THE STRONG HEART STUDY
Cardiovascular Disease in American Indians
(Phase III)

Operations Manual
Volume Eight
Carbon Monoxide Determination and Asthma Sub-study

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EXPIRED AIR CARBON MONOXIDE (CO) DETERMINATION
MANUAL OF OPERATIONS
STRONG HEART STUDY, PHASE III 1997

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TABLE OF CONTENTS

BACKGROUND ................................................................. 1
PRINCIPAL OF OPERATION OF THE CO ANALYZER .................. 2
PERFORMANCE SPECIFICATIONS OF THE CO ANALYZER ............. 2
STEPS TO MEASURE THE BREATH CO LEVEL ........................... 3
CO ANALYZER MAINTENANCE AND TROUBLESHOOTING .............. 5
THE CALIBRATION PROCEDURE ........................................... 6
BACKGROUND CO ............................................................. 7
BACKGROUND

Cigarette smoking is one of the strongest risk factors for cardiovascular disease and all cause mortality. Self-report of smoking status (via questionnaire) results in a certain degree of mis-classification due to misrepresentation by some study participants. There are several methods of biochemical validation of self-reported non-smoking. The most commonly used by epidemiological studies are analysis of blood, urine, or saliva samples for nicotine (or one of its metabolites, usually cotinine), thiocyanate, or the measurement of carbon monoxide (CO) in blood samples or in exhaled breath. The Strong Heart Study has chosen breath CO measurement since it is non-invasive, sample collection is quick, it provides immediate results, and it is relatively inexpensive. A false negative result will occur if the participant has not smoked cigarettes during the previous 24 hours. A false positive result will occur if the participant was recently exposed to excessively high levels of CO in their environment. Sources of high levels of environmental CO include poorly vented gas appliances (kerosene room heaters, water heaters, central heaters, or gas ranges), indoor wood-burning, or gasoline engines with leaking exhaust systems. Detection of these sources in non-smoking participants with high CO levels may be accomplished using commercially available home CO monitors ($30-60 each). Recent exposure to second-hand smoke from other smokers (cigarette, pipe, or cigar) results only in small elevations of breath CO.

The carboxyhemoglobin concentration (COHgb) is elevated in the blood of smokers because the inhaled smoke contains carbon monoxide (CO). The hemoglobin within red blood cells binds CO much more avidly it does oxygen. The average half-life of CO in the blood is about 4 hours, so that when a person smokes a cigarette, their CO level will remain higher than that of a non-smoker (more than 10 ppm, parts per million) for at least 8 hours following their last cigarette. A measurement of the concentration of CO in the exhaled breath provides a quick non-invasive estimate of COHgb. A direct measurement of COHgb would require a blood sample and a large expensive analyzer (called a co-oximeter). Hand-held battery operated CO analyzers (like the unit chosen for this study, made by Vitalograph) measure ambient or exhaled CO in the range of 0-500 ppm, although the highest levels normally seen in smokers, immediately after smoking, are about 50 ppm.
Principle of Operation of the CO Analyzer

The Vitalograph EC50 CO Monitor is a compact, portable instrument powered by either alkaline or rechargeable batteries. A simple sampling system traps the last portion of an exhaled breath (an "alveolar" sample) in a T-piece which is adjacent to the surface of the instrument's sensor. Diffusion of the sample into the sensor results in an electrical signal directly proportional to the CO concentration. The sensor is an electrochemical polarographic type cell. The cell electro-oxidizes carbon monoxide to carbon dioxide in direct proportion to the partial pressure of CO in the sample area. The resulting signal is amplified, temperature compensated, and then is displayed in parts per million on the liquid crystal display.

Performance Specifications of the Vitalograph CO Analyzer

<table>
<thead>
<tr>
<th>Gas Detected</th>
<th>Carbon Monoxide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concentration Range</td>
<td>0-500 ppm</td>
</tr>
<tr>
<td>Detection Principle</td>
<td>Sealed electrochemical sensor</td>
</tr>
<tr>
<td>Meter</td>
<td>Liquid crystal display</td>
</tr>
<tr>
<td>Sampling System</td>
<td>Two flutter valve T-piece</td>
</tr>
<tr>
<td>Mouthpieces</td>
<td>Cardboard, disposable</td>
</tr>
<tr>
<td>Warm-up Time</td>
<td>Less than 10 seconds</td>
</tr>
<tr>
<td>Response Time</td>
<td>Less than 30 seconds to 97% of final reading</td>
</tr>
<tr>
<td>Drift</td>
<td>Less than 1% of signal per month at constant temperature</td>
</tr>
<tr>
<td>Operating Temp Range</td>
<td>0-40 degrees centigrade</td>
</tr>
<tr>
<td>Operating Pressure</td>
<td>Atmospheric</td>
</tr>
<tr>
<td>Humidity Range</td>
<td>0-100% relative humidity (a hydrophobic filter protects sensor from condensed water vapor)</td>
</tr>
<tr>
<td>Life of the Sensor</td>
<td>2-3 years (guaranteed 6 months)</td>
</tr>
<tr>
<td>Sensor Selectivity</td>
<td>Negligible interference from alcohol and other organic species under normal situations. A high capacity carbon filter is available to remove unusually high concentrations of alcohol. 20 ppm hydrogen gives less than a 4 ppm reading.</td>
</tr>
<tr>
<td>Power Supply</td>
<td>9 volt Alkaline battery</td>
</tr>
</tbody>
</table>
Steps to Measure the Breath CO Level of a Study Participant

1) Push the black on/off switch, located above the display on the top of unit, to "On" position. The display will start at a high number, then rapidly fall to around "000" (±2).

2) When the unit has reached "000" (±2), attach the blue T-valve. Record the ambient reading; record the + or - sign in the first field, and the reading in the second field (see figure 1). The open end of the T-valve should face away from the display, towards the "Breath CO" logo.

3) Attach a new disposable cardboard mouthpiece to the open end of the T-valve.

4) Instruct the participant to exhale completely, then to inhale deeply and hold the breath for 20 seconds.

5) Instruct the participant to go on the cardboard mouthpiece, and seal their lips tightly around the mouthpiece.

6) Instruct them to exhale as completely as possible through the sampling system (approximately 15 seconds).

7) At the end of the participant's expiratory breath, record the reading after it reaches its peak (after about 30 seconds). The reading obtained is the concentration of carbon monoxide in the participant's breath (an "alveolar" sample).

8) Allow your participant to "catch their breath" between trials (approximately 30 seconds to 1 minute).

9) Two trials are completed for each participant; repeat steps 4 through 7.

10) If the first 2 trials are within 4 ppm (±4), record both results on the study form (see figure 1a, "1st" and "2nd"), and record "X" in trials 3 and 4. If they are not within 4 ppm, both trials should be repeated with careful coaching and recorded. No more than two sets of 2 trials should be done even if the second set also differs by more than 4 ppm.

Note: It is not necessary to wait for the instrument to return to zero before another test is performed.
11) When doing sampling:

- Turn off the display (using the black on/off display switch)
- Disassemble the sampling equipment, and discard the mouthpiece.

<table>
<thead>
<tr>
<th>Breath CO:</th>
<th>+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ambient:</td>
<td>CO [ppm]:</td>
</tr>
<tr>
<td><strong>circle</strong></td>
<td>1st</td>
</tr>
</tbody>
</table>

*figure 1a*
CO Analyzer Maintenance and Troubleshooting

- Turn the unit OFF after each participant, unless you plan to use it again within ONE HOUR.

- Typically, the 9 volt Alkaline battery has a life of 250 - 500 hours of use. The unit will display "low battery" when it needs to be replaced. To replace the battery:

  On the back of the unit, press down on the compartment panel marked "OPEN" and slide cover in the direction of the arrow. Then, lift cover from the unit. Remove and discard the old battery. Replace with a new 9 volt battery. Tuck the wires neatly away before replacing the compartment cover.

- **Storage and Transporting.** The unit should always be turned off when stored. The battery should be removed if you don't intend to use it for several weeks. If the machine is used for field work, the padded carrying case is highly recommended. Avoid leaving the machine in freezing temperatures or temperatures above 80 degrees. Always carry 2 sets of spare batteries.

- **Sensor Cell Replacement.** The sensor cell should last 2-3 years, and is guaranteed for 6 months. A loss in sensitivity will generate erratic readings and an inability to be calibrated correctly. These signals indicate that replacement of the sensor cell is necessary. Ship the instrument to Vitalograph for maintenance.

- **T-valve Sterilization.** The T-valves should be sterilized each week.

  1) Using a test tube brush and a solution of mild detergent and warm water, scrub each T-valve inside and out.
  2) Rinse and then immerse them in a sterilizing solution (i.e. Lysol I.C., glutaraldehyde) for 20 minutes.
  3) Thoroughly rinse each T-valve again, and air dry and wrap in paper towels for storage. To avoid skin irritation or allergic sensitization, always wear rubber gloves when removing T-valves from the sterilizing solution.

- **Erratic Readings.** If an instrument does not display a background reading between +2 and -2 ppm, let the instrument sit with the unit on, for up to 30 minutes. Usually the background reading will fall to within the range of acceptable drift. If not, follow the calibration procedure.
The Calibration Procedure

Equipment needed:

- Tank of 50 ppm CO Test Gas with regulator, hose
- Calibration Check Chart and Log
- Small screwdriver
- 2 minute count up/down timer
- T-valve

The CO analyzer must be calibrated at least monthly, and more often if excessive drift is noted.

1) If the Vitalograph has been used recently to measure CO, allow it to sit for at least 30 minutes with the unit off. This provides sufficient time for any CO remaining within the sensor to be consumed.

2) Turn the unit ON and take a reading. Record the reading in the "zero valve" spot on the calibration check chart and log sheet.
   - If the zero reading is not between -2 and +2 ppm, (the acceptable drift range) adjust the zero potentiometer located on the front panel (black slide above the "Vitalograph" logo) to give a reading of "000". DO NOT ADJUST the zero if within +/-2 ppm, simply record the reading. Once it reads "000" (±2), tape down the black slide bar so it can not be adjusted between calibration checks.

3) Attach the T-valve. Fit the calibration cap into the end of the T-valve which accepts the mouthpiece. Open the regulator valve, releasing gas, until the needle is rests at 10 psi. The calibration gas will enter the T-valve.

4) Start timer, and leave the gas on for the 1 minute. This will allow the unit to achieve a stable reading.

5) When timer goes off, note the reading, then turn off the gas tank.

6) Allow 30 seconds to pass before noting the reading (allows the unit to achieve its peak reading). Record the result on the calibration check chart and log sheet.
   - If the reading is between 48 to 52 ppm, DO NOT ADJUST THE SPAN, just record the reading. If the CO reading is NOT between 48 to 55 ppm, use a miniature screwdriver to adjust the span potentiometer located on the back of the unit to give a reading of 50 ppm.

