quality on at least 10 different participants. Training PFTs can be done on staff members, friends, or volunteers.

- **Examiners should not administer albuterol during these practice tests.**
- Examiners may not use the same person multiple times for the 10 certification PFTs.
- Examiners should perform a minimum of 1-2 PFTs per week until the study start date to maintain proficiency in both spirometry and DLCO.

- The Reading Center will accept spirometry and DLCO tests separately for those examiners who would like to start certification testing for spirometry while they wait for their gas tanks.

See **Section M** for information on how to submit data to the Reading Center for certification.

Following the Reading Center review of certification tests, certification results will be sent to each site.

- Examiners will receive certification reports along with comments from the Reading Center for each individual test performed.
- Examiners will need to show PFT testing proficiency in order to be initially certified, and will need to maintain proficiency throughout the study to ensure that they will be allowed to continue administering PFTs.
- Decisions about each examiner's PFT testing proficiency will be at the discretion of the Reading Center, and will be based on the quality of the PFTs produced by the examiner.
- Testing proficiency is best represented by the grades assigned to each PFT test by the EasyOne Pro system:
  - A-grade data is the most representative data of an individual's lungs (the most accurate).
  - B-grade data is slightly downgraded, but due to the sensitivity of the EasyOne Pro sensor, is still usually highly accurate, though it may contain some artifact (i.e., coughs).
  - As quality grades are further downgraded, there is not as much reproducibility and less confidence in the data.

## **H. MATERIALS AND EQUIPMENT**

- EasyOne Pro<sup>®</sup> Device
  - Single Breath DLCO system
    - Standard two-year warranty
- CGA 973 Regulator
  - For use with small (E) cylinder of DLCO
- CGA 500 Regulator
  - For use with (H/K) cylinder of DLCO
- Case of 200 Spirettes<sup>®</sup>
  - Single patient use only
- Case of 100 Barriettes<sup>®</sup>
  - Single patient use only

- Nose clips, 25 count
  - Single patient use only
- HP OfficeJet 6100E for Pro/LAB (suggested printer) or Windows compatible printer
- 3-Liter Calibration Syringe and Calibration Adapter
- Calibration Adapter
- DLCO Gas Cylinder
  - H cylinder or E cylinder with H/E cylinder regulator (holder)
- Portable 5-Wheel Rolling Cart (optional)
  - Includes: Swivel and tilt mounting plate, easy grip handle, tray for disposables, printer clamp, small (E) cylinder tank holder, and 4-outlet power strip
- Albuterol and Spacers (purchased by sites locally)

#### **I. DISTRIBUTION OF MACHINES TO SITE**

Machines will be shipped individually as requested by each site. Please communicate with Kevin Hodgdon at ndd (919-480-3616), [khodgdon@nddmed.com](mailto:khodgdon@nddmed.com), or the appropriate ndd representative for your region, for any shipping questions or machine ordering.

#### **J. ALBUTEROL AND SPACERS**

Albuterol MDI (metered-dose inhaler):

- Should be purchased locally from a pharmacy
- Should be stored at room temperature; has an expiration date
- Delivers a specific number of puffs, depending on the size ordered (e.g., 200 puffs per canister is the most common); the number of puffs left in inhaler can be tracked by counting each puff used
- Can be tested to verify if there is medicine remaining before administering the 4 puffs to each participant; Do this by dispensing one puff into the air and listening for the sound of aerosolized medicine being released

Calculation of puffs: If the MDI has 200 puffs, then 1 test puff into the air, plus delivery of 4 puffs, would be:

- 1 test puff + 4 delivered puffs = 5 puffs per participant
- 200 puffs per MDI/5 puffs per participant = approximately 40 participants for each 200-puff MDI

It is recommended to keep two albuterol MDIs on site at all times in case of malfunction, or if the albuterol MDI runs out unexpectedly.

Spacer – One “valved spacer” is required for each participant

- Dispose of spacer after one use

- Allows accurate delivery of albuterol; Ensures that each subject gets the same amount of albuterol
- Avoids mouth contact with the albuterol MDI
- May have a whistle which will sound if the participant is inhaling too fast, indicating that less albuterol is getting into the lungs

The price of spacers varies (e.g., \$6, \$10, \$30) so you should shop around. If you are able to buy in bulk (e.g., through a medical center purchasing department), you may get a better price.

## K. ELIGIBILITY AND QUESTIONNAIRES

### 1. INCLUSION CRITERIA

All WIHS participants seen at the UCSF, UNC, and Atlanta sites during Visit 48 are eligible for this study.

### 2. EXCLUSION CRITERIA

See *PFT Screening Form* (PFTSCR) in **Appendix A** for definitions of the conditions below:

- Inability to complete study procedures
- Recent pneumothorax, myocardial infarction, or heart condition
- Recent surgery on eyes, chest, or abdomen
- Active TB
- Current retinal detachment
- Uncontrolled hypertension
- Current respiratory infection
- Currently pregnant
- Non-participating site

Site staff should complete the *PFT Screening Form* (PFTSCR) (**Appendix A**) to determine participant eligibility. If the participant responds “Yes” to any of Questions A6-A14, then the participant is not eligible for spirometry or DLCO.

If the participant is currently pregnant she is not eligible for spirometry or DLCO. If the participant is currently breastfeeding she should not be given Albuterol and her results will be recorded as pre-bronchodilation only.

If the participant is excluded due to having uncontrolled hypertension, she may return after blood pressure is controlled.

### 3. QUESTIONNAIRE ADMINISTRATION

Two questionnaires that ask about respiratory symptoms and related health and behavior will be administered to each participant. Questionnaires should be completed on paper or in Apollo, as appropriate, and will take up to 30 minutes to complete (these

forms can be completed on paper and entered into Apollo at a later time). Timing of each questionnaire is as follows:

- *Modified Medical Research Council (MMRC)*, 1-5 minutes, interviewer-administered via paper form or DDE (**Appendix B**)
- *St. George's Respiratory Questionnaire (SGRQ)*, 20-25 minutes, self-administered via paper form (**Appendix C**)

There is a 15-minute wait time after the albuterol is administered and before the post-bronchodilation test. During this time, the site may administer the MMRC and/or the SGRQ. If a participant is approaching 30 minutes on the SGRQ, stop, do the post-bronchodilation test, and then continue with the questionnaire after testing is done.

All participants completing the SGRQ and MMRC must be consented before answering the questions.

Site staff should complete the *PFT Disposition Notification Form (PFTNOTI)* (**Appendix D**) regardless of whether the PFT was performed or not. Answers should be based on the results of the exam and questionnaire completion.

## L. TESTING PROCEDURES

### 1. PFT TESTING

The ndd EasyOne Pro testing system measures lung function with the flow-volume loop recorded, before and after bronchodilator administration. DLCO will be measured after bronchodilator administration using the automated single-breath procedure of the EasyOne Pro.

When starting a new spirometry exam, follow the steps outlined below. Most participants will have two sets of spirometry maneuvers performed, one before bronchodilation and one after.

If participant reports recent bronchodilator use (see below), then only one set of spirometry maneuvers is collected which will be considered "post-bronchodilator testing." Please note, the EasyOne Pro refers to the first spirometry done on each participant as the "Pre-bronchodilator spirometry" and this cannot be changed, even when the participant is already bronchodilated.

### 2. BLOODWORK

Hemoglobin and carboxyhemoglobin levels in the blood will need to be collected in order to analyze results of the DLCO test. The carboxyhemoglobin should be collected as close to the actual DLCO testing as possible, and must be collected on the same day as the PFT testing to maintain the best DLCO results possible. The *hemoglobin* values tested as part of the core WIHS visit can be submitted if preferred, as long as they are collected within 60 days of the PFT date and no hospitalizations or serious illnesses/conditions have occurred in the interim. See **Section M, Procedure after Visit** for information about the transfer of bloodwork results to WDMAC.

Data from the blood draw should be recorded on the *PFT Blood Specimen Collection Form* (PFT29) (**Appendix J**). For carboxyhemoglobin levels testing, sites should draw EDTA whole blood in a 4 mL lavender-top tube. This should be the first tube drawn and needs to be a dedicated tube for the carboxyhemoglobin test only. The tube cannot be opened. The tubes for carboxyhemoglobin should be shipped to the local lab at room temperature.

If hemoglobin needs to be tested on the same day as PFT testing, sites should draw EDTA whole blood in a separate 3 mL lavender-top tube. This should be the second tube drawn. The tubes for hemoglobin should be shipped to the local lab at room temperature.

Sites should ship all specimens to their local testing lab within the timeframe noted on the local lab guidelines for these clinical tests.

Results should be recorded on the *PFT Lab Results Form* (PFTLAB) (**Appendix K**) and entered into Apollo.

### 3. PRE- VS POST-BRONCHODILATION TESTING

As part of the screening process, staff should take a blood pressure and heart rate measurement from the participant. If the participant's systolic blood pressure is > 180 mm HG or her diastolic blood pressure is > 100 mm HG, ask the participant to rest for 5 minutes. After 5 minutes, repeat the blood pressure measurement. If the average of the two systolic blood pressure readings is still > 180 mm HG or the average of her diastolic blood pressure readings is > 100 mm HG, the participant is not eligible for PFT testing. The examiner will note this on Question A13 on the *PFT Screening Form* (PFTSCR).

During screening, staff will ask whether the participant has used a short acting bronchodilator within the last 4 hours and/or a long-acting bronchodilator in the last 12-24 hours on the *PFT Screening Form* (PFTSCR) (**Appendix A**). If participant answers "Yes" to any of Questions A15-A17, record the time taken, and then proceed with post-bronchodilator spirometry only. If the participants answers "No" to all three questions, staff will proceed with pre-bronchodilator testing and DLCO.

If the screening indicates that the participant's medication is still effective and the participant is already bronchodilated, then only one spirometry test should be performed, which will be considered post-bronchodilator spirometry.

- a) Pre-bronchodilator testing: Perform spirometry to ATS/ERS standards and as outlined below (**Pre-Bronchodilation Spirometry**).
- b) Post-bronchodilator testing: Repeat spirometry 15 minutes after inhalation of 4 puffs of albuterol delivered by a metered dose inhaler (MDI) with spacer. See **Post-Bronchodilation** below for details.

To determine if the participant is eligible for post-bronchodilator testing only, follow the prompts on the *PFT Screening Form* (PFTSCR). This decision is based on the participant reporting the use of an inhaler in the last 4, 12, or 24 hours in Questions A15-17.

If the participant reports an allergy to albuterol or levalbuterol, no bronchodilator will be given. Results will be recorded as pre-bronchodilator testing.

#### 4. PREPARATIONS

If possible (e.g., in a visit reminder letter or phone call), ask the participant not to smoke the day of their WIHS PFT visit, as it can interfere with the breathing tests. However, this is not required.

During the testing, the participant should be relaxed and should not wear tight clothing. It is recommended that the participant sit in a chair with arms. Watch the participant closely in the event that she becomes dizzy or lightheaded during the test.

After the blood draw and for the duration of the PFT testing, the participant should not take a break to smoke.

Spirometry and bronchodilator testing require active participation from the participant, so it is very important to explain and demonstrate all test maneuvers and leave time for participant questions. Explain the purpose of the testing thoroughly (Appendix E).

#### 5. SETTING UP THE NDD EASYONE PRO DEVICE

See **Section 2.3-2.4** of the EasyOne Pro Manual for details on how to set up the device and gas supply. Once the device has been set up, you can connect a keyboard and mouse directly to the machine's USB port. You will need to connect the printer via USB port as well. Detailed information on this is in **Section 2.6** of the EasyOne Pro Manual.

#### 6. PREPARE EQUIPMENT: START-UP AND CALIBRATION

1. Turn on the device. There should not be any warmup time needed.
2. Machine should display a **Login** screen, followed by **Startup** screen. Be sure to log in and out after each use so that the correct Examiner ID is attached to each pulmonary function test.
3. Be sure to compare the values on the gas cylinder with the values displayed by following the path **Utilities → Configuration →** before beginning.
4. Using the calibration adaptor, connect the sensor to the syringe. The piston must be fully inserted and at the stop position.
5. In the **Utilities** menu, click **Calibration Check**, then select **Multiflow**.
6. Wait until baseline has been set. Then execute one full inspiratory pump stroke followed by one full expiratory pump stroke.
7. Three trials each at different flow rates are required for the **Multiflow** calibration check.
8. You should see "**Accuracy Confirmed**" on the device along with the % deviation and the average flow velocity of the pump stroke. You should reach +/-3.5 % accuracy.
9. Equipment should be checked once daily, before first use. Value must be within calibration limits ( $\pm 3.5\%$ ). Calibration checks only need to be done on days the

device is used for testing. The site should maintain documentation of repairs, computer software or hardware updates or changes. If the equipment is altered or relocated, document calibration checks and quality-control procedures on equipment before further participant testing. The machine automatically calibrates all gas analyzers before each test.

## 7. ENTERING PARTICIPANT DEMOGRAPHICS

1. From the Main Menu, click **Patients** and add a new participant by selecting **New** in the bottom left corner of the **Patients** Screen.
2. You will be required to enter the following information to create a new Patient ID:
  - a. Patient ID (use WIHSID)
  - b. Last name (use WIHSID)
  - c. First name (use WIHSID)
  - d. Gender
  - e. Ethnicity
  - f. Year of Birth
  - g. Height
  - h. Weight
3. Once demographic information is entered, press **OK** to return to the participant list and select the correct participant. If data is entered incorrectly, it can be edited at a later date.

## 8. EXAMINERS: COACHING AND PROVIDING FEEDBACK

Examiners are encouraged to do the following when testing participants:

1. Demonstration by examiner of the FVC maneuver before participant's first attempt.
2. Vigorously coach to obtain a full inspiration followed by a "blast" at outset of maneuver.
3. Provide encouragement of complete exhalation by saying "squeeze everything out."
4. Observe participant throughout the maneuver.
5. Offer enthusiastic feedback to encourage maximal efforts.

The EasyOne Pro provides an integrated feedback system to the examiner during maneuvers; they receive an immediate score: "A / B" grade meets the most stringent 2005 ATS/ERS spirometry quality criteria, "C" meets less stringent 1994 ATS criteria, and "D / F" are not acceptable. In addition to a grade, the device also provides feedback suggestions after each maneuver, such as "Blow out longer" or "Take a deeper breath," thus helping examiners troubleshoot at the point of care.



## 9. PRE-BRONCHODILATION SPIROMETRY

1. Disconnect the DLCO valve assembly.
2. Insert the spirette so that the upwards pointing arrow on the spirette matches the arrow on the sensor. Be sure to leave plastic wrapper around mouthpiece of the spirette to avoid flow during initialization of the test.
3. Once you have entered the participant's demographic information, click on her Patient ID, followed by the "Test." You will see a screen with various tests available. To select a spirometry test, select FVL (ex/in).
4. Confirm the environmental measurements (Body Temperature & Pressure Saturated (BTPS) on the screen. Please note that the machine will also direct you to block the spirette (keep packaging on) until prompted. This is for the first trial only. It is to ensure baseline has been set.
5. Explain the purpose of the test as well as the test maneuver, as it is important for the participant to understand and participate fully. Because this will likely be the participant's first time using the EasyOne Pro to perform a spirometry test, it is important to explain the instructions fully and allow time for participant questions. It is important for the participant to maintain an upright position for the duration of the testing with her head upright (no leaning forward, bending head forward, etc.). A general description of the procedure for spirometry is below; see **Appendix E** for coaching tips and techniques:
  - a. Participant will need to breathe normally initially, then fill lungs fully, inhaling completely.
  - b. They will have a minimal pause (<1 second) with full lungs briefly, then exhale as forcefully and quickly as possible (within the first second), continuing to blow out until lungs are completely empty, maintaining an upright posture.
  - c. Once empty, participant will again inhale completely and rapidly and the examiner will manually stop the test.
  - d. This test will need to be completed successfully at least three times to ensure accuracy.
    - i. ATS/ERS spirometry guidelines for high-quality spirometry require 3 acceptable (defined below) and 2 reproducible tests. If such criteria cannot be obtained within 8 attempts, further testing will not be productive, and may be terminated at the judgment of the examiner. Inability to perform spirometry should be reported on the *PFT Disposition Form* because it may affect participation in the study.
6. Instruct the participant to put on the nose clip and sit upright, with both feet planted firmly on the floor. Once the trial starts, the monitor will display "**Setting Baseline, Avoid Flow.**"

7. When **“Start Test”** displays on the monitor, instruct the participant to remove the plastic wrap around the mouthpiece and place her teeth firmly around the mouthpiece. Ask her to place the spirette on top of her tongue and seal her lips around it to avoid leaks, making sure not to block the opening or bite down excessively.
8. The participant will perform the procedure as outlined above. Provide the participant with motivating feedback and remind her that this test has to be repeated successfully at least two more times.
  - a. For each additional trial, click **“Add Trial”** to start the process over again until three successful trials have been completed. Please note that trials can only be added for same-day testing. If a participant needs a break, she must complete the remaining trials during this same day.
9. After the third acceptable spirometry trial, the machine will display the message **“Session Complete.”** Let the participant know this part of the testing is over. They should be instructed to breathe normally and relax.
10. After bronchodilation, when you return to the spirometry (FVL) test, click **“Add Post”** rather than **“Add Trial.”**

#### 10. ACCEPTABILITY OF PFT TEST

1. During testing, a quality grade and variability information will be displayed. This will indicate the session quality and session interpretation.
2. After each trial, the screen will display a quality grade and system interpretation. Session comments can be added in the **Comment** section next to **Test Information**. The examiner should add comments here if a participant attempted to perform a trial but was unsuccessful, or refused to participate in any of the trials. This should also be noted on the *PFT Disposition Notification Form* (PFTNOTI) (**Appendix D**) at the end of testing.
3. The session will be graded with A, B, C, D, or F. Acceptable trials have the following characteristics:
  - a. Good start of test (sharp upward peak on flow-volume curve indicating deep, quick inhale).
  - b. Good end of test (plateau on volume-time graph indicating no more air is being exhaled).
  - c. Artifact free (no coughs, dips on flow-volume curve that indicate stopping exhalation prematurely).
4. An acceptable session is 3 acceptable trials with the 2 best having a FEV1 and FVC that are repeatable within 150 mL. Do not worry about these numbers, the machine will let you know when you have achieved this. At this time, a session complete message will be displayed.