7) Detach the hose from T-valve, and switch the unit off.
8) Record your tech ID code and data on the calibration check chart and log sheet.

If you have difficulty in obtaining zero or 50 ppm readings, replace the battery and repeat the entire calibration procedure. If you still have difficulty, the sensor may need replacement. Call Vitalograph for advice.

**Background CO**

Background (ambient) CO is that CO which is present in the room air at the time a CO sample is collected. Normal background CO levels are 0-4 ppm. We define the background CO level as the reading immediately prior to testing the first participant of the day. The background reading is made before attaching the T-valve.

Environmental factors such as car exhaust and faulty heating systems will influence background CO levels. If the background CO level is greater than 4 ppm, take the machine outside a building and rezero the meter. (See step 2 of the cal check procedure.)

**Standard Equipment, Service, and Maintenance**

- Vitalograph CO Monitor $1000
- T-valve, miniature common screwdriver
- Additional T-valves can be bought from the company $4
- Mouthpieces #20.202 (box of 210) $30
- Calibration gas cylinder 50 ppm CO $85
  (15-20 calibrations per tank)
- Count up/down timer (Radio Shack Cat# 63-878 or similar unit) $12

All apparatus and replacements are available from Vitalograph Medical Instruments, 8347 Quivira Road, Lenexa, Kansas, phone 1-800-255-6626
APPENDIX

WHAT IS CARBON MONOXIDE?

Carbon monoxide (CO) is a colorless, odorless, poisonous gas produced by burning organic material. It is one of the three main constituents of tobacco smoke along with tar and nicotine. All three represent some risk to health. Carbon monoxide mainly effects the heart, blood vessels, and lungs.

Carbon monoxide is found in atmospheric pollution. It is produced by burning petrol and gas so that all modern cities will have at least some CO in the air. Compared to the concentrations found in tobacco smoke, however, the levels found in the body from pollution are low.

Some carbon monoxide is produced naturally by the body. So even non-smokers in country areas will not have a level of zero. However, the levels produced naturally are so small that they could not be confused with those resulting from smoking.

What this means in practice is that the level of carbon monoxide in the body shows the amount of tobacco smoke inhaled. Even moderate CO levels are rare in non-smokers except in unusual circumstances.

When tobacco smoke is inhaled into the lungs, carbon monoxide passes through the lining of the lung into the bloodstream, where it becomes attached to hemoglobin (Hb) - the red blood cells. The function of the red cells is to carry oxygen around the body. However, they have a much more powerful chemical attraction to CO than to oxygen (200 times greater) so if there is any CO in the blood at all, it becomes attached to hemoglobin in the place of the oxygen forming carboxyhemoglobin or COHb.

The percentage of COHb is the proportion of red blood cells carrying CO rather than oxygen. Thus, if you have five percent COHb this means that your body is five percent short of oxygen: five percent of your red cells are carrying CO and not oxygen.

This places extra strain on the system. The heart has to work harder to make up for the oxygen loss, and it has to do this extra work when its own blood supply is short of oxygen. There is a double effect.

SOME EXAMPLES OF CARBON MONOXIDE LEVELS

1. In The Country Air

Natural free CO can be measured where there is no major industry or motor vehicles and air is fairly pollution-free - mountain regions, remote rural areas or offshore islands without cars. Such places show less than one part per million (ppm) CO. These on non-smoking inhabitants show an average Carboxyhemoglobin (COHb) level of 0.68 percent (5 ppm CO), produced naturally by the body, mainly from breakdown of hemoglobin.
2. **In a Small, Badly Ventilated "Smoking" Office**

In a controlled test, 12 non-smokers and eight smokers were confined in an unventilated room for nearly 80 minutes, during which 80 cigarettes and two cigars were burned or smoked. The average COHb level of non-smokers rose from 1.6 percent (10 ppm) to 2.6 percent (17 ppm) in that time.

This one percent increase is approximately the amount of CO a smoker obtains from one cigarette. It is also similar to the CO intake by a driver working for a whole day in a major city, or by policeman after three hours of traffic duty.

3. **In Heavy Smokers**

Tests showed that smokers attending a London stop smoking clinic had an average COHb level of eight percent (45 ppm).

**Summary - Distinguishing Smokers from Non-smokers**

CO levels will vary a little in non-smokers because of pollution, including passive smoking. The best cut-off point for dividing smokers and non-smokers is around 1.6 percent COHb or 8 ppm of CO. Levels above this normally indicate an unusual level or source of pollution, or smoking.

**MEASURING CARBON MONOXIDE**

Holding your breath for a short while allows the CO concentration in the lungs and the blood vessels to equalize. You then blow into the instrument which registers your CO level almost immediately.

As you stop smoking, you will see your CO level drop dramatically.

**WHAT THIS READING MEANS**

The average level for smokers is about 5.5 percent (33 ppm), but this does not translate exactly into the number of cigarettes smoked per day. How heavy a smoker you really are depends on the amount of smoke inhaled and not on the number of cigarettes smoked.

The cut off point will not always be exactly 1.6 percent or 8 ppm, but this is the level which separates smokers and non-smokers best. Normally, non-smokers will only have higher levels due to unusual factors.

Levels above 15 percent are uncommon except in cigar and pipe smokers (because cigar and pipe smoke have a high CO concentration). This is why switching from cigarettes to cigars or pipe is useless, or be even more dangerous. Measuring CO will show if those who have switched are still inhaling. Most do.

Symptoms of intoxication start at around 20 percent and levels above 30 percent are approaching danger (from asphyxiation).
ASTHMA SUBSTUDY - SPIROMETRY

MANUAL OF OPERATIONS

STRONG HEART STUDY, PHASE III  1998

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Spirometer
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Renaissance Spirometry System
11150 Thompson Avenue
Lenexa, KS 66219-2301
(800) 225-6773
Software Version F Serial Number: RU707012

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TABLE OF CONTENTS

BACKGROUND ........................................................................................................... 1
DEFINITIONS (GLOSSARY) ...................................................................................... 2
DESCRIPTION OF THE SPIROMETER ....................................................................... 3
PARTICIPANT INFORMATION at the MAIN MENU ...................................................... 3
PARTICIPANT PREPARATION .................................................................................... 4
BASELINE SPIROMETRY .......................................................................................... 4
PRINTING RESULTS .................................................................................................. 5
GIVING A BRONCHODILATOR .................................................................................. 5
POST-BRONCHODILATOR SPIROMETRY .................................................................. 6
MANEUVER QC GRADES .......................................................................................... 6
SPIROMETRY INTERPRETATION .............................................................................. 6
MONDAY CALIBRATION CHECKS ............................................................................. 8
WEEKLY BIOLOGICAL CONTROL .......................................................................... 8
CLEANING AND CARE OF THE EQUIPMENT .......................................................... 9
TECHNICIAN CERTIFICATIONS .............................................................................. 9
QUALITY CONTROL .............................................................................................. 9
DOWNLOADING OF MEMORY CARDS .................................................................... 10
REFERENCES .......................................................................................................... 11
APPENDIX ............................................................................................................. 12
SUPPLIES .............................................................................................................. 13
INDEX .................................................................................................................. 14
FORWARD:

This manual serves three purposes:

- a study guide for training of physicians, nurses and technicians to perform spirometry (pre & post bronchodilator, BD).
- a practical "how-to" reference guide to be used during the study
- documentation of the procedures for analyses and manuscript preparation.

BACKGROUND:

Spirometry is the simplest, most effective test for assessment of lung function. That is why it has been included in many cardiovascular epidemiology studies, including SHS.

Spirometry (without bronchodilator) was measured during SHS Phase II for the original cohort. Spirometry reference values are being developed from the healthy subset of American Indian participants.

Spirometry records the relationship between airflow (FEV1) and the exhaled volume of air during a breathing maneuver called the FVC maneuver (forced vital capacity maneuver). The most common lung diseases reduce forced expiratory flows. Such "obstructive" lung diseases include asthma, bronchitis, and emphysema. The ratio of FEV1/FVC is very sensitive for detecting mild airways obstruction.

NEW PROCEDURES

1. Baseline Spirometry will be done on all substudy participants including controls. For those with abnormal results on baseline spirometry, 2 puffs (from an asthma inhaler) will be given to the participant, with spirometry repeated 10 minutes later (post BD).

SUB-STUDY SPIROMETRY CHANGES

When compared to spirometry testing done during SHS Phase II,

1. A maximum of 5 maneuvers will be done (not 8). Maneuvers will last only 6 seconds (not 10).
**DEFINITIONS (GLOSSARY)**

**ALBUTEROL** (official generic name in the U.S.) is an asthma medication for the relief of bronchospasm in patients with reversible obstructive airway disease (asthma). After administering albuterol, an improvement of 15% or greater in FEV1 values indicates precedence of asthma.

**ALLERGEN**: a substance that causes an allergy.

**ANTIGEN**: a liquid made from an allergen that when introduced onto the skin stimulates the production of an antibody.

**ATS** is short for American Thoracic Society, the scientific branch of the American Lung Association (ALA). The ATS promotes accurate spirometers by recommending spirometry standards. The ATS and ALA divorced in 1997.

**BD**: is short for bronchodilator.

**BIOLOGIC CONTROL CALIBRATION CHECK** is a baseline spirometry done by a non smoker and non asthmatic tech. The same tech should be used every Monday morning before the 1st participant.

**CALIBRATION SYRINGE** is a large plastic cylinder with a rubber sealed piston used to check the volume accuracy of spirometers.

**COPD** stands for Chronic Obstructive Pulmonary Disease, a general term for lung disease caused by cigarette smoking - a mixture of emphysema, bronchitis, and hyper reactive airways (asthma).

**FEV1**: Forced Expiratory Volume in 1 Second (liters). The volume of air exhaled in the first second of an FVC maneuver.

**FEV1/FVC RATIO** is the most sensitive and specific index of airways obstruction measured by a spirometer. It is normally above 70% in adults.

**FLOW SENSOR** see pneumotach

**FVC** is the Forced Vital Capacity, the volume of air exhaled during the maneuver named after it. The subject takes as deep a breath as possible and then quickly exhales (BLAST) as much air as possible. The FVC is reduced with restrictive disorders.

**MDI** is a meter dose inhaler, a small pressurized cannister commonly used to deliver asthma medications directly to the airways. Also called "asthma puffers".

**OBSTRUCTION** is a decrease in maximal airflow rates caused by airway narrowing. The FEV1/FVC ratio and the FEV1 are both decreased.

**PEF** stands for Peak Expiratory Flow, the highest flow measured during the FVC maneuver. It is a good index of blast effort.

**PF** is short for Pulmonary Function (lung tests).

**PNEUMOTACH** is the white plastic "trumpet" mouthpiece that is used with the Renaissance Spirometer.

**PRED** is short for the predicted value of a PF parameter. It is determined from the regression equation from a large population study of supposedly normal people.

**RESTRICTION** is a decrease in lung volumes. Scarring of lung tissue (fibrosis), heart failure (CHF), pneumonia, and simple obesity are some of many causes. The FVC is reduced while the FEV1/FVC ratio is normal or increased.

**SPACE** is a device attached to a MDI asthma inhaler, designed to improve deposition of the drug deeper into the patient's lungs.
DESCRIPTION OF THE SPIROMETER

The PB100 Spirometer weighs about one pound and complies with ATS standards for spirometer accuracy: Volume: ± 3% of reading or ± 50ml, whichever is greater. FEV1 measured by back extrapolation. It has an internal rechargeable NiCad battery pack, and an AC adaptor/charger.

The PB110 Base Station weighs 19 oz, and provides docking for the spirometer to charge the NiCad battery pack and also sends reports to a printer.

The PB130 Patient Data memory card stores participant test information for future printing; interfaces with the PB100 spirometer or the PB110 base station. It stores approximately 65-75 participant tests. All results will be stored on the memory cards, and mailed at the end of each month to the Reading Center in Tucson, Arizona. Data will be downloaded from the memory card and returned to the site within 2 weeks.

Disposable pneumotach (FS200). The Renaissance system uses pre-calibrated, white plastic disposable pneumotachs. These single-participant use pneumotachs eliminate the need to clean or sterilize any part of the spirometry system.

The Printer - Canon model is a color capable ink jet printer. We will use BJ02 Black Ink printer cartridges.

PARTICIPANT INFORMATION at the MAIN MENU

After the calibration check, a MAIN MENU is automatically displayed.

You usually move forward within a program by pressing either the Enter key or the test key. Directions are given for each step in the spirometry’s screen. If you make a mistake, you can usually get back to the MAIN MENU by pressing the TEST key. Calibration, configuration, and previous participants’ data are stored after each use.

The MAIN MENU displays

| ID: | UP TO 10 DIGITS |
|----|-----------------

1. Type the participant’s ID number, press ENTER.

<table>
<thead>
<tr>
<th>AGE:</th>
<th>(yr)</th>
</tr>
</thead>
</table>

2. Type in the age, then ENTER.

<table>
<thead>
<tr>
<th>HEIGHT:</th>
<th>(in)</th>
</tr>
</thead>
</table>

3. Type in the height (in inches), then ENTER. Confirm the participant’s height in feet and inches.

<table>
<thead>
<tr>
<th>SEX:</th>
<th>1=MALE 2=FEMALE</th>
</tr>
</thead>
</table>

4. Select the participant’s gender, press ENTER.

<table>
<thead>
<tr>
<th>WEIGHT:</th>
<th>(lb)</th>
</tr>
</thead>
</table>

5. Type the participant’s approximate weight, press ENTER.

<table>
<thead>
<tr>
<th>RACE ADJUST:</th>
<th>1=YES 2=NO</th>
</tr>
</thead>
</table>

6. Select 2 for no correction, press ENTER. (Race correction is used ONLY for African Americans).

<table>
<thead>
<tr>
<th>ROOM TEMP:</th>
<th>70 F</th>
</tr>
</thead>
</table>

7. Press ENTER (no need to change this).
PARTICIPANT PREPARATION

You, the technician, are the critical part of the pulmonary function testing system, since you must guide the participant through breathing maneuvers which are highly dependent on their effort. You must coach the participant to inhale maximally and then to BLAST out their air. To obtain accurate results, the testing must be done in a standardized fashion.

Note: This manual refers to the participant as "he" or "him" for easy reading. Of course SHS participants are both women and men.

Wash your Hands Participants will appreciate your consideration if you make a point of washing your hands before testing them. Do this as you enter the room if it has a sink.

Explain the Procedure Explain that the purpose of the next test is to determine how hard and fast he can exhale air, "Like blowing out candles on a birthday cake." Explain that, he should take in as deep a breath as possible, and when his lungs are completely full, quickly position the pneumotach, and exhale his air as hard and fast as possible.

Suggest to women that they may wish to go to the bathroom first, especially if their bladder is full (to avoid stress incontinence).

Position the Participant Testing will be done in the sitting position without nose clips.

Any tight clothing (a tie, bra, vest, belt) which might restrict maximal breathing efforts should be loosened. Dentures, if they are loose, should be removed and placed in a clean denture cup, since they will prevent a tight seal from being formed around the pneumotach. If dentures are not loose, leave them in place.

Always Demonstrate the Maneuver First ask the participant to watch you perform the FVC maneuver with your own pneumotach. Stand up straight. Take a deep breath, throw back your shoulders, widen your eyes, and stand on your toes to emphasize the maximal depth of inhalation. Then, stick out your tongue, place the pneumotach on it. Seal your lips around it, and dramatically BLAST out as hard and as fast as you can for a couple of seconds.

Your vigorous demonstration will prevent their time and effort from being wasted on unacceptable forced maneuvers.

BASELINE SPIROMETRY

1. Ask the participant to remove the plastic bag covering the white pneumotach. Attach it to the grey rubber adaptor at the end of the clear tubing.

2. Press TEST.

3. Press the FVC (1) key.

   KEEP PNEUMOTACH STEADY! ZEROING

   The participant should not move the white flow sensor at this time.

   BLOW ! ! !

   When the screen shows "BLOW ! ! !", its ready to test.

4. Instruct the participant to take in as deep a breath as possible. Watch them put the pneumotach in their mouth, seal their lips around and make a tight seal. Ensure that their fingers are not touching the white filter paper of the sensor.

5. Then yell BLAST out!
Review the flow-volume curves for evidence of poor efforts. To perform additional maneuvers, press FVC (1) and follow the instructions (steps 1-8 above). If the interpretation is NORMAL, they are done with spirometry testing. Discard their pneumotach.

If baseline spirometry interpretation was NOT NORMAL, explain to the participant that you would like them to inhale a breathing medication and see if it improves their results in 10 minutes. If they agree, administer albuterol.

**GIVING A BRONCHODILATOR**

Show the patient how to correctly use a metered dose inhaler (MDI). Attach a clean spacer to the Albuterol MDI canister.

1. Instruct the participant to exhale completely, then put the canister in front of their lips.
2. Instruct the participant to seal their lips around the spacer.
3. Instruct them to SLOWLY take a big breath. As soon as they begin inhaling, press the canister to release the albuterol.
4. Have the participant hold their breath for 5 seconds, as you count to 5 slowly.
5. Allow them to breathe normally for about a minute.
6. Repeat steps 1 through 4 (for a second "puff" of the medication).
7. Using the timer, wait 10 minutes before performing the post-bronchodilator spirometry.

**PRINTING RESULTS:**

Be sure that the base station is turned on and that the printer is connected, with paper in the hopper and the ON-LINE glowing green.

1. Press PRINT SEND.
2. Select 2 ('BEST TEST SUMMARY'), then press ENTER.
3. SENDING DATA

Wait for the report to be printed.
POST-BRONCHODILATOR SPIROMETRY

1. Press POST (6) key.

DO POST MED:  
1 = YES 2 = NO

2. Select 1, then press ENTER.

3. Select FVC (1) key.

4. Repeat all steps in BASELINE SPIROMETRY starting on page 4 (using the same flow sensor).

5. Print a final report and discard the baseline printed report. Discard their pneumotach. Offer to send a copy of the report to their physician.

MANEUVER QC GRADES

Coach every participant to obtain at least three maneuvers that are "acceptable" including two that are "reproducible". The best test summary report includes 2 test grades (A to F). The FEV1 grade, the first letter, indicates the reliability of the reported FEV1.

Errors in maneuver performance are identified by the system and displayed after each test (QC grades).

QC Message  

Criterion

Start faster  
Extrapolated volume is > 5% of FVC and > 100ml. Participant is hesitating or lips are not sealed around pneumotach before blasting

BLAST out harder  
The time from the beginning of test to peak flow is > 90 msec. Participant must BLAST out the air more quickly at the beginning of test.

Avoid coughing  
Substantial drop and recovery in flow within first second. Ask the participant to clear their throat and offer a drink of water.

Blow out longer  
Exhalation time is too short. Coach the participant to blow out for at least 6 seconds.

Abrupt ending  
The participant quit before lungs were completely empty. Ignore this message for this study.

FEV1 Variable  
FEV1 value is at least 5% less than their best FEV1. Coach participant to take a deeper breath before the next maneuver.

FVC Variable  
FVC value is at least 5% less than their best FVC.

PEF Variable  
Peak expiratory flow is at least 10% less than their best PEF. Loudly coach the participant to BLAST air out.

GOOD TEST!!!  
No problems detected. Good job!

Maximum Number of Maneuvers. Don't exhaust the participant by asking them to perform more than FIVE maneuvers (5 baseline plus 5 post BD). Make a note on the printed report why the participant couldn't perform the maneuvers.

SPIROMETRY INTERPRETATION

Making a diagnosis of asthma. Symptoms which suggest asthma include intermittent episodes of shortness of breath with wheezing, chest tightness, and/or cough. In patients with these symptoms, spirometry is recommended to help confirm a diagnosis of asthma. If baseline spirometry shows airways obstruction in such a patient, and administration of an inhaled bronchodilator is followed by a 12% or greater increase in the FEV1 (post BD), the patient is likely to have asthma. The bronchodilator acts to quickly relieve the constriction of airway smooth muscle. However, the lack of a "significant" response to the bronchodilator is not helpful in excluding the possibility of asthma, since chronic inflammation of the airways due to asthma may not respond quickly to inhaled bronchodilator. The patient may then be asked to take inhaled or oral corticosteroids every day for a few weeks, and then return for repeat spirometry to see if the FEV1
improved due to the anti-inflammatory therapy.

Many persons with asthma have only mild intermittent episodes (only a few times each year). Spirometry in such patients may be entirely within normal limits (a normal FEV1/FVC) during periods (or seasons) when they have no symptoms. In order to obtain objective test data to confirm asthma in such patients, a 45 minute methacholine challenge test may be performed in a hospital-based pulmonary function laboratory. Alternatively, the patient may be given a peak flow meter to use at home for a few weeks. The results may show excessive variability in lung function, confirming asthma. SHS participants in the asthma substudy will be given an electronic peak flow meter for this purpose.