## 11. ALBUTEROL ADMINISTRATION

1. Use albuterol (90 µg x 4 doses) via MDI with new spacer.
2. Shake MDI well.
3. Activate inhaler in air to check for adequate operation.
4. Attach spacer to MDI.
5. Instruct participant to blow out any remaining air in lungs and then insert the spacer mouthpiece into participant's mouth.
6. Instruct participant to inhale slowly; examiner activates inhaler during inspiration and delivers 1 puff of albuterol.
7. Have participant hold breath for 10 seconds before exhaling after each puff.
8. Wait 10-30 seconds and repeat process 3 more times, for a total delivery of 4 puffs of albuterol.
9. Wait at least 15 minutes after last inhalation before beginning the post-bronchodilator spirometry testing.
10. Use the **Albuterol Administration Checklist** in **Appendix E** for tips on this procedure.
11. While you are waiting to perform the post-bronchodilation spirometry (FVL) test, you may elect to administer the MMRC and/or SGRQ questionnaires.
12. If participant identifies a concern about side effects because of her health history (e.g., heart rate, tremor, history of arrhythmias), albuterol will not be used (i.e., only pre-bronchodilator set of spirometry maneuvers will be obtained), but this should be logged in the comments section of the EasyOne Pro and on the *PFT Screening Form* (PFTSCR).

After albuterol administration, the examiner should take another heart rate and blood pressure measurement from the participant. If the participant's systolic blood pressure is > 180 mm HG or her diastolic blood pressure is > 100 mm HG or her heart rate is > 100 beats per minute, the testing should be stopped. Discretion should be used to determine if the increase in blood pressure/heart rate is due to the albuterol and should be considered an adverse event or not. For example, if the participant's initial heart rate was 95 beats per minute and increases to 101 beats per minute post albuterol administration, this is likely not a drug reaction. Testing should still be stopped, however. If the participant's initial heart rate was 60 beats per minute and increases to 101 beats per minute post albuterol administration, it is more likely due to a drug reaction and testing should stop. The examiner will then fill out the *PFT Adverse Event Form* (PFTAER).

## 12. POST-BRONCHODILATION FOLLOWING PRE-BRONCHODILATION SPIROMETRY

Administer four puffs of albuterol by a metered dose inhaler (MDI) attached to a spacer (see above). Then repeat spirometry between 15-30 minutes after the albuterol inhalation was completed (15 minutes is preferred).

1. On the Main Screen, click **“Patients”** and select the appropriate participant. Before performing Bronchodilation testing (post-test), forced spirometry (pre-test) should already be measured, unless the participant is only eligible for Post-Bronchodilation Spirometry, so you will not need to add participant information for this test again. In the event that the participant is not eligible for albuterol administration, you will have to select a new patient as outlined above and note in the session comments section that the test is a “Post-only” test.
2. Once you have selected the appropriate participant, select the **“FVL Test”** as you did for forced spirometry testing earlier. In this case, you will select **“Add Post”** rather than **“Add Trial”** in the bottom right-hand corner of the screen since you are adding a new trial post-bronchodilation with albuterol. You will be able to see all of the **“Pre-Tests”** performed earlier.
3. Conduct the test as outlined in the **Pre-Bronchodilation Spirometry** section of this manual above and use the **Coaching Tips/ Techniques in Appendix E** as a resource. An acceptable session is 3 acceptable trials with the 2 best having a FEV1 and FVC that is repeatable within 150 mL. Do not worry about these numbers, the machine will let you know when you have achieved this. At this time, a session complete message will be displayed.

### 13. POST-BRONCHODILATION WITHOUT PRE-BRONCHODILATION SPIROMETRY

In the event that a participant is not eligible for bronchodilation per the *PFT Screening Form* (PFTSCR) (**Appendix A**), examiners will need to select **“Add Trial”** and perform the Pre-Bronchodilation Spirometry as outlined above (but note that this is actually a post test). Examiners will need to note in the EasyOne Pro session comments section that the participant was not eligible for pre-bronchodilation spirometry and the session reflects post-bronchodilation spirometry. They will also note this on the *PFT Disposition Notification Form* (PFTNOTI) after all testing is complete (**Appendix D**).

### 14. EVALUATION AND REPORTING OF SPIROMETRY

1. Acceptability (within maneuver evaluation): Three acceptable tests are required for an adequate spirometry maneuver. Examples of acceptability criteria are listed below, along with suggested criteria for implementing computerized checks.
  - a. Slow start of test: Participant did not begin her initial peak flow early enough; repeat, coaching for a more forceful and abrupt start (“BLAST it out”). This error occurs when volume at the back extrapolated zero-time is more than 5% of the FVC or greater than 150 mL.
  - b. Cough: This causes abrupt irregularities in flow, and is a reason to reject the test when it occurs during the first second of the effort. Coach the participant to make the effort without coughing.
  - c. Abrupt end of test: At the end of exhalation, the participant stopped blowing out too abruptly, ending her effort too soon. Coach the

participant to maintain her expiratory effort to the very end until told to stop by the examiner.

- d. Short expiratory time: Participant did not continue her expiration for at least 6 seconds or did not reach a volume plateau. In participants with severe COPD, the expiration often does not reach a plateau in reasonable time. In this case, 6 seconds of effort is the minimal duration of effort but 10 to 12 seconds of effort is reasonable.
  - e. Low peak flow: The participant did not achieve an adequately forceful blast. Repeat the effort, coaching to blow harder and faster if possible.
2. Reproducibility (between maneuver evaluations): Reproducibility criteria are used to determine when more than 3 acceptable FVC maneuvers are needed. The nnd EasyOne Pro will indicate if the results do not meet reproducibility quality.
  3. Abnormal Spirometry Review: A pulmonologist at each site will review printed results at regular intervals. If any abnormal results are discovered during this testing, a member of the research team will notify the participant or the participant's primary care physician, who will assess the need to provide additional evaluation.

#### 15. DLCO (POST-TEST)

This test should be completed after the post-bronchodilation spirometry.

1. To perform this test, you will need to attach the DLCO barriette to the DLCO Unit, making sure that the highlighted arrow connects correctly to the sensor. The barriette is necessary to avoid contamination of the tubing of the DLCO unit.
2. Mount the DLCO unit onto the flow sensor before performing this test.
3. On the Home Screen, click "**Select Patient**" and select the appropriate participant. Before performing a DLCO test, Spirometry (pre or post-bronchodilator only in some cases) should already be measured, so you will not need to add a new patient for this test.
4. On the screen, select DLCO to begin testing. In the BTPS (Body Temperature & Pressure Saturated) window, you can confirm the humidity, temperature, and atmospheric pressures by selecting "**Confirm.**" Initializing and gas flushing will take place, roughly 20-30 seconds, and the monitor will display "**Initializing...**" and "**Test Preparation...**" until it is ready for the participant to begin breathing normally (**Tidal Breathing**).
5. Attach the nose clip to the participant and explain the test procedures thoroughly, allowing time for practice and/or questions. Be sure the participant is sitting upright with her feet placed firmly on the floor. General instructions are below, but see **Appendix E for Coaching Tips/ Techniques**:

- a. Breathe normally for a few breaths, avoiding deep inspirations, then exhale completely (unforced exhalation) until the sensor clicks or the examiner instructs you to stop exhaling.
  - b. Inhale deeply and quickly (~2 seconds), and begin holding breath for 10 seconds.
  - c. Exhale normally (3-5 seconds) and inhale again to stop the test.
  - d. This test will need to be performed a minimum of two times successfully.
6. During initialization of the test (after you press **Start**), direct the sensor away from the participant, allowing the equipment to automatically calibrate.
7. When the screen displays the **“Tidal breathing”** message, instruct the participant to hold the sensor straight in front of her mouth, and insert the spirette in between her teeth, allowing her lips to seal around the spirette. Instruct the patient to avoid blockage of the opening with her tongue and teeth, to avoid leaks, or biting down excessively. After normal, steady breathing, for 3-4 breaths, the **Activate** button appears.
8. Instruct the participant to fully exhale. During exhalation, press **“Activate.”** The valve will automatically close at the end of exhalation and you will hear a clicking sound. Make sure the valve is closed before proceeding with the next step.
9. Then instruct the participant to inhale fully and quickly until her breathing curve surpasses the horizontal blue dotted line (where FVC ~85%) but before the curve reaches the vertical blue dotted line. Upon full inhalation, instruct the participant to hold her breath for 10 seconds. A display on the screen will count down time remaining for this portion of the testing.
10. After 10 seconds, the valve will open and the patient should exhale normally for 3-5 seconds (try to avoid unnaturally rapid/slow exhalation) and inhale into the spirette again to stop the test. You will know the test has stopped when you see the message **“Good Effort”** on the display screen. Provide the participant with motivational feedback on the successful completion of Trial 1 of the DLCO testing.
  - a. Wait time between trials (remember that there are only 2 successful trials needed for DLCO Testing) will be displayed on the monitor, but must be at least 4-5 minutes to allow test gas to eliminate from lungs. The device will alert you when four minutes has passed. The test should not be repeated more than five times consecutively on one participant.
  - b. In participants with severe obstructive lung disease, a longer interval (10 minutes) between repeat testing should be allowed. Generally, the examiner should allow the participant adequate time between testing (i.e., until they say they are ready to perform the next trial).
11. Successful completion of the test should display an output. The various steps in the DLCO procedure are highlighted and distinguished by color.

## 16. ADVERSE EVENT

- Definition: An “Adverse Event” is a significant medical event which is felt to be at least possibly related to the research study.
- Example: Shortness of breath that causes the participant to be unable to continue the PFT testing.
- Describe the adverse event in the Adverse Event Form (PFTAER) (**Appendix F**) if the participant reports an adverse event while participating in the PFT procedure

## 17. PFT DISPOSITION FORM (Appendix D)

- Complete this form following the PFT.
- Indicate whether the testing was performed successfully (Pre-Bronchodilation, Post-Bronchodilation, DLCO).
- Indicate the participant’s preference for having PFT result letters sent to herself and/or her doctor.

## M. PROCEDURE AFTER VISIT

### 1. PFT DATA TRANSFER

#### a. **Timing**

Each site is expected to upload their Easy on-PC data file at the end of each day. There is no need for sites to select individual tests; all tests in the Easy on-PC database will be sent to the Reading Center for cleaning and quality control.

#### b. **Site Responsibilities**

Sites should upload all PFT testing results to their remote site directory (altwihs, bkwih, bxwihs, chwihs, dcwihs, miawih, mswih, sfwihs, uabwihs, and uncwihs) for Reading Center review. See more detailed information below.

#### c. **Reading Center Responsibilities**

- Retrieve the PFT data uploaded to each site’s remote directory
- Process and clean the testing results data to ensure quality control
- Send cleaned data to WDMAC via a clinic-specific ACCESS database
- Create reports for each site examiner based on quality of PFT testing results

#### d. **WDMAC Responsibilities**

- Provide Reading Center access to all site results (via PFT folder in remote site directories) and email Reading Center on a daily basis regarding new database uploads by sites
- Receive the cleaned PFT data from the Reading Center and generate data edits

- Communicate with sites and Reading Center regarding data edits and generate data file once complete
- Compare number of participants reported to have PFT testing done to the actual data received by the Reading Center (inform sites and Reading Center of any discrepancies)
- Generate monthly progress reports of PFT progress for the Pulmonary Working Group (PWG)

#### e. Steps for Data Transfer to WDMAC

1. The full PFT database should be exported to a removable drive (e.g., USB port) at the end of each day (i.e., cumulative transmission). On the home screen, select **Utilities** → **Advanced**. Enter the password “8005” and login. Then choose **Export Data** → **Patient Data** (uncheck everything else) → **Export**. Browse until you find the removable drive that you will be using, select it, and hit **OK**. You will receive a message that the export was completed successfully. This version should be maintained at the site and not uploaded to WDMAC.
2. Make a copy of the full PFT database. This version will be uploaded to WDMAC. Use the following naming convention:
  - a. **Site#\_DATE(YYYYMMDD)\_WIHS** (e.g., 10\_20180221\_WIHS)
  - b. Use the following site numbers:
    - i. 10 = Bronx
    - ii. 20 = Brooklyn
    - iii. 30 = Washington, DC – Georgetown
    - iv. 31 = Washington, DC – Inova
    - v. 32 = Washington, DC – Montgomery County
    - vi. 50 = UCSF – Scott Street
    - vii. 51 = UCSF - EBAC
    - viii. 60 = Chicago - Main
    - ix. 61 = Chicago - Rush
    - x. 80 = UNC – Raleigh
    - xi. 81 = UNC – Durham
    - xii. 82 = Emory
    - xiii. 83 = Miami
    - xiv. 84 = UAB
    - xv. 85 Jackson



3. Upload the full PFT database to WDMAC using FTP client software such as “SSH Secure File Transfer” or “FileZilla FTP Client.” Securely log in to WDMAC’s FTP server using the username and password assigned to your site. Use the host name **statepi5.jhsph.edu** and the port **22**.
4. After you log in, you should see a list of directories and files on the computer you are using in the left pane, as well as a list of directories on WDMAC’s server in the right pane. On the WDMAC server (right pane), navigate to the directory called **PFT**. Click and drag the file you want to transfer from the left pane into **PFT**.

**f. Bloodwork Data and Results**

Carboxyhemoglobin must be collected on the same date as the PFT testing. Hemoglobin from the WIHS visit can be used as long as it was collected within 60 days of the PFT data and no hospitalization or serious illness/conditions have occurred in the interim. If the hemoglobin result from the WIHS visit cannot be used, hemoglobin will need to be collected on the date of the PFT testing.

Sites will enter data from the PFT29 into Apollo in real time on the day of the PFT testing. Lab results will be entered into Apollo on the PFTLAB form as they are received at the sites. It is necessary for these results to be entered in a timely manner as the data is required for the Reading Center to properly calculate values.

WDMAC will download the lab results (PFTLAB) at least every two weeks to provide to the Reading Center.

**g. Questionnaire Data**

Sites will enter questionnaire data in Apollo, which will be downloaded by WDMAC as needed.

**h. Data Transfer for PFT Certification**

Sites will transfer their certification data from the Easy on-PC at the end of each day for Reading Center review and certification following the instructions listed above. Examiners are required to submit 10 PFT sets of sufficient quality on at least 10 different people. The naming convention for the file will be:

**999\_xxx\_EXID**

‘xxx’ are sequential, 3-place digits, beginning with a 001 and increasing by 1 each time the examiner starts a new set of certification test sets (10 sets required).

‘EXID’ is the unique examiner ID assigned and distributed by WDMAC.

Example: 999\_002\_142

**i. Clean PFT Data**

The cleaned PFT data will be transferred back to WDMAC and a data file will be created to store this information. From the cleaned data, reports for the data received/expected will be generated for all sites and provided to each site and the Reading Center.

## 2. PROCEDURE FOR PRODUCING RESULTS AND RESULTS LETTERS

Sites will be able to print reports for local pulmonologist review, or alternatively export and send the pdf electronically. There are several layouts available for the EasyOne Pro display (1-2 page summaries), and sites will need to decide locally with their pulmonologist which is the best for their interpretation of the results. (See **Appendix G** for a recommended EasyOne Pro Report format).

At regular intervals (weekly suggested), sites will:

- Collect PFT hard copies.
- Send hardcopy or electronic report to local reading pulmonologist for reading.
- Record-keeping as per site (example: count, date sent, person sending).

Reading Pulmonologist Procedure (NOTE: Centers may tailor procedures)

- Receive regular delivery of PFT hard copies or electronic copies (recommended weekly).
- Handwrite, send electronically, or use another method to indicate the type of result letter that should be produced; confirm with signature or other method.
  - Suggest establishing deadlines for turnaround times by the pulmonologists.
- Return printout to site or send electronic indication of final interpretation to be used for result letter.
- Sites coordinate with their local pulmonologist for clinical interpretation of the research test results.
- Use pulmonologists' final interpretation to generate result letters.

Site Procedure

- Receive delivery of PFT hard copies or electronic version of reading pulmonologist signature.
- Use Final Interpretation Notes to produce results letter (**Appendix I**).
  - Suggest establishing deadlines.
  - Site may select to include more specific findings in participant results letter by using terms written on the PFT printout along with the description of these terms (see **Appendix H**: Glossary of PFT Terms).

Participant Result Letter: Each site will create a customized participant letter using the Participant Letter Templates (**Appendix I**).

Doctor Result Letter: Each site will create a customized doctor's letter using the Doctor Letter Templates, which will include findings per local pulmonologist (**Appendix I**).

Sites will be given the option to opt out of sending normal results letters to participants and doctors. If the site chooses not to send normal results letters, the participant must be told that she will be notified, by either phone or letter, if the local pulmonologist reports any abnormal findings.

**APPENDIX A**

**WOMEN'S INTERAGENCY HIV STUDY  
FORM PFTSCR: PFT SCREENING FORM**

- A1. PARTICIPANT ID:                   |\_|-|\_|\_|-|\_|\_|\_|\_|-|\_|\_|
- A2. WIHS CORE VISIT NUMBER DURING WHICH PFT IS COMPLETED:   |\_|\_|
- A3. FORM VERSION:                   **04/01/18**
- A4. FORM COMPLETED BY:         |\_|\_|\_|\_|
- A5. DATE:                             |\_|\_|\_| / |\_|\_|\_| / |\_|\_|\_|  
  M                   D                   Y

**INSTRUCTIONS:** ASK THE PARTICIPANT THE FOLLOWING SET OF QUESTIONS BEFORE SPIROMETRY/DLCO TESTING TO DETERMINE ELIGIBILITY AND TO INFORM TESTING RESULTS.

**PROMPT:** IF THE PARTICIPANT ANSWERS YES TO ANY OF QUESTIONS A6-A13, SKIP TO THE END OF THE FORM. THE PARTICIPANT IS NOT ELIGIBLE FOR SPIROMETRY OR DLCO.

- A6. Are you currently experiencing a respiratory infection such as pneumonia, bronchitis or sinusitis, or symptoms such as dyspnea (difficulty breathing), cough, fever (temperature > 100.4°F [38°C])?  
      YES.....1 **(END)**  
      NO .....2
- A7. Are you currently being treated for tuberculosis?  
      YES.....1 **(END)**  
      NO .....2
- A8. Have you had pneumothorax (collapsed lung) within the past 3 months?  
      YES.....1 **(END)**  
      NO .....2
- A9. Have you had a myocardial infarction (heart attack) within the past 3 months?  
      YES.....1 **(END)**  
      NO .....2
- A10. During the past 4 weeks, have you experienced or been told you have a heart condition (e.g., tachycardia [fast heart rate, resting heart rate > 110], angina [chest pain/discomfort], or unstable arrhythmia [irregular heart beat])?  
      YES.....1 **(END)**  
      NO .....2
- A11. Do you currently have a retinal detachment (when the retina in your eye is pulled away from its normal position)?  
      YES.....1 **(END)**  
      NO .....2

WIHSID

A12. Have you had surgery on your eyes, chest, or abdomen in the past 3 months?

YES.....1 (END)

NO .....2

A13. DOES THE PARTICIPANT HAVE UNCONTROLLED HYPERTENSION (DEFINED AS SYSTOLIC > 180 MM HG OR DIASTOLIC > 100 MM HG FROM AN AVERAGE OF TWO OR MORE READINGS)?