**Categorizing asthma severity.** In patients who are known to have chronic asthma, and are taking asthma medication, spirometry is used to provide an objective measurement which helps to determine the severity of their asthma (or the degree of disease control). Mild obstruction suggests mild asthma (or reasonable control); moderate obstruction suggests moderate asthma; and severe obstruction suggests severe asthma (or poor control). Moderate or severe chronic asthma suggests the need for better control, which usually means the daily use of inhaled anti-inflammatory medications (controller meds).

**The printed interpretation.** The spirometer interprets the numeric results automatically and prints an interpretation message after the numeric results. These interpretations are based on widely recognized clinical practice guidelines (ATS 1991) but assume that the instrument was calibrated and the test sessions were performed with good quality (QC grades of A or B). Falsely positive interpretations may be printed if these conditions were not met. (The participant is disease free but the report says that they have obstruction or restriction.) Likewise, the degree of BD response may be misinterpreted if either the baseline or post BD maneuvers were of poor quality. For these reasons, technicians and nurses should not be fully confident in the computer interpretations during discussions with study participants. Always suggest that the participant take a copy of the spirometry results to their primary care physician for interpretation. Doctor Enright at the Reading Center will then be happy to discuss the spirometry results with the participant's physician.

Here then are the criteria used by the computer in the spirometer to interpret the spirometry results:

<table>
<thead>
<tr>
<th>Interpretation</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal spirometry</td>
<td>FEV1/FVC ratio ≥70% and FEV1≥80% pred and FVC ≥80% pred</td>
</tr>
<tr>
<td>Borderline obstruction</td>
<td>FEV1/FVC ratio &lt; 70% but FEV1≥80% pred</td>
</tr>
<tr>
<td>Mild obstruction</td>
<td>FEV1/FVC ratio &lt; 70% and FEV1 60% to 79% pred.</td>
</tr>
<tr>
<td>Moderate obstruction</td>
<td>FEV1/FVC ratio &lt; 70% &amp; FEV1 of 41% to 59% pred.</td>
</tr>
<tr>
<td>Severe obstruction</td>
<td>FEV1/FVC ratio &lt; 70% and FEV1 &lt; 40% pred</td>
</tr>
<tr>
<td>Reduced vital capacity</td>
<td>FVC &lt; 80% pred (in addition to obstruction)</td>
</tr>
<tr>
<td>Mild restriction</td>
<td>FVC 60% to 79% pred, with FEV1/FVC ratio ≥ 70%</td>
</tr>
<tr>
<td>Moderate restriction</td>
<td>FVC 51% to 59% pred, with FEV1/FVC ratio ≥ 70%</td>
</tr>
<tr>
<td>Severe restriction</td>
<td>FVC 50% or less than pred with FEV1/FVC ratio &gt; 70%</td>
</tr>
<tr>
<td>Bronchodilator response</td>
<td>Post-BD shows a 12% increase in FEV1</td>
</tr>
</tbody>
</table>
MONDAY CALIBRATION CHECKS

To perform a calibration (cal) checks you need the calibration syringe and a FS200 calibration pneumotach: marked "for calibration use only".

1. Connect the pneumotach to the calibration syringe using the adaptor.

2. Press TEST.

3. Press CAL (4). Carefully follow the messages.

   CAL TYPE: 1=CHECK 2=DISB

4. Press 1 (1=CHECK), then ENTER.

   ROOM TEMP: 0 F
   (32 - 113)

5. Enter the room temperature, then ENTER.

   KEEP PNEUMOTACH STEADY! ZEROING

6. Don’t move the syringe and pneumotach until the “STEADY” message disappears.

7. Pull out the syringe plunger completely (until it “clicks”), then press any key to start the cal check.

   DO EXP CAL

8. Push the syringe plunger in evenly and completely while counting “one Mississippi”.

9. The screen will display a message regarding calibration.

   Message here

10. Place the calibration pneumotach back into a protective plastic baggie.

If the Volume Check Fails

Possible reasons for the volume check to fail (in order of decreasing likelihood) include:

• Failure to completely fill and/or discharge the syringe into the spirometer. Make sure the syringe clicks against the stops with each stroke, but don't "bang" it too forcefully.

• Differences in the air temperature between the spirometer and the syringe. Reflush and repeat the check.

• Try a new flow sensor (pneumotach).

• An air leak in the calibration syringe (see "Cleaning and care of the equipment").

WEEKLY BIOLOGIC CONTROL

The Bio-Control tech must not be a smoker and must not have asthma. The same Bio-Control tech should do a spirometry test each week.

1. On Monday mornings following the CAL Check, use the following assigned ID number (enter on main menu as "ID") for your location:

   999001 = Arizona

   999010 = S. Dakota at Eagle Butte
   999020 = S. Dakota at Pine River

   999100 = Oklahoma at Anadarko
   999200 = Oklahoma at Lawton

2. Do 3 good FVC maneuvers (QC grade A or B).

3. Ensure that your current FEV1 is within 0.2L of the mean of your previous 5 values. If not, repeat using a new pneumotach. If still not, do a 3
flow calibration check, and repeat the test.

4. Print 1 copy of the report. The test automatically saved to the memory card. Place the report in the Biologic Control Log 3-Ring Binder.

CLEANING AND CARE OF THE EQUIPMENT

Cleaning the Spirometer. Use a damp cloth and wipe down the external face of the system. Use water or a mild detergent solution.

Calibration Syringe Care

The 3.00 liter calibration syringe should be stored near the spirometer so that it remains at the same temperature as the spirometer. Store the syringe with the plunger pushed all the way in. Take care not to drop it.

DO NOT attempt to make any adjustments to the syringe. Do not loosen the metal rings on the shafts, since this will spoil the factory calibration.

Periodically check each syringe for leaks. Fill it with air, hold your palm against the outlet snout, and try to empty it. If you can expel any air with the outlet plugged, the syringe has a leak and must be repaired. Notify the Reading Center.

TECHNICIAN CERTIFICATION

The certification examination includes 50 multiple choice questions based on this Manual of Procedures, and a practical demonstration of skills including calibration checks, cleaning, biological control and testing of a naïve subject (50 points). A passing score of at least 75 points is necessary for certification. Only certified technicians will perform pulmonary function testing.

Certification of new technicians after the initial central training session may be performed by a centrally trained, certified PF technician. The written exam will be administered locally, and the first 20 PF tests performed will be observed by a certified PF technician and then examined by the Reading Center and found to be satisfactory before the new technician is certified. The results of the first 20 spirometry test sessions performed by each technician will be closely examined at the Reading Center. Copies of suboptimal quality test sessions (where QC grades are less than B) with comments for improvements will be mailed to the technician as they are evaluated.

A site visit to the clinical/site centers will be made early during phase, and mid-way through Phase III. Complete calibration, biological control QC check, and complete PF testing of at least three participants by each PF certified technician will be observed and reviewed. More efficient methods as well as protocol violations will be discussed during the site visits and later in a written report.

QUALITY CONTROL

Need for Spirometry QC. Examination of spiromgrams from the Framingham study revealed that more than 18% were of clearly unacceptable quality. Two more recent studies, with over 12,000 adults each, found that 40 - 50% of the spirometry maneuvers were of unacceptable quality. Deviations in test performance and lack of regular leak checking and calibration checks can result in loss of study data.

Feasibility of QC Procedures. The Renaissance spirometry system assists the pulmonary technician with quality control of maneuvers when spirometry testing is being performed, calculates the PF variables, suggests interpretations, formats and prints reports, and compresses graphics data for archival storage. The computerization of spirometry QC procedures dramatically...
decreases the overhead time associated with spirometry testing.

**Implementation of QC Procedures.** There are five separate levels of quality control implemented for spirometry testing which address the four factors known to influence the results:

1. Daily volume calibration checks using a 3.00 liter syringe as the "gold standard".

2. QC grading of maneuver acceptability and reproducibility immediately after every maneuver.

3. The PF technician is trained to recognize the patterns of unacceptable maneuvers, watching the participant during the performance, and reviewing the QC grades and resulting printed flow-volume curves.

4. The results of the calibration checks, biologic control and the best 3 FVC maneuvers are stored and sent to the Reading Center for review by the QC Supervisor. Results are reported to the Data Coordinating Center.

5. Each week biologic control. The results will be compared with their prior mean values for FVC and FEV1.

**DOWNLOADING OF MEMORY CARDS**

On the first Monday of each month, mail the previous month's memory card to the Reading Center. The Reading Center will download all PF data for participants tested during the previous month into a database (Renaissance DB). The data is deleted from the memory card, and the memory card is mailed back to the site.
REFERENCES: Please call the PF Reading Center for a copy of any of these references.


APPENDIX

Spirometer Configuration: The spirometry system comes to you set with the standard configuration. You should, however, go through the configuration routine to set the correct date and time. This shows the correct settings for the SHS Asthma Sub-Study settings:

1. Press TEST.
2. Press the forward arrow key ▲.
   To retain the current configuration, press ENTER.
   To change the configuration press the number of the desired option, then press ENTER.
3. TECH CODE: 2 (2=NO)
4. UNITS: 1 (1=English)
5. INTERP: 1 (1=YES)
6. DATE FORMAT: 1 (1=Amer)
7. TIME FORMAT: 2 (2=12HR)
8. TIME: XXXX (HHMM)
9. AM/PM: 1=AM, 2=PM
10. DATE: XX XX XX (mm dd yy)
11. ADULT NORMS: 2 (2=Knudson)
12. KNUDSON REF: 2 (2=1983)
13. PED NORMS: 2 (2=Polgar)
14. PEF UNITS: 2 (2=LPM)
15. REPORT: 2 (2=INDS)
16. BESTVAL: 1 (1=VAL)
17. GRAPH FORM: 1 (1=Flow-Vol)
18. GRAPH SIZE: 2 (2=Validation)
19. SCALE GRAPH: 2 (2=NO)
20. NUM CURVES: 3
21. OVERLAY CRV: 1 (1=YES)
22. PRED POINTS: 1 (1=YES)
23. PRINTER: 4 (4=HP)
24. GRID: 2 (2=NO)
25. LUNG AGE: 2 (2=NO)
26. SYR VOL: 3
27. QC GRADES: 1 (1=YES)
28. INS INCNT: 2 (2=NO)
29. AUDIO INCENT: 1 (1=YES)
30. RACE ADJUST: 85
31. ALL DATA: 1 (1=YES)
32. ALL CURVES: 2 (2=No)
33. PRES: 730 Arizona
       730 Oklahoma
       675 S. Dakota
34. CUST HEADER: 1 (1=YES)
    using the 7 (advances 1 letter), 9 (back 1 letter) and both arrows (forward/back in sentence), enter the header as “Strong Heart Study”
SUPPLIES

Attach the spirometer cable to the computer with the two screws on the connector, otherwise it will fall off easily. Attach the printer cable to the rear of the PC. Attach all power plugs to the switched outlet strip.