YES.....1 (END)

NO .....2

A14. Have you ever had an allergic reaction to albuterol or levalbuterol?

YES.....1

NO .....2

**PROMPT:** IF PARTICIPANT REPORTS AN ALLERGIC REACTION TO ALBUTEROL OR LEVALBUTEROL, NO BRONCHODILATOR WILL BE GIVEN. RESULTS WILL BE RECORDED AS PRE-BRONCHODILATOR TESTING.

A15. In the last 4 hours, have you used a rescue intermediate-acting inhaled beta-agonist, including one of the following:

Albuterol (Proair, Ventolin, Proventil) .....1

Levalbuterol (Xopenex)..... 2

Ipratropium (Atrovent or Combivent)..... 3

None of the above.....4 (A16)

Other..... 5 (SPECIFY)

**SPECIFY:** \_\_\_\_\_

**PROMPT:** IF PARTICIPANT REPORTS THE USE OF ANY DRUGS LISTED IN QUESTION A15 IN THE LAST 4 HOURS, PARTICIPANT HAS ALREADY BEEN BRONCHODILATED. NO PRE-BRONCHODILATOR TESTING WILL BE PERFORMED AND NO ALBUTEROL WILL BE GIVEN. RESULTS WILL BE RECORDED AS POST-BRONCHODILATOR TESTING.

A15a. Time taken? |\_\_|\_\_|:|\_\_|\_\_| AM..... 1

PM..... 2

A16. In the last 12 hours, have you used a rescue long-acting inhaled beta-agonist, including one of the following:

Budesonide + formoterol (Symbicort) .....1

Fluticasone + salmeterol (Advair)..... 2

Mometasone + formoterol (Dulera)..... 3

Glycopyrrolate + formoterol (Bevespi)..... 4

Glycopyrrolate + indacaterol (Utibron)..... 5

Salmeterol (Serevent)..... 6



A18. When did you last smoke (cigarette, cigar, pipe, marijuana)?

- I don't smoke.....1 **(A19)**
- More than one day ago..... 2 **(A19)**
- Yesterday..... 3 **(A19)**
- Today..... 4

A18a. How many hours ago did you last smoke today? |\_\_|\_\_| HOURS

A19. Have you consumed any caffeinated beverages or medications (e.g., Anacin, Darvon, Esgic, Excedrin, Fiorinal, Fioricet, NoDoz, Norgesic, Vivarin) in the last 8 hours?

- YES.....1
- NO .....2

A20. Have you consumed any food or beverages containing alcohol in the last 8 hours?

- YES.....1
- NO .....2

A21. Have you used any antihistamines, oral decongestants, or cold remedies in the last 48 hours?

- YES.....1
- NO .....2

**APPENDIX B**

**WOMEN'S INTERAGENCY HIV STUDY  
FORM MMRC: MODIFIED MEDICAL RESEARCH COUNCIL**

- A1. PARTICIPANT ID:                   |\_|-|\_|\_|-|\_|\_|\_|\_|-|\_|\_|
- A2. WIHS CORE VISIT NUMBER DURING WHICH PFT IS COMPLETED:   |\_|\_|
- A3. VISIT DATE:                    |\_|\_|/|\_|\_|/|\_|\_|  
  M  D  Y
- A4. FORM VERSION:                   **04/01/18**
- A5. FORM COMPLETED BY:       |\_|\_|\_|\_|

**INSTRUCTIONS:** THIS FORM SHOULD BE COMPLETED BETWEEN PRE AND POST-BRONCHODILATION TESTING.

- A6. Please answer YES or NO for each of the following questions:
- |   | <u>YES</u> | <u>NO</u> |
|---|------------|-----------|
| a. Do you get breathless with strenuous exercise?.....  | 1          | 2         |
| b. Do you get short of breath when hurrying on level ground or up a slight hill? .....  | 1          | 2         |
| c. Do you walk slower than people your same age on level ground because of breathlessness or do you have to stop for breath when walking at your own pace on level ground?..... | 1          | 2         |
| d. Do you stop for breath after walking 100 yards or after a few minutes on level ground?.....  | 1          | 2         |
| e. Are you too breathless to leave the house?.....  | 1          | 2         |

- A7. In general, would you say your health is (select one):
- Excellent .....1
  - Very good .....2
  - Good.....3
  - Fair .....4
  - Poor .....5

- A8. How many days **during the previous week** did you perform lower-extremity endurance exercises such as walking or cycling?                   |\_|\_| days **(if 0 days END)**
- a. If greater than 0, how many minutes each day?       |\_|\_|\_|\_| minutes



**APPENDIX C**

**WOMEN'S INTERAGENCY HIV STUDY  
FORM SGRQ: ST. GEORGE'S RESPIRATORY QUESTIONNAIRE**

A1. PARTICIPANT ID:                   |\_|-|\_|\_|-|\_|\_|\_|\_|-|\_|\_|

A2. WIHS CORE VISIT NUMBER DURING WHICH PFT IS COMPLETED:   |\_|\_|

A3. VISIT DATE:                   |\_|\_|/|\_|\_|/|\_|\_|  
  M                   D                   Y

A4. FORM VERSION:                   **04/01/18**

A5. FORM COMPLETED BY:       |\_|\_|\_|\_|

**INSTRUCTIONS TO PARTICIPANT:** This questionnaire is designed to help us learn much more about how your breathing is troubling you and how it affects your life. We are using it to find out which aspects of your illness cause you the most problems, rather than what the doctors or nurses think your problems are.

Please read the instructions carefully and ask if you do not understand anything. Do not spend too long deciding about your answers.

Before completing the rest of the questionnaire:

A6. Please select one response to show how you describe your current health:

- Very good .....1
- Good.....2
- Fair .....3
- Poor.....4
- Very Poor .....5

**PART 1**

Questions about how much chest trouble you have had over the past 3 months (*Select one response for each question*).

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A7. Please ask yourself, "Over the <u>past 3 months</u> , I have...."	Most days a week	Several days a week	A few days a month	Only with chest infection	Not at all
a. coughed:	1	2	3	4	5
b. brought up phlegm (sputum):	1	2	3	4	5
c. had shortness of breath:	1	2	3	4	5
d. had attacks of wheezing:	1	2	3	4	5

A8. During the <u>past 3 months</u> , how many severe or very unpleasant attacks of chest trouble have you had? ( <i>Select one response</i> )	More than 3 attacks	3 attacks	2 attacks	1 attack	No attacks
	1	2	3	4	5 (skip to A9)
a. How long did the worst attack of chest trouble last? ( <i>Select one response</i> )	A week or more	3 or more days	1 or 2 days	Less than a day	
	1	2	3	4	

A9. Over the <u>past 3 months</u> , in an average week, how many good days (with little chest trouble) have you had? ( <i>Select one response</i> )	No good days	1 or 2 good days	3 or 4 good days	Nearly every day is good	Every day is good
	1	2	3	4	5

A10. If you have a wheeze, is it worse in the morning?

YES.....1  
 NO..... 2  
 Not applicable ..... 3 (**check if answered "not at all" to Question A7d**)

**PART 2**

**Section 1**

A11. How would you describe your chest condition?

The most important problem I have..... 1  
 Causes me quite a lot of problems..... 2  
 Causes me a few problems..... 3  
 Causes me no problem..... 4

A12. If you have ever had paid employment, please choose one of these answers:

- My chest trouble made me stop work altogether..... 1
- My chest trouble interferes with my work  
or made me change my work..... 2
- My chest trouble does not affect my work..... 3

**Section 2**

The following are questions about what activities make you feel breathless these days. For each item, please answer either TRUE or FALSE as it applies to you.

Activity	TRUE	FALSE
A13. Sitting or lying still	1	2
A14. Getting washed or dressed	1	2
A15. Walking around the house	1	2
A16. Walking outside on level	1	2
A17. Walking up a flight of stairs	1	2
A18. Walking up hills	1	2
A19. Playing sports or games	1	2

**Section 3**

Some more questions about your cough or breathlessness these days. For each item, please answer either TRUE or FALSE as it applies to you.

	TRUE	FALSE
A20. My cough hurts	1	2
A21. My cough makes me tired	1	2
A22. I am breathless when I talk	1	2
A23. I am breathless when I bend over	1	2
A24. My cough or breathing disturbs my sleep	1	2
A25. I get exhausted easily	1	2

**Section 4**

Questions about other effects that your chest trouble may have on you these days. For each item, answer either TRUE or FALSE as it applies to you.

	TRUE	FALSE
A26. My cough or breathing is embarrassing in public	1	2
A27. My chest trouble is a nuisance to my family, friends or neighbors	1	2
A28. I get afraid or panic when I cannot get my breath	1	2
A29. I feel I am not in control of my chest problems.	1	2
A30. I do not expect my chest to get any better	1	2
A31. I have become frail or an invalid because of my chest	1	2
A32. Exercise is not safe for me	1	2

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	TRUE	FALSE
A33. Everything seems too much of an effort	1	2

A34. Are you currently using any breathing medications (e.g., inhaler or oxygen)?  
YES.....1  
NO..... 2

**If you aren't using any breathing medications, go to Section 6.**

**Section 5**

Questions about your medication. For each item, please answer either TRUE or FALSE as it applies to you.

	TRUE	FALSE
A35. My medication does not help me much	1	2
A36. I get embarrassed using my medication in public	1	2
A37. I have unpleasant side effects from my medication	1	2
A38. My medication interferes with my life a lot	1	2

**Section 6**

These are questions about how your activities might be affected by your breathing. For each question, please answer TRUE if one or more parts apply to you because of your breathing. Otherwise, answer FALSE.