Spirometry Major Components

1. PB100 Renaissance spirometer
2. PB110 Renaissance base station
3. PB130 Memory card (qty 2)
4. AC Adapter
5. Pressure tube and spare
6. Canon BJ240 inkjet printer, printer cable and 1 extra BJ-02 Black Ink cartridges
7. Hans Rudolph 3.00 L calibration syringe
8. MDI spacers, box of 100 (6 inch lengths of ventilator tubing)
9. PB Spirometry video
10. A pneumotach marked “FOR CALIBRATION ONLY”
11. SASE padded mailing envelopes (qty 15) for sending memory cards to the Reading Center

Spirometry Supplies

FS200 disposable pneumotachs, box of 250
Power strip with 4 outlets
Denture cups (qty 50)
8½" x 11" paper; a ream of standard copier paper
Electronic timer; Radio Shack catalog # 63-896
# SPIROMETRY REPORT

Patient ID: 6663  
Age: 41  
Height (in): 65  
Weight (lbs): 135  
Sex: Female  
Race Correction: No  
Sensor: FS200  
Resp Sci  
PB100 SW Rev: J-D  
UofA Med College Resp Sci  
SCOR Specialized Center of Research  
TEST DATE: 02/27/98  
TIME: 02:46 PM

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Premed QC</th>
<th>TRIAL 1</th>
<th>TRIAL 2</th>
<th>TRIAL 3</th>
<th>Pred</th>
<th>%Pred</th>
<th>PostMed QC</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC (L)</td>
<td>A</td>
<td>1.86*</td>
<td>3.66</td>
<td>3.16</td>
<td>112%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV1 (L)</td>
<td>A</td>
<td>2.03*</td>
<td>2.48</td>
<td>2.48</td>
<td>105%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>%FEV1 (%)</td>
<td></td>
<td>78.49</td>
<td>78.45*</td>
<td>78.42</td>
<td>80.19</td>
<td>94%</td>
<td></td>
</tr>
</tbody>
</table>

Variability: Premed: FVC = 1.61%  
FEV1 = 1.74%  
PEF = 3.04%

**PREMED**

![Graph](chart.png)

**FLOW (L/S)**

.25 CM/L/S

**VOLUME (L)** .5 CM/L

**Interpretations:**

PREMED: Testing indicates normal spirometry.

**Comments:**
FORWARD:

This manual serves three purposes:

- a study guide for training of physicians, nurses and technicians to perform ambulatory PF monitoring.
- a practical "how-to" reference guide to be used during the study
- documentation of the procedures for analyses and manuscript preparation.

BACKGROUND:

*Participant selection.* The Data Coordinating Center (the DCC at UOK) has preselected a subset of SHS participants for the Asthma Substudy. These participants include all of those who reported asthma or a history of episodes of wheezing with shortness of breath during the Phase II exam (n=600). Participants who report asthma or wheezing at the time of the Phase III exam (recent onset) will also be added to the asthma substudy. All asthma substudy participants will be asked to perform ambulatory PF monitoring at home for two weeks following their clinic visit.

There is no risk to the test. It is merely inconvenient.

*Rationale for Ambulatory PF Monitoring.* Asthma is a disease of variable airways obstruction. Many patients with asthma have only mild intermittent asthma. Such patients have long intervals without symptoms, during which lung function is often normal. Baseline spirometry is then normal and there is no bronchodilator (BD) response. The only objective evidence of asthma may then be excessive lability of pulmonary function (PF, which includes both PEF and FEV1). This lability (hyperreactivity) may be measured within 30 minutes by administering a methacholine challenge test in a hospital PF laboratory. An easier method of detecting PF lability is to measure diurnal variation in lung function over a couple of weeks in the patient’s own environment (at home). Most patients with asthma have larger than normal "morning dips" in lung function, which may be measured by ambulatory PF monitoring. A morning dip in PEF of more than 20% in adults usually indicates excessive airway lability.

In patients with mild to severe persistent asthma, baseline spirometry usually shows airways obstruction, with a large acute (10 minute) response to an inhaled bronchodilator (albuterol). However, this response may be blunted by the recent use of an asthma inhaler or by chronic airway inflammation. The severity of asthma may then be measured by the severity of the morning dip in lung function during ambulatory monitoring. A morning PEF dip of more than 30% is associated with moderate to severe asthma.

Ambulatory PF monitoring has two primary purposes: #1) to assist asthma management, or #2) to help establish the diagnosis of asthma or determine the severity of asthma. Peak flow meters and the new electronic PF monitors (like AirWatch) were designed for asthma management; however, we will be using the AirWatch in this study only for purpose #2.

During the two weeks we ask a participant to use the AirWatch unit, we do not want those who have asthma to use the results to adjust their asthma medications (as they would for asthma management purposes). However, if following the study they and their physician decide that they would like to use a peak flow meter for asthma management, we will provide one without charge.

Airway lability is calculated for each day as the highest minus the lowest PEF, divided by the average PEF. The lowest PEF during the day is almost always the early morning value, because blood adrenaline and cortisol levels are lowest in the early morning, and because indoor allergens such as house dust mites and molds are inhaled from bedding during the night. This means that
for a valid measure of PF lability, PF must be measured at least twice a day, including once in the early morning. Since compliance is better if the AirWatch is kept in the bathroom, and not taken to the workplace, we will ask only for early morning and evening or bedtime measurements (when most people brush their teeth).

In order to obtain reasonable sensitivity, PF must also be measured for several days, because high levels of allergens may be inhaled only during a couple of days or nights during any given week. Studies have also found a "learning effect" of low PF values and high PF lability during the first 3 days of a study, and rather poor compliance after 2-3 weeks of daily PF measurements, so two weeks seems an optimal duration of testing.

When compared to diagnostic spirometry testing, ambulatory PF testing requires only one second maneuvers (not 6 seconds), since only the PEF and FEV1 are measured, and not the vital capacity. Also, the participant is asked to perform only 3 blows during each test session (not up to 8). The deep inhalation and BLAST efforts remain important, so teaching the participant to use the AirWatch will be done immediately after spirometry testing during their clinic visit.

Most previous epidemiologic studies of ambulatory PF monitoring have used inexpensive mechanical peak flow meters along with a written asthma diary. However, the recent introduction of relatively inexpensive electronic spirometers allows automatic storage of the results, improving compliance and accuracy. They also allow measurement of the FEV1 which is more accurate, more reproducible, and more sensitive to bronchoconstriction when compared to the PEF. Spirometry is the simplest, most effective test for assessment of lung function. That is why it has been included in many cardiovascular epidemiology studies, including SHS.

Spirometry (without bronchodilator) was measured during SHS Phase II for the original cohort. Spirometry reference values are being developed from the healthy subset of American Indian participants.

Spirometry records the relationship between airflow (FEV1) and the exhaled volume of air during a breathing maneuver called the FVC maneuver (forced vital capacity maneuver). The most common lung diseases reduce forced expiratory flows. Such "obstructive" lung diseases include asthma, bronchitis, and emphysema. The ratio of FEV1/FVC is very sensitive for detecting mild airways obstruction.

NEW PROCEDURES
1. Ambulatory PF monitoring of the participant for 2 weeks.
2. The AirWatch is very small.
3. The AirWatch will be returned to the clinic for downloading of the data, cleaning and reissue. The participant will be paid $0.25 per GOOD test ($0.50 per day for a total of $7.00).
DEFINITIONS (GLOSSARY)

ALBUTEROL (official generic name in the U.S.) is an asthma medication for the relief of bronchospasm in patients with reversible obstructive airway disease (asthma). After administering albuterol, an improvement of 15% or greater in FEV1 values indicates a decrease in asthma.

BD: is short for bronchodilator.

COPD stands for Chronic Obstructive Pulmonary Disease, a general term for lung disease caused by cigarette smoking - a mixture of emphysema, bronchitis, and hyper reactive airways (asthma).

FEV1: Forced Expiratory Volume in 1 Second (liters). The volume of air exhaled in the first second of an FVC maneuver.

FEV1/FVC RATIO is the most sensitive and specific index of airways obstruction measured by a spirometer. It is normally above 70% in adults.

FVC is the Forced Vital Capacity, the volume of air exhaled during the maneuver named after it. The subject takes as deep a breath as possible and then quickly exhales (BLAST) as much air as possible. The FVC is reduced with restrictive disorders.

MDI is a meter dose inhaler, a small pressurized cannister commonly used to deliver asthma medications directly to the airways. Also called "asthma puffers".

OBSTRUCTION is a decrease in maximal airflow rates caused by airway narrowing. The FEV1/FVC ratio and the FEV1 are both decreased.

PEF stands for Peak Expiratory Flow, the highest flow measured during the FVC maneuver. It is a good index of blast effort.

PF is short for Pulmonary Function (lung tests).

MOUTHPIECE is the blue plastic part off the end of the AirWatch. This is where the participant blows. When the mouthpiece is fully open or closed, it will click into place when you rotate it.

NUMBER LINE shows either (1) the date and time, or (2) the peak flow, or (3) FEV1 measurement.

PRED is short for the predicted value of a PF parameter. It is determined from the regression equation from a large population study of supposedly normal people.

RESTRICTION is a decrease in lung volumes. Scarring of lung tissue (fibrosis), heart failure (CHF), pneumonia, and simple obesity are some of many causes. The FVC is reduced while the FEV1/FVC ratio is normal or increased.

SPACER is a device attached to a MDI asthma inhaler, designed to improve deposition of the drug deeper into the patient's lungs.

WILBY is the coach. He looks like a mutated Pac-Man or an eraser head.
DESCRIPTION OF THE AIRWATCH

The AirWatch \textsuperscript{TM} is a hand-held electronic spirometer the size of a stopwatch. It costs about $120. When a person blows into the attached blue plastic flow sensor, lung function (PEF and FEV1) is measured, displayed, and stored, along with the date and time of day. The unit is usually configured to store the highest FEV1 and the highest PEF from multiple maneuvers performed during a 10 minute period of time (during a single test session). During each test session, the patient may indicate if the maneuvers were performed before or after inhaling a bronchodilator (pre or post-BD).

The AirWatch was designed to assist the patient with asthma to monitor the severity of airways obstruction at home, as a guide to the need for asthma medications, and to periodically send the results to the primary care physician, via telephone and FAX. However, during this study we will not ask the participants to connect the AirWatch unit to a telephone, and we will not send the results to their physician.