	TRUE	FALSE
A39. I take a long time to get washed or dressed	1	2
A40. I cannot take a bath or shower, or I take a long time	1	2
A41. I walk slower than other people, or else I stop for rests	1	2
A42. Jobs such as housework take a long time, or I have to stop for rests	1	2
A43. If I walk up one flight of stairs, I have to go slowly or stop	1	2
A44. If I hurry or walk fast, I have to stop or slow down	1	2
A45. My breathing makes it difficult to do things such as walk up hills, carrying things up stairs, light gardening such as weeding, dance, bowl, or play golf	1	2
A46. My breathing makes it difficult to do things such as carry heavy loads, dig in the garden or shovel snow, jog or walk at 5 miles per hour, play tennis, or swim	1	2
A47. My breathing makes it difficult to do things such as very heavy manual work, run, cycle, swim fast, or play competitive sports	1	2

**Section 7**

We would like to know how your chest usually affects your daily life. Please answer either TRUE or FALSE as it applies to you because of your chest trouble. Remember that TRUE only applies to you if you cannot do something because of your breathing.

	TRUE	FALSE
A48. I cannot play sports or games	1	2
A49. I cannot go out for entertainment or recreation	1	2
A50. I cannot go out of the house to do the shopping	1	2
A51. I cannot do the housework	1	2
A52. I cannot move far from my bed or chair	1	2

Here is a list of other activities that your chest trouble may prevent you doing. You do not have to choose; they are just to remind you of ways in which your breathlessness may affect you.

- Going for walks or walking the dog
- Doing things at home or in the garden
- Sexual intercourse
- Going out to church, pub, club or place of entertainment
- Going out in bad weather or into smoky rooms
- Visiting family or friends or playing with children

A53. Please write in any other important activities that your chest trouble may stop you from doing **(leave blank if n/a)**.

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A54. Choose (only one) which you think best describes how your chest trouble affects you:

- It does not stop me doing anything I would like to do..... 1
- It stops me doing one or two things I would like to do..... 2
- It stops me doing most of the things I would like to do..... 3
- It stops me doing everything I would like to do..... 4

**APPENDIX D**

**WOMEN'S INTERAGENCY HIV STUDY  
FORM PFTNOTI: PFT DISPOSITION NOTIFICATION FORM**

A1. PARTICIPANT ID:                   |\_|-|\_|\_|-|\_|\_|\_|\_|-|\_|

A2. WIHS CORE VISIT NUMBER DURING WHICH PFT IS COMPLETED:   |\_|\_|

A3. FORM VERSION:                   **04/01/18**

A4. FORM COMPLETED BY:       |\_|\_|\_|

A5. DATE:                           |\_|\_|/|\_|\_|/|\_|\_|  
  M          D          Y

A6. DID THE PARTICIPANT CONSENT TO PARTICIPATE IN THE PFT STUDY?

YES.....1 **(A7)**

NO .....2

A6a. IF NO, WHY NOT:

PARTICIPANT NOT ELIGIBLE FOR SPIROMETRY OR

DLCO TESTING AT THS TIME.....1 **(END)**

HAS HAD PFT PREVIOUSLY..... 2 **(END)**

SAFETY CONCERN..... 3 **(END)**

INSUFFICIENT TIME OR ROOM NOT AVAILABLE..... 4 **(END)**

NOT INTERESTED/REFUSED..... 5 **(END)**

OTHER..... 6 **(SPECIFY)**

**SPECIFY:** \_\_\_\_\_

A7. DID PARTICIPANT COMPLETE THE MMRC QUESTIONNAIRE?

YES.....1 **(A8)**

NO .....2

A7a. IF NO, WHY NOT: \_\_\_\_\_

A8. DID PARTICIPANT COMPLETE THE SGRQ QUESTIONNAIRE?

YES.....1 **(A9)**

NO .....2

A8a. IF NO, WHY NOT: \_\_\_\_\_

A9. WAS THE PRE-BRONCHODILATION SPIROMETRY TEST SUCCESSFULLY COMPLETED?

YES.....1 **(A10)**

NO .....2

A9a. IF NO, WHY NOT:

- PARTICIPANT NOT ELIGIBLE FOR PRE-BRONCHODILATION SPIROMETRY (PREVIOUS BRONCHODILATION) .....1
- HARDWARE MALFUNCTION..... 2
- SAFETY CONCERN.. .....3
- NO TIME..... 4
- ROOM NOT AVAILABLE ..... 5
- NOT INTERESTED/REFUSED ..... 6
- LACK OF SUPPLIES..... 7
- HAS HAD PFT PREVIOUSLY..... 8
- PARTICIPANT BEGAN TESTING BUT UNABLE TO COMPLETE..... 9
- PARTICIPANT BEGAN TESTING BUT REFUSED TO COMPLETE..... 10
- OTHER..... 11 (SPECIFY)

**SPECIFY:** \_\_\_\_\_

A9b. WERE ANY PRE-BRONCHODILATION SPIROMETRY DATA COLLECTED (IF PARTIALLY COMPLETED)?

- YES.....1
- NO .....2

A10. WAS ALBUTEROL ADMINISTERED?

- YES.....1
- NO .....2 (A10b)

A10a. TIME OF ALBUTEROL ADMINISTRATION: |\_\_|\_\_| : |\_\_|\_\_| AM.....1  
 PM.....2 (A11)

A10b. PRIMARY REASON ALBUTEROL NOT ADMINISTERED:

- PARTICIPANT HAD RECENTLY TAKEN A BRONCHODILATOR..... 1
- NO TIME..... 2
- SAFETY CONCERN..... 3
- NOT INTERESTED..... 4

A10c. COMMENTS ABOUT ALBUTEROL: \_\_\_\_\_

\_\_\_\_\_

A11. WAS THE POST-BRONCHODILATION SPIROMETRY TEST SUCCESSFULLY COMPLETED?

- YES.....1 **(A12)**
- NO .....2

A11a. IF NO, WHY NOT:

- HARDWARE MALFUNCTION..... 1
- SAFETY CONCERN ..... 2
- NO TIME..... 3
- ROOM NOT AVAILABLE..... 4
- NOT INTERESTED/REFUSED ..... 5
- LACK OF SUPPLIES..... 6
- HAS HAD PFT PREVIOUSLY..... 7
- PARTICIPANT BEGAN TESTING BUT  
UNABLE TO COMPLETE..... 8
- PARTICIPANT BEGAN TESTING BUT  
REFUSED TO COMPLETE..... 9
- OTHER..... 10 **(SPECIFY)**

**SPECIFY:** \_\_\_\_\_

A11b. WERE ANY POST-BRONCHODILATION SPIROMETRY DATA COLLECTED (IF PARTIALLY COMPLETED)?

- YES.....1
- NO .....2

A12. WAS THE DLCO TEST SUCCESSFULLY COMPLETED (SELECT N/A IF SITE IS NOT DOING DLCO)?

- YES.....1 **(A13)**
- NO .....2
- N/A .....3 **(A13)**

A12a. PRIMARY REASON DLCO NOT COMPLETED:

- HARDWARE MALFUNCTION..... 1
- SAFETY CONCERN ..... 2
- NO TIME..... 3
- ROOM NOT AVAILABLE..... 4
- NOT INTERESTED/REFUSED ..... 5
- LACK OF SUPPLIES..... 6
- HAS HAD PFT PREVIOUSLY..... 7
- PARTICIPANT BEGAN TESTING BUT  
UNABLE TO COMPLETE..... 8
- PARTICIPANT BEGAN TESTING BUT  
REFUSED TO COMPLETE..... 9
- OTHER..... 10 **(SPECIFY)**



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**SPECIFY:** \_\_\_\_\_

A12b. WERE ANY DLCO DATA COLLECTED (IF PARTIALLY COMPLETED)?

YES.....1

NO..... 2

A13. WILL RESULTS LETTER BE SENT TO:

YES      NO

DOCTOR..... 1      2

PARTICIPANT..... 1      2

A14. EXAMINER NAME (FORMAT: NAME, EXAMINER ID, SITE NAME):