The AirWatch was designed to be just as accurate as an office spirometer (FEV1s are measured with 3\% accuracy or better). However, spirometry requires acceptable FVC maneuvers, as judged by the apparent degree of effort during inhalation and subsequent forced exhalation (Blast), and by the pattern of the resulting flow-volume curves. There is no coach to help the participant perform acceptable FVC maneuvers at home, and flow-volume curves are not stored or printed by AirWatch, so the results are usually not of optimal diagnostic quality when compared to office spirometry. The AirWatch developers are planning to include maneuver quality checks, similar to those incorporated in many spirometers. We will switch to those improved units when they become available later in 1998.

The two quarter-size AirWatch batteries last about one year with daily use and are easily replaced. It automatically goes into standby mode to conserve battery power after about 30 seconds of inactivity. Press any of the 3 blue buttons to turn it on again.

Recent studies in Denver found that about 10\% of the units become inoperative during one year of use in the field, half due to the electronics and half due to the blue sensor, which is easily replaced. A 3 liter calibration syringe cannot be used to check the AirWatch accuracy. However, correct and accurate operation is conveniently verified by comparing the PEF and FEV1 values obtained by the participant during spirometry testing with those obtained using the AirWatch.

AIRWATCH PROTOCOL

AirWatch Setup. Please view the 20 minute AirWatch videotape and review the "Getting Started with AirWatch" manual to learn how to install the batteries, attach or replace the mouthpiece, and set the date and local time. During the setup, set the personal best PEF to 100 LPM, leave the first zone boundary at 80\%, the second zone boundary at 50\%, set the session length to 10 (minutes), and set the phone dialing method to tone (not pulse). The final number is the unit's serial number (verify but don't change).

Look for a battery symbol in the upper right corner of the display. If there is the display is blank or if the battery symbol is displayed, replace the batteries with two new 3 volt batteries, type CR2032, both with + sides up. Then recheck for correct setup. To enter the setup mode, press and hold the two outside buttons for 5 seconds.

A demonstration unit was given to each site during training. Keep the "demo" unit in the "DEMO" ziplock. Each staff member should have his/her own blue mouthpiece stored in a ziplock labeled with their name.

Teaching the Participant. Teach the participant how to use the AirWatch immediately following spirometry testing, after
administering the bronchodilator, while waiting the 10-15 minutes for it to take effect, or following post-BD spirometry.

Tell the participant, "We have a new little gadget to test your lungs at home." Show them the AirWatch. "You push one of these blue buttons and then blow into it just like you did into this spirometer." Point to the Renaissance spirometer. "Asthma causes variations in lung function throughout the day, and we would like to measure those variations. You would keep this gadget in the bathroom and use it when you brush your teeth in the morning and in the evening."

Say, "we'd like you to use it twice a day for two weeks and then mail it back to us in this envelope." Show them a self-addressed stamped padded envelope. "Do you think that you could do this?"

If they agree, open the package of a clean AirWatch, take its log sheet and confirm the correct serial number (printed on the back of each AirWatch unit). Write down the date, the participant's name, and their ID number.

Install a clean blue mouthpiece on the AirWatch. Be certain to align the two small (nearly invisible) triangles, pointing the mouthpiece downwards, before gently snapping the mouthpiece onto the spirometer.

Next say "Let me show you how easy it is to use this gadget. I will also give you this instruction sheet in case you forget. First, push any of these 3 blue buttons to turn on the unit. You will then see this little man displayed. Our asthma doctor calls him eraser head, but his real name is Wilby. Rotate the blue mouthpiece like this, until it snaps open. Take as deep a breath as possible. Quickly put you teeth around the blue mouthpiece and seal your lips around it. Blast out your air as fast as you can for one or two seconds."

Take the demonstration unit, attach your blue mouthpiece with your name on it and show them how it is done. Then hand their unit to them and coach them to do a test. Stop their exhalation after two seconds. Look for numbers on the display and a smiling Wilby. Wait for a minute and blow into the gadget again. Wait for another minute and repeat the test for a third time. State, "the goal is to get Wilby to smile three times, then you are done with that test session."

Store your blue mouthpiece in your labeled ziplock, and place it and the demonstration unit into "DEMO" ziplock.

Validating AirWatch Accuracy. On their baseline spirometry printed report, write down the best PEF (in LPM) displayed on the AirWatch. Then press down on the center blue button for 3 seconds to view and record the best FEV1 from the test session. Compare the two PEF results (Renaissance and AirWatch values) to ensure that they match within 50 LPM (about 10%). Compare the two FEV1 results to ensure that they match within 0.3 liters.

If the results from the two spirometers do not compare favorably, the problem could be either differences in participant effort (submaximal inhalations or blasts), bronchodilator response, or instrument inaccuracy. Following the post bronchodilator spirometry, replace both the white Renaissance flow sensor and the blue AirWatch sensor and coach the participant to repeat 3 maneuvers using the AirWatch. Press the right-hand blue button to indicate a post-BD test session, note that an MDI symbol appears above Wilby. Then compare the post-BD PEF and FEV1 values and write the AirWatch values on the post-BD spirometry report. Note on the report that you replaced the flow sensor. Hopefully the results will match this time.

Ask the participant, "any questions? Please call me later if you have any problems or questions using the gadget during the next two weeks." Place the AirWatch and instruction sheet inside the padded envelope and hand it to them to take home.
Follow-up. If possible, call the participant three days later and ask if they have had any problems using the gadget. Discuss how important it is to blow into it at least twice a day. If you have not received the unit three weeks later, call them to remind them to place it in the mail.

Receipt and Data Transmission. Upon receipt of an AirWatch from a participant, gently detach the blue mouthpiece and place it into the Tupperware container which is full of disinfectant cleaning solution. There is no need to keep the mouthpieces and AirWatch units paired together. Any mouthpiece should be accurate when attached to any other AirWatch unit.

Find the AirWatch Log Sheet for that unit, verify the serial number, and write down the Return Date. Remove the blue rubber connector cover and attach the unit to an analog telephone line (like the one attached to your FAX machine or computer modem). Press any blue button. Confirm that the phone is connected by noting the phone symbol displayed next to Wilby's ear. Press any blue button to begin transmission. The phone symbol will blink during the transmission, which should last less than one minute. If the transmission was successful, Wilby smiles and a star is displayed above his head. On the log sheet, write down the time of the phone call.

If Wilby frowns, the call to the central computer was not successful. Press any button to try again. If transmission is still unsuccessful, call the AirWatch toll-free help line at (800) 267-9452. Don't worry, the unit stores the last 500 test sessions until the batteries are dead.

Thoroughly wipe the AirWatch with a damp cloth to clean it. Press a button and verify that the batteries are still good (the low battery symbol is not displayed). Wash your hands. Obtain a clean dry blue mouthpiece, gently attach it to the unit and place them in a new sandwich bag. Place a new instruction sheet, the Log Sheet, and the AirWatch into a new padded envelope, ready for the next participant.
REFERENCES: Please call the PF Reading Center for a copy of any of these references.


APPENDIX

AIRWATCH LOG SHEET

Unit ____ Serial # ______

<table>
<thead>
<tr>
<th>Log Out Date</th>
<th>Participant Name</th>
<th>ID number</th>
<th>Reminder Call</th>
<th>Return Date</th>
<th>Phone Time</th>
</tr>
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<tbody>
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<td></td>
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<td></td>
</tr>
</tbody>
</table>
AIRWATCH INSTRUCTION SHEET

Please use twice a day for two weeks.
Early in the morning and in the evening.

1. Press any button to turn it on.
2. Take a very deep breath.
3. Seal your lips around the blue mouthpiece.
4. BLAST out your air, for 1-2 seconds. Wait for a minute and blow into it again.
5. Wait again and blow into it a third time. The goal it to make Wilby smile 3 times.

The unit will turn off by itself.
You don't need to clean the unit. We will.
Return the unit after using it for 2 weeks.
If problems or questions, please call:

[clinic phone number and staff name here]
SUPPLIES

AirWatch Major Components

1. AirWatch™ Airway Monitoring System
2. Mouthpiece

AirWatch Supplies

- Tubberware or plastic container
- Disinfectant cleaning solution
- Demo Ziplock (large ziplock) containing:
  - 1 demonstration unit (1/site)
  - 3 blue mouthpieces in 3 small ziplocks (to be labeled with tech's name)
ASTHMA SUBSTUDY - ALLERGY SKIN TESTING
MANUAL OF OPERATIONS
STRONG HEART STUDY, PHASE III 1998

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(800) 438-0088

Bayer Corporation
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Allergy Products
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# TABLE OF CONTENTS

BACKGROUND ........................................................................... 1
DEFINITIONS (GLOSSARY) .................................................. 2
WEEKLY PROCEDURES ...................................................... 2
THE DERMAPIK SYSTEM. .................................................... 2
ANTIGEN STORAGE ............................................................ 3
ANTIGEN EXPIRATION DATES ........................................... 3
PARTICIPANT PREPARATION .............................................. 3
TEST PREPARATION .......................................................... 3
PREPARING THE ARM .......................................................... 4
APPLYING ANTIGENS ......................................................... 4
RECORDING THE RESULTS ................................................ 5
HISTAMINE CONTROL ....................................................... 6
STOP THE ITCHING ............................................................ 6
EQUIPMENT CLEANING .................................................... 6
TECHNICIAN CERTIFICATION .......................................... 6
REFERENCES ........................................................................ 7
SUPPLIES ............................................................................ 8
FORWARD:

This manual serves three purposes:

- a study guide for training of physicians, nurses and technicians to perform allergy skin testing.
- a practical "how-to" reference guide to be used during the study

BACKGROUND:

Many patients with asthma and hayfever are allergic to aeroallergens -- plant or animal derived "antigens" which are small enough to be inhaled. A person with multiple allergies is often referred to as being "atopic." These allergies often develop during the first few years of life, but the onset of allergic symptoms may begin at any age. It is worthwhile to determine exactly which antigens a given patient is allergic to, because they may then be able to avoid exposure to the sources of these antigens -- thereby reducing the frequency and severity of symptoms and perhaps, the need for medication. Of course, many patients have already identified some animals, plants, or seasons which trigger their symptoms, but the test results remain useful to confirm what experience (by trial and error) has taught them.

Two tests are available and standardized to determine which antigens a patient is allergic to: 1) allergen skin testing and 2) serum (blood) levels of specific IgEs (immunoglobulin E). Results in a half hour and low cost (for a large number of antigens) are the primary advantages of allergen skin testing. The cost of analyzing 20 specific IgE levels is about $200 for a single patient and the results are usually not available for a couple of weeks. Disadvantages of allergen skin testing are that it is takes more technician time than drawing a sample of blood, and the subject often has an itchy arm or back for about a half hour (where the allergic skin reactions occurred).

The second National Health and Nutrition Survey (NHANES II) performed allergen skin testing of 8 common aeroallergens for 4300 young participants. Asthma was most strongly associated with positive skin tests to Alternaria (a mold) and to house dust mite, but asthmatic subjects were also more likely than other subjects to be skin test positive to dog, cat, oak, bermuda grass, rye grass, and ragweed. The followup NHANES III study performed skin testing for many other antigens. We have chosen to use allergen skin testing for the 19 antigens which have been reported by local allergists to be positive most frequently at each SHS site.

The concentration of each antigen is standardized and was selected to produce a rather small skin reaction (about ½ inch in diameter) if a patient is allergic to that antigen. The "immediate hypersensitivity reaction" is produced by the release of histamine from mast cells present in the skin. The resulting inflammation causes swelling (called a wheal) centered on the point of antigen entry (the skin prick site) with a larger area of redness (erythema or flare) surrounding the bump. A large wheal and flare are produced when the patient is very sensitive to that antigen, so the diameter of the wheal is measured as the degree of skin test response.

About 5% of persons will have a small reaction to the skin prick by itself (without any antigen) and so this wheal to the "negative control" must be subtracted from any antigen response. A few persons are "anergic" and have no skin test response of any kind, probably because they don't have any mast cells in their skin, or their histamine response has been blocked by medications. For this reason, a dilute concentration of histamine is also applied as a "positive control."

Several methods of applying the antigens just below the surface of the skin, without drawing blood, have been developed. We have chosen a method (the DermaPik) which has the following advantages when compared to other methods: speed of
application, small chance of accidentally switching antigens, lack of cross-contamination (single-use DermaPIKs), high sensitivity, and good repeatability.

NEW PROCEDURES

1. Allergy skin test will be done using 21 antigens and controls.

DEFINITIONS (GLOSSARY)

ALLERGEN: a substance that causes an allergy.

ANTIGEN: a liquid made from an allergen that when introduced onto the skin stimulates the production of an antibody.

CONTROL (made from glycerine): used to identify participants who have sensitive skin which might give the false impression of positive skin test results.

CONTROL PARTICIPANT: to verify asthma in an asthmatic participant (those who indicate they have asthma or have been told that they have asthma) by conducting the same procedures on a participant without asthma.

HISTAMINE (the end product of the allergic reaction): checks to be certain that the skin's ability to react positively to an antigen has not been blocked by the participant's use of other medications. Taking an antihistamine 1 or 2 days before skin testing may block the test results, as well as taking certain medications.

WEEKLY PROCEDURES

Daily:
- After each participant, replace with new DermaPIKs
- Wash your hands

Friday: After last participant:
- Refill supplies (70% alcohol, cotton balls, sterile pads, tissue, hydrocortisone, antihistamine lotion)

REPLACEMENT OF DERMAWELLS
FEBRUARY (STARTUP) & AUGUST 1998
FEBRUARY 1999

- New DermaWells will be placed in the DermaRAK in February 1998 at startup.
- Replace the DermaWells every 6 months for this study. DO NOT REFILL DERMAWELLS. When wells are emptied they should be discarded and replaced with new ones.
- Each DermaWell should be filled with approximately 0.05 cc of the appropriate extract. At least 1.0 cc of each extract has been provided. Filled DermaWells (0.5cc) provide sufficient antigen for approximately 100 skin tests.
- Always wash your hands after handling the antigens.

THE DERMAPIK SYSTEM

The Greer DermaPIK is a plastic, single use "toothpick" with six tiny tines arranged at the tip in a 2 mm circle for epicutaneous allergy skin testing. There is 1 DermaPIK per antigen; 21 DermaPIKs per participant.

The Greer DermaWell is a plastic container that seats into the DermaRAK. Each DermaWell is assigned an antigen and holds approximately 0.5cc of the antigen. A DermaPIK seals each DermaWell. Each DermaWell is marked with its antigen (G1-3, W1-4, T1-4, F1-4, C1-7, C- and C +). The Greer DermaRAK is a plastic rack containing 21 DermaWells.

The Antigens we are using were carefully picked using high percentage of positive reactions seen in the Phoenix and Tucson areas, and adjusting for localized pollens within the same family.

G = grass pollens
G1 Bermuda
G2 Timothy
G3 Bluegrass, Kentucky
PARTICIPANT PREPARATION

In order to obtain valid and useful skin testing results, the participant must discontinue the use of certain medications for 72 hours before skin testing. OTC (over the counter) and prescription medications such as:

**Antihistamines** - includes Benadryl, ChlorTrimeton, Allerest, ARM, Contact, Extendryl, Sedane, Claritin, Bromfed, and other OTC and prescription antihistamine/decongestant medications.

**Cough preparations** - any type, OTC or prescription.

**But they shouldn’t stop these:**

**Stomach medications** - such as Zantac, Tagamet.

**Antidepressants and Tranquilizers**

If participant has taken any of the above, note them on the Skin Test (ST) worksheet.

TEST PREPARATION

**Wash your Hands** Participants will appreciate your consideration if you make a point of washing your hands before testing them. Do this as you enter the room if it has a sink.

**Explain the Procedure** Explain that the purpose of the next test is to determine if they are allergic to trees, molds, grasses, animal or insects. The test using 21 “toothpicks” will be lightly pushed on their skin. Each of the toothpick has a drop of antigen made of a tree, mold, grass, or animal. If they are allergic to one of the antigens, after 15 minutes, you will circle any raised bump (will look and feel like a “mosquito” bite). We will measure the bump, then we will wash your arm. If you are still itchy, we have lotion that will take away the itchiness.
PREPARING THE ARM

1. Ask the participant to bare their non-dominant forearm.

2. Using the 70% alcohol and cotton balls, clean the inside of the forearm gently. Stop cleaning the area when the cotton ball(s) come up clean.

3. Using 4x4s or 2x2s gauze pads, gently dry the area.

4. Using the template on the “Skin Test Worksheet” (left side), line up the 1st mark (darker line under “template”) with the antecubital fossa (the crease between the forearm and upper arm). Then, place template down the middle of the forearm.

5. Using an ink pen, mark the template on the arm. Make the marks 1" wide.

6. Mark the antecubital mark with an “X”.

7. 1" from the line above the wrist (stay clear of creases & veins), mark an “+”. If there is not enough room, you may place the “+” above the elbow, or on the other arm, or if the arm is wide enough, place the “+” on the side (at least 1 ½ " away from the other marks).

APPLYING THE ANTIGENS

Allergy testing with the DermaPIK, as with any skin test device, requires that the proper technique be used. Proper contact between the DermaPIK and the skin is required to ensure that the antigen bearing tines of the DermaPIK penetrate the first layer of the epidermis to deliver the antigen to the underlying reactive dermis layer of the skin, but proper test technique will not cause bleeding.

1. Match up the DermaRAK with the arm (left side marked on the DermaRAK is your left side [participant’s right side of their forearm]).

2. Hold the participant’s arm steady at the palm with your non-dominant hand.

3. Starting with the left side; Using your dominate hand and starting at the 1st line past the antecubital line, remove the DermaPIK from the DermaWell, and briefly inspect to assure that a small amount of the liquid antigen is present between the tines.

4. Place the antigen to the appropriate spot 1" at the left of the line. Make a SLIGHT DIMPLE (IMPRESSION) into the skin with the DermaPIK ensuring that all six tines are in contact and gently twist, rotating the DermaPIK approximately one-quarter turn.

5. Discard used DermaPIK in the paper cup.

6. Proceed down the left side using the above technique. Then, proceed down the right side.

7. Following the application of all the antigens and controls, set the timer for 15 minutes.

8. Remind the participant not to scratch
or move their arm.

9. Administer the 2-4 page Asthma Questionnaire.

10. Discard the contents of the paper cup into a SHARPS container.

8. At the ‘+’ mark near the participant’s wrist, place the scotch tape on the skin over their marked reaction.

9. Press down on the scotch tape so it adheres to the skin.

10. Pull the left-side up just a little, making sure the ink marks are coming up with it. If ink marks are not coming up with the tape, press the scotch tape back down and press harder across the tape.

RECORDING THE RESULTS

1. At the end of the 15 minutes, set the scotch tape dispenser next to the arm.

2. Using the ink pen, carefully circle each reaction (the raised part that looks like a mosquito bite).

11. Pull the left-side up and off the arm (see the actual “reaction” template left on the tape).

12. Under the ‘left-side’ column on the participant’s ST worksheet, match the line. Press the scotch tape onto the ST worksheet.

13. Do steps 9 and 12 for the right-side.

14. Under the ‘right-side’ column on the participant’s ST worksheet, match the line. Press the scotch tape onto the ST worksheet.

15. Pull the ‘+’ strip up just a little, making sure the ink marks are coming up with it. If ink marks are not coming up with the tape, press the scotch tape back down and press harder across the tape.

16. Pull the ‘+’ strip up and off the arm.

17. Under the ‘+’ column on the participant’s ST worksheet, press the scotch tape onto the ST worksheet.

3. Cut a piece of scotch tape approximately 8½” to 9” long.

4. Running down the left side (your left-side; their right-side) from a little above the antecubital line to the wrist, press the scotch tape on the skin.

5. Press down on the scotch tape so it adheres to the skin (picking up the ink circles/marks).

6. Repeat steps 3-6 for the right side.

7. Cut a third piece of scotch tape approximately 1½” long.
HISTAMINE CONTROL

All participants should have a reaction to the Histamine Control (C+).

1. If there is no histamine reaction, redo the Histamine (C+) at another location on the arm using the same method as described in PREPARING THE ARM AND APPLYING THE ANTIGENS.

2. Wait at least 5 minutes.

3. Record the reaction using the method described in RECORDING THE RESULTS.

4. If Histamine Control is still negative, carefully go over the medications listed in PARTICIPANT PREPARATION section with the participant and record any changes.

STOP THE ITCHING

1. Cleanse the forearm with 70% alcohol and cotton balls, wiping gently. The participant will appreciate this procedure since their arm will be itchy where they had reactions.

2. Apply 1% hydrocortisone cream or the anti-itching lotion to the area. You can also apply ice to the area.

3. Severe reactions are rare. If a severe reaction has occurred (flushing, low blood pressure, shortness of breath, chest tightness) administer Benadryl liquid (adult dosage is 2 teaspoons). The Benadryl often causes drowsiness (see PDR). Watch the participant for at least 30 minutes before releasing them. Don’t let them drive.

CLEANING EQUIPMENT

Cleaning the DermaRAK. Using an alcohol prep or the 70% alcohol on a cotton ball, wipe down the external face of the DermaRAK.

Quarterly replacement of the DermaWells. The DermaWells will be replaced every 6 months (February, August 1998) during this substudy.

TECHNICIAN CERTIFICATION

The certification examination includes 10 multiple choice questions based on this Manual of Procedures, and a practical demonstration of skills including cleaning and testing of a naive subject (50 points). Only certified technicians will perform allergy skin testing.