\_\_\_\_\_

**APPENDIX E: COACHING TIP & TECHNIQUES, ALBUTEROL CHECKLIST**

Action	Coaching Tip/ Technique
<b>Spirometry Testing (FVL) Purpose: We are going to do a breathing test to see how much air your lungs hold and how fast you can blast all of that air out.</b>	
Before test begins	Explain test maneuver fully & <u>let participant know it's OK to forget</u> , you will coach them ( <b>Demonstrate the actions while you are explaining</b> ): -Breathe normally for 3-5 breaths, making sure lips sealed tightly around spirette -Then fill lungs fully and rapidly, holding with a very minimal pause (<1s) -Exhale rapidly and forcefully until lungs are COMPLETELY empty -Breathe in again to stop the test -Repeat this procedure at least 2 more times for a total of 3 acceptable trials
Normal breathing	"Now take a <b>deep breath in</b> " or " <b>fill your lungs up, up, up, up, up</b> "
Lungs full (sitting upright, shoulders back)	"Now <b>blast out</b> ", " <b>Blow! Blow! Blow!</b> " " <b>Push, push, push!</b> "
While Blasting out (sitting upright, shoulders back)	" <b>keep going, keep going, keep going</b> "
Once lungs empty	" <b>Good job!</b> Now take a deep breath in & relax"
After trial has finished	It's important to <b>motivate the participant</b> throughout the testing, especially between trials
<ul style="list-style-type: none"> <li>• Imagery is important for participants to understand the maneuvers:                             <ul style="list-style-type: none"> <li>○ Take the deepest breath in that you can, imagine you're being pushed overboard and have to take a deeeeeeeep breath in</li> <li>○ Now blast out, blast out, empty your lungs like a deflating balloon, all the way out</li> </ul> </li> <li>• Encouragement is key to:                             <ul style="list-style-type: none"> <li>○ Ensuring the inhalation is deep (lots of air to exhale)</li> <li>○ Ensuring the exhalation is rapid (steep curve) and full (plateau at the end of the volume-time graph)</li> </ul> </li> </ul>	
<b>DLco Testing Purpose: This test is going to measure how well your lungs are able to exchange gas (like oxygen)</b>	
Before test begins	Explain the test maneuver fully: -Breathe normally for 3-5 breaths (Device will display 'tidal breathing'), making sure lips sealed tightly around spirette -Inhale normally, then exhale fully, emptying the lungs (Device will display 'Activate' which examiner will press while participant continues to exhale) -Once lungs completely empty, the device will close (clicking sound) and participant will inhale quickly and deeply (device will display 'take a deep breath in) until the curve goes to the dotted blue line (85% VC) -Hold breath for 10s (Countdown clock on device will monitor this) -Exhale 4-5sec into the spirette -Take a small or normal breath in to end the test -Repeat this procedure after 4 minutes (Device will monitor this)
Normal breathing	"Take a <b>slightly deeper breath in</b> " and then "Now <b>blast out, out, out, empty those lungs all the way</b> " while examiner hits " <b>Activate</b> "
Lungs empty (after clicking of closing valve)	"Now take a <b>deep breath in, in, in</b> " until his breathing curve goes to the individualized dotted blue line

Once lungs full	<b>“Hold your breath for 10sec, keep going, keep going”</b> and show them the countdown clock
After 10sec	<b>“Now exhale normally</b> and then breathe in normally to end the test”
After trial has finished	<b>“Good job! Now take a break, we will repeat this test in 4 minutes or when you are ready”</b>

<b>Albuterol Administration Checklist</b>	
<input type="checkbox"/>	Explain bronchodilator to participant. Say: “I am now going to give you a dose of an inhaler which will help open up your airways and allow us to test your best lung function.”
<input type="checkbox"/>	Demonstrate inhaler technique to participant. Say: “You will need to breathe all the way out. Then, bring this spacer to your mouth and seal your lips over the end of the spacer. When I say “breathe,” I want you to take a nice, <i>slo-o-o-w</i> deep breath in. Once your lungs are full, hold your breath for 10 seconds, or as long as you can comfortably hold it. Then breathe out normally. We will do this four times.”
<input type="checkbox"/>	Test inhaler to make sure it is working properly.
<input type="checkbox"/>	Seat participant.
<input type="checkbox"/>	Shake canister.
<input type="checkbox"/>	Attach clean spacer to inhaler (do not touch participant end of spacer).
<input type="checkbox"/>	Have participant empty lungs fully.
<input type="checkbox"/>	Bring spacer/inhaler to participant’s lips and have participant make a good seal.
<input type="checkbox"/>	Deliver <b>one</b> puff while participant starts breathing in through the spacer/inhaler.
<input type="checkbox"/>	Instruct on slow, deep breath over 3-5 seconds.
<input type="checkbox"/>	Instruct participant to hold breath for up to 10 seconds. Remove spacer/inhaler while participant holds breath.
<input type="checkbox"/>	Allow participant to exhale.
<input type="checkbox"/>	Wait approximately 30 seconds.
<input type="checkbox"/>	Repeat three times (for a total of 4 puffs only).
<input type="checkbox"/>	Clean inhaler properly before storing; discard spacer.

**APPENDIX F**

**WOMEN'S INTERAGENCY HIV STUDY  
FORM PFTAER: PFT ADVERSE EVENT REPORTING FORM**

A1. PARTICIPANT ID:                   |\_|-|\_|\_|-|\_|\_|\_|\_|-|\_|

A2. WIHS CORE VISIT NUMBER DURING WHICH PFT IS COMPLETED:   |\_|\_|

A3. FORM VERSION:                   **04/01/18**

A4. FORM COMPLETED BY:         |\_|\_|\_|

A5. DATE OF EVENT:                 |\_|\_|/|\_|\_|/|\_|\_|  
  M          D          Y

A6. DATE OF DISCOVERY  
OF EVENT:  
  
  |\_|\_|/|\_|\_|/|\_|\_|  
  M          D          Y

**INSTRUCTIONS:** THIS FORM SHOULD BE FILLED OUT BY WHOEVER IS NOTIFIED OF OR OBSERVES AN ADVERSE EVENT THAT IS FELT TO BE AT LEAST POSSIBLY RELATED TO THE RESEARCH STUDY. THIS FORM SHOULD BE SENT TO WDMAC WITHIN 24 HOURS OF AN EVENT. PLEASE ALSO NOTIFY THE SITE PI OF ALL ADVERSE EVENTS.

- A7. WIHS SITE REPORTING EVENT:
- BRONX.....1
  - BROOKLYN..... 2
  - WASHINGTON, DC..... 3
  - SAN FRANCISCO..... 4
  - CHICAGO..... 5
  - UNC..... 6
  - ATLANTA..... 7
  - MIAMI..... 8
  - UAB-MS (BIRMINGHAM)..... 9
  - UAB-MS (JACKSON)..... 10

A8. DETAILED DESCRIPTION OF EVENT (E.G., DIZZINESS AFTER HOLDING BREATH):

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

A9. WHAT IS THE CURRENT STATUS OF THE PARTICIPANT?

---

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A10. DID THE EVENT RESOLVE?

- YES.....1
- NO .....2 **(A11)**
- UNKNOWN .....3 **(A11)**

A10a. DATE OF RESOLUTION:   |\_\_|\_\_| / |\_\_|\_\_| / |\_\_|\_\_|  
  M           D           Y

A10b. HOW DID IT RESOLVE (TREATED, RESOLVED ON ITS OWN, ETC.)?

---

---

---

A11. WAS THIS EVENT ANTICIPATED (LISTED IN THE CONSENT FORM RISK SECTION)?

- YES.....1
- NO .....2 **(A12)**
- UNKNOWN .....3 **(A12)**

A11a. IF ANTICIPATED, WAS THE EVENT ANY OF THE FOLLOWING:

- SHORTNESS OF BREATH..... 1
- DIZZINESS ..... 2
- OTHER EVENT LISTED IN CONSENT FORM..... 3

A12. IS IT MORE LIKELY THAN NOT THAT THIS PROBLEM/EVENT WAS RELATED TO THE RESEARCH PROCEDURES OR INTERVENTIONS:

- YES.....1
- NO.....2 **(A13)**
- UNKNOWN..... 3 **(A13)**

A12a. IF YES, CHOOSE THE STRENGTH OF ATTRIBUTION TO THE STUDY:

- NOT RELATED..... 1
- PROBABLY NOT RELATED ..... 2
- POSSIBLY RELATED..... 3
- PROBABLY RELATED..... 4
- DEFINITELY RELATED..... 5

A13. ALL UNANTICIPATED ADVERSE EVENTS SHOULD BE REPORTED TO YOUR LOCAL IRB. WAS THIS EVENT REPORTED TO YOUR LOCAL IRB?

- YES.....1
- NO .....2 (**PROMPT**)
- UNKNOWN..... 3

**PROMPT:** NOTIFY WDMAC WHEN THE IRB HAS BEEN NOTIFIED OF THIS UNANTICIPATED EVENT.

# APPENDIX G: RECOMMENDED PFT REPORT

## Premeir Medical Specialists

200 High Street  
Farmington, MA 02830  
(800) 275-5800



**Masiello, Jerry**

**ID: #0047 Age: 63 (9/17/1954)**

Gender	Male	Height	66 in	Asthma	No
Ethnicity	Caucasian	Weight	190 lb	COPD	No
Smoker	No				

### FVL Tidal

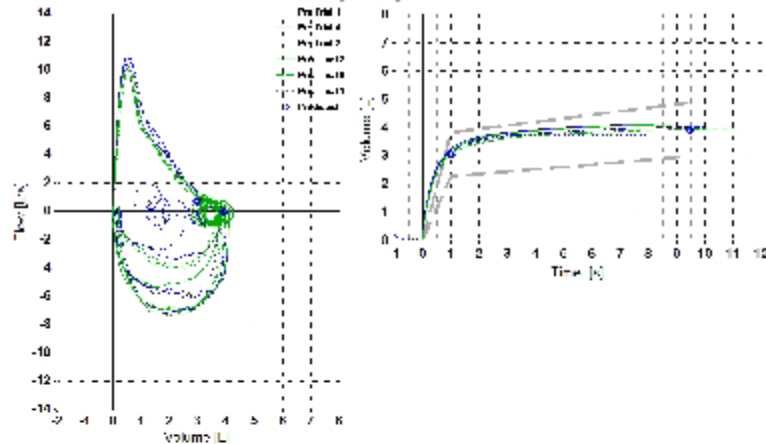
**Your FEV1 / Predicted: 106 %**

Test Date	2/20/2018 12:55:23 PM	Interpretation	GOLD(2008)/Hardie	Value Selection	Best Trial
Post Time	2/20/2018 12:58:54 PM	Predicted	Quanjer (GL), 2012	BTPS (IN/EX)	1.10/1.02