Certification of new technicians after the initial central training session may be performed by a centrally trained, certified technician. The written exam will be administered locally, and the first 5 allergy skin tests performed will be observed by a certified technician and then examined by the Reading Center and found to be satisfactory before the new technician is certified. The results of the first 5 allergy skin test sessions performed by each technician will be closely examined at the Reading Center.

A site visit to the clinical/site centers will be made early during phase, and mid-way through Phase III. Complete allergy skin testing of a participant by each allergy certified technician will be observed and reviewed. More efficient methods as well as protocol violations will be discussed during the site visits and later in a written report.
REFERENCES: Please call the Allergy Reading Center for a copy of any of these references.


SUPPLIES

Skin Testing Major Components

1. DermaPIK
2. DermaRAK
3. DermaWells
4. Antigens (scratch testing formula):

<table>
<thead>
<tr>
<th>SHSid#</th>
<th>Common Name</th>
<th>Bayer Item#</th>
<th>Concentration</th>
<th>Qty</th>
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<tbody>
<tr>
<td>G1</td>
<td>Bermuda</td>
<td>1142</td>
<td>1:20</td>
<td>5ml</td>
</tr>
<tr>
<td>G2</td>
<td>Timothy</td>
<td>2597</td>
<td>1:20</td>
<td>5ml</td>
</tr>
<tr>
<td>G3</td>
<td>Bluegrass, Kentucky</td>
<td>1190</td>
<td>1:20</td>
<td>5ml</td>
</tr>
<tr>
<td>W1</td>
<td>Russian Thistle</td>
<td>2363</td>
<td>1:20</td>
<td>5ml</td>
</tr>
<tr>
<td>W2</td>
<td>Mixed Ragweed</td>
<td>2297</td>
<td>1:20</td>
<td>5ml</td>
</tr>
<tr>
<td>W3</td>
<td>Sagebrush mix</td>
<td>2428</td>
<td>1:20</td>
<td>5ml</td>
</tr>
<tr>
<td>W4</td>
<td>Careless Weed (Amaranth palmeri)</td>
<td>1298</td>
<td>1:20</td>
<td>5ml</td>
</tr>
<tr>
<td>T1</td>
<td>Mulberry</td>
<td>1885</td>
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</tr>
<tr>
<td>T2</td>
<td>Cottonwood</td>
<td>1436</td>
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</tr>
<tr>
<td>T3</td>
<td>Elm</td>
<td>1541</td>
<td>1:20</td>
<td>5ml</td>
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<tr>
<td>T4</td>
<td>Ash</td>
<td>1081</td>
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<td>5ml</td>
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<tr>
<td>F1</td>
<td>Alternaria tenuis</td>
<td>5009</td>
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<td>Aspergillus fumigatus</td>
<td>5021</td>
<td>1:10</td>
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<tr>
<td>F3</td>
<td>Helminthosporium interseminatum</td>
<td>5125</td>
<td>1:10</td>
<td>5ml</td>
</tr>
<tr>
<td>F4</td>
<td>Hormodendrum cladosporioides</td>
<td>5129</td>
<td>1:10</td>
<td>5ml</td>
</tr>
<tr>
<td>C1</td>
<td>Cat (Fel d 1)</td>
<td>4810TR</td>
<td>10,000 BAU</td>
<td>5ml</td>
</tr>
<tr>
<td>C2</td>
<td>Dog hair and dander</td>
<td>4825</td>
<td>1:50 AP</td>
<td>5ml</td>
</tr>
<tr>
<td>C3</td>
<td>House Dust mite; D. farinae</td>
<td>6720UP</td>
<td>30,000 AU/ml</td>
<td>5ml</td>
</tr>
<tr>
<td>C4</td>
<td>Cockroach mix (Amer&amp;German)</td>
<td>6585</td>
<td>1:10</td>
<td>5ml</td>
</tr>
</tbody>
</table>

5. Controls
   - C - glycerine 6806ED 50% gly. 5ml
   - C + histamine 7099ED 5ml

6. Additional antigens
   - C5 House Dust mite; pteronyssinus 6692UP 30,000 AU/ml 5ml
   - C6 Horse Hair and Dander 4856AP 1:50 AP 5ml
   - C7 Cattle Hair and Dander 4812AP 1:50 AP 5ml

Skin Testing Supplies

- 70% Alcohol
- Cotton balls
- Antihistamine lotion
- Hydrocortisone cream (1%)
- Benadryl (12.5mg/5ml)
- Black Ink pen
- 3/4" Scotch tape
- Paper cups
- 4x4 or 2x2 sterile gauze pads
- 15 minute Timer
<table>
<thead>
<tr>
<th>LEFT SIDE</th>
<th>RIGHT SIDE</th>
<th>CONTROL +</th>
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<tbody>
<tr>
<td>C - DILUENT</td>
<td>T3 ELM TREE</td>
<td>C + HISTAMINE</td>
</tr>
<tr>
<td>G1 BERMUDA GRASS</td>
<td>T4 ASH TREE</td>
<td>EXTRA</td>
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<tr>
<td>G2 TIMOTHY GRASS</td>
<td>F1 ALTERNARIA MOLD</td>
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<tr>
<td>G3 KENTUCKY BLUEGRASS</td>
<td>F2 ASPERGILLUS MOLD</td>
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<tr>
<td>W1 TUMBLERWEED</td>
<td>F3 HELMHITOSPORIUM MOLD</td>
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<tr>
<td>W2 RAGWEED</td>
<td>F4 N. CIADOSPORIUM MOLD</td>
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<tr>
<td>W3 SAGEBRUSH MIX</td>
<td>C1 CAT</td>
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<tr>
<td>W4 CARELESS WEED</td>
<td>C2 DOG</td>
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<tr>
<td>T1 MULBERRY TREE</td>
<td>C3 HOUSEDUST MITE</td>
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<tr>
<td>T2 COTTONWOOD TREE</td>
<td>C4 COCKROACH</td>
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SHS-III Asthma Sub-Study Screening Questions

SHS ID: [ ]

1. Have you been diagnosed as having asthma since the Phase II exam?  
   1=Yes 2=No
   [ ]

2. Are you aware of shortness of breath with wheezing at night?  
   1=Yes 2=No
   [ ]

3. Have you had an attack of wheezing with shortness of breath  
   during the last 12 months?  
   1=Yes 2=No
   [ ]

4. Have you used any asthma inhalers during the last 12 months?  
   1=Yes 2=No
   [ ]

If the answer to any of these four questions is "YES",  
participation is eligible for the asthma sub-study.

Date: [ ]/ [ ]/ [ ]
   mo day year
STRONG HEART STUDY PHASE III

Asthma Sub-Study Questionnaire

SHS ID: __________

1. Was this questionnaire administered in a language other than English? Yes [ ] No [ ]

2. Do you ever have trouble with your breathing?
   If “YES”, how often do you have this trouble?
   __________ = continuously so that your breathing is never quite right
   __________ = repeatedly, but it gets completely better
   __________ = only rarely

3. Does your chest ever sound wheezy or whistling apart from colds? Yes [ ] No [ ]

4. Have you ever had an attack of wheezing that made you feel short of breath? Yes [ ] No [ ]

5. At any time during the last 12 months, have you had wheezing or whistling in your chest? Yes [ ] No [ ]
   If so, was this wheezing brought on or made worse by exposure to any of the following (check all that apply):
   __________ colds or sore throats
   __________ exercise or exertion
   __________ house dust
   __________ fumes
   __________ smoke
   __________ contact with animals
   __________ contact with plants or pollens
   __________ other, specify: _______________________________________

6. Was this wheezing worse during a particular season of the year? Yes [ ] No [ ]
   If so, which season: winter [ ] spring [ ] summer [ ] fall [ ]
7. Does shortness of breath or chest tightness ever wake you up? Yes [ ] No [ ]

8. Have you had an attack of shortness of breath that came on soon after you finished a strenuous physical activity (especially in cold weather)? Yes [ ] No [ ]

9. Have you had hay fever or any other allergy that makes your nose runny or stuffy apart from colds? Yes [ ] No [ ]
   1. If yes, how much were you bothered by hay fever or allergy? very little [ ] somewhat [ ] very much [ ]
   2. Did you take any of the following medications for your hay fever or allergy?
      1. antihistamine pills by prescription? Yes [ ] No [ ]
      ii nose sprays by prescription? Yes [ ] No [ ]
      iii decongestant pills (like Sudafed)? Yes [ ] No [ ]

10. Have you had problems with your sinuses during the last 12 months? Yes [ ] No [ ]

11. Do you have heartburn (gastroesophageal reflux)? Yes [ ] No [ ]

12. Which best describes the building in which you live? (check one)
   [ ] 1 = a home in which more than one family lives
   [ ] 2 = a mobile home or trailer
   [ ] 3 = a one family home
   [ ] 4 = an apartment
   [ ] 5 = a nursing home
   [ ] 6 = other, specify: ________________________________

13. What do you use for heating in your home? (check all that apply)
   [ ] a. a fireplace or a woodstove
   [ ] b. a gas, oil, or coal burning furnace
   [ ] c. a gas or kerosene space heater
   [ ] d. electric heat
   [ ] e. nothing
14. What do you use for cooling in your home? (check all that apply)
   □ a. an evaporative (swamp) cooler
   □ b. room air conditioners
   □ c. a central air conditioner
   □ d. fans or nothing

15. Is there an exhaust fan in both your kitchen and bathroom?  Yes ____, No ____

16. Does your bedroom (or where you sleep) have wall-to-wall carpeting?  Yes ____, No ____

17. Has there been any water damage to your home, for example, from broken pipes, roof leaks, or floods?  Yes ____, No ____

   don’t know ____

   if yes, which year did this occur?  19 __________

18. Is there mold or mildew on any walls inside your home?  Yes ____, No ____

19. Do you ever see any of the following pests in your home? (check all that apply)
   □ a. mice
   □ b. rats
   □ c. cockroaches
   □ d. none

20. What types of animals or pets stay inside your home? (check all that apply)
   □ a. one or more cats
   □ b. birds
   □ c. one or more dogs
   □ d. other furry animals
   □ e. none

21. Have you ever had asthma?  Yes ____, No ____

   1. If “NO”, you are done with this questionnaire.  GO TO Q42.
   2. If “YES”, do you still have asthma?  Yes ____, No ____

   If “YES”, please complete the rest of the questions.
   If “NO”, go to Q42.
22. How old were you when you had your first episode of asthma? [ ] [ ] age in years

23. How old were you when you had your most recent episode of asthma? [ ] [ ] age in years

24. Are any of your relatives (living or deceased) known to have asthma? Yes