Parameter	Pred	LLN	Pre Best			%Pred	Post Best			%Pred	%Chg
			Trial 1	Trial 4	Trial 2		Trial 2	Trial 3	Trial 1		
FVC [L]	3.91	2.96	4.11	4.01	3.73	105	4.11	3.97	3.84	105	0
FEV1 [L]	3.04	2.26	3.22	3.15	3.19	106	3.13	3.02	3.06	103	-3
FEV1/FVC	0.776	0.651	0.783	0.785	0.857	101	0.761	0.760	0.797	98	-3
FEF25-75 [L/s]	2.53	1.19	2.80	2.76	3.50	111	2.49	2.37	2.71	99	-11
PEF [L/s]	-	-	10.47	11.07	10.89	-	10.08	10.27	10.16	-	-4
FET [s]	-	-	9.4	9.9	7.8	-	9.9	11.3	7.6	-	5
FVC [L]	3.91	2.96	4.05	3.72	3.65	104	3.87	3.95	3.61	99	-5
PIF [L/s]	-	-	6.03	7.18	6.11	-	6.91	7.13	7.42	-	15

Session Quality Pre B (FEV1 Var=0.02L (0.7%); FVC Var=0.10L (2.4%))  
Post B (FEV1 Var=0.08L (2.4%); FVC Var=0.14L (3.5%))

System Interpretation Pre Normal Spirometry  
Post Normal Spirometry



**APPENDIX H: GLOSSARY OF PFT TERMS**

<b>Term</b>	<b>Definition</b>
Chronic Obstructive Pulmonary Disease (COPD)	Lung disease characterized by chronic obstruction of lung airflow that interferes with normal breathing and is not fully reversible.
Emphysema	A condition in which the air sacs of the lungs are damaged and enlarged, causing breathlessness.
Impaired Pulmonary Diffusing Capacity	An impaired transfer of gas from air in the lung to the red blood cells in lung blood vessels.
Pulmonary Function Test (PFT)	PFTs are designed to measure how well the lungs are working. PFTs gauge how the lungs are expanding and contracting and measure the efficiency of the exchange of oxygen and carbon dioxide between the blood and the air within the lungs.
Diffusing Capacity for Carbon Monoxide (DLco)	A test of the diffusing capacity of the lungs for carbon monoxide (CO).
Vital Capacity (VC)	The greatest volume of air that can be expelled from the lungs after taking the deepest possible breath.
Flow Volume Loop (FVL)	A graph of the rate of airflow as a function of lung volume during a complete respiratory cycle consisting of a forced inspiration followed by a forced expiration.
Forced Vital Capacity (FVC ex only)	The amount of air that can be forcibly exhaled from the lungs after taking the deepest breath possible. <b>FVC</b> is used to help determine both the presence and severity of lung diseases.
Forced Expiratory Volume in the first second (FEV1)	The volume of air that can be forced out in one second after taking a deep breath in.
FEV1/FVC Ratio	A ratio that represents the proportion of a person's VC that they are able to expire in the 1 <sup>st</sup> second of expiration.
Forced Expiratory Flow (FEF)	The rate of airflow recorded in the measurements of FVC, usually calculated as an average flow over a given portion of the expiratory curve. FEF25%-75% is called the maximal midexpiratory flow.
Tidal Breathing	Regular breathing, or the volume of air moved in/out of the lungs during quiet breathing.
Residual Volume (RV)	The volume of air remaining in the lungs after a maximal exhalation.
Metered Dose Inhaler (MDI)	A device that delivers a measured amount of medication as a mist the patient can inhale.



APPENDIX I – PFT PARTICIPANT LETTER TEMPLATE



[DATE]

Dear [PARTICIPANT NAME]:

Thank you for your participation in the Women's Interagency HIV Study (WIHS). This letter provides you with the results of the pulmonary function testing you recently had done in the WIHS. A copy has also been sent to your doctor (if you requested that we do so).

**Pulmonary function tests (PFTs) performed as a part of the study had findings that were:**

**(Select one)**

**Normal**      or      **Possibly Abnormal**      or      **Unable to interpret due to suboptimal quality**

**[OPTIONAL: INCLUDE THE FOLLOWING IF REQUESTED BY PARTICIPANT]:**

We have sent a copy of the detailed report to your doctor. These findings may or may not be new. Please review them with your doctor, who may consider additional work-up as clinically indicated. You may contact the [WIHS SITE NAME] office at [PHONE NUMBER] if you, or your doctor, have any questions about this report.

*Please note that these studies were performed as part of a research study and may not be the same tests done as part of your clinical care.*

Thank you.

Sincerely,  
[SITE SIGNATURE]

cc: Referring physicians (if requested)

**APPENDIX I – PFT PHYSICIAN LETTER TEMPLATE**



[DATE]

Dear [PHYSICIAN NAME]:

Your patient, [PARTICIPANT NAME], is a participant in our research study. She has requested that we send you the results of her pulmonary function test (PFT) which was administered as part of the study. We are also sending you the detailed PFT report.

*Please note that these studies are not performed at a clinically-certified PFT lab and should not be made a part of the medical record. Clinical PFT testing should be performed to follow up any abnormalities.*

**Pulmonary function testing performed as a part of the study had findings that were:**  
(Select one)

**Normal**            or            **Abnormal**

**If Abnormal:** (check all that apply)

<b>Abnormal Outcome</b>	<b>Possible</b>	<b>Mild</b>	<b>Moderate</b>	<b>Severe</b>
Airflow obstruction	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Restriction	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Decreased Diffusing Capacity	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Extra-Thoracic Obstruction	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Intra-Thoracic Obstruction	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Please contact us at [PHONE NUMBER] if you have any questions about this report.

Thank you.

Sincerely,  
[SITE SIGNATURE]

APPENDIX J

WOMEN'S INTERAGENCY HIV STUDY  
FORM PFT29: PFT BLOOD SPECIMEN COLLECTION FORM

- A1. PARTICIPANT ID: |\_\_|\_|\_|-|\_\_|\_|\_|-|\_\_|\_|\_|-|\_\_|\_|\_|
- A2. WIHS CORE VISIT NUMBER DURING WHICH PFT IS COMPLETED: |\_\_|\_|
- A3. FORM VERSION: 04/01/18
- A4. FORM COMPLETED BY: |\_\_|\_|\_|

The hemoglobin blood draw must be within 60 days of the carboxyhemoglobin blood draw in order for the results to be valid. If > 60 days, the entire PFT protocol is void.

**PROMPT: IF THE CORE VISIT BLOOD WAS DRAWN GREATER THAN 60 DAYS FROM TODAY'S DATE, YOU WILL NEED TO DRAW BLOOD FOR HEMOGLOBIN TESTING AND REPORT THE DATE ON QUESTION A6. THE BLOOD DRAW FOR CARBOXYHEMOGLOBIN MUST BE THE SAME DAY AS SPIROMETRY/DLCO.**

- A5. WAS THE CORE VISIT BLOOD DRAW GREATER THAN 60 DAYS FROM TODAY'S DATE?  
YES.....1 (A6)  
NO .....2 (A5a)

A5a. DATE OF PREVIOUS BLOOD DRAW FOR HEMOGLOBIN:

|\_\_|\_|\_| / |\_\_|\_|\_| / |\_\_|\_|\_| (A7)  
M D Y

A6. DATE OF BLOOD DRAW FOR HEMOGLOBIN:

|\_\_|\_|\_| / |\_\_|\_|\_| / |\_\_|\_|\_|  
M D Y

A7. DATE OF BLOOD DRAW FOR CARBOXYHEMOGLOBIN:

|\_\_|\_|\_| / |\_\_|\_|\_| / |\_\_|\_|\_|  
M D Y

WIHSID

<u>TEST TYPE</u>	<u>TUBE TYPE</u> (TUBE/VOL)	<u>WHOLE</u> <u>BLOOD</u> <u>VOLUME</u>	<u>SPECIMEN</u> <u>COLLECTED</u>			<u>REQUIRED</u> <u>VOLUME</u> <u>COLLECTED</u>		<u>ESTIMATED</u> <u>VOLUME</u> <u>COLLECTED</u>
			<u>YES</u>	<u>NO</u>	<u>N/A</u>	<u>YES</u>	<u>NO</u>	
A8. Hemoglobin	Lavender-Top (3 mL)	2.5 mL	1	2 (a)	3	1 (A9)	2	__ __  mL
	IF NO, SPECIFY REASON		a. _____					
A9. Carboxyhemoglobin	Lavender-Top (4 mL)	4.0 mL	1	2 (a)		1 (END)	2	__ __  mL
	IF NO, SPECIFY REASON		a. _____					

APPENDIX K

WOMEN'S INTERAGENCY HIV STUDY  
FORM PFTLAB: PFT LAB RESULTS FORM

- A1. PARTICIPANT ID: |\_\_|\_|-|\_\_|\_|-|\_\_|\_|-|\_\_|\_|-|\_\_|\_|
- A2. WIHS CORE VISIT NUMBER DURING WHICH PFT IS COMPLETED: |\_\_|\_|
- A3. FORM VERSION: **04/01/18**
- A4. FORM COMPLETED BY: |\_\_|\_|\_|
- A5. HEMOGLOBIN BLOOD DRAW DATE:  
|\_\_|\_| / |\_\_|\_| / |\_\_|\_|  
M D Y
- A6. HEMOBLOBIN RESULT:  
|\_\_|\_|. |\_\_| (GM/DL)
- A7. CARBOXYHEMOGLOBIN BLOOD DRAW DATE:  
|\_\_|\_| / |\_\_|\_| / |\_\_|\_|  
M D Y
- A8. CARBOXYHEMOGLOBIN RESULT:  
|\_\_|\_|. |\_\_| (%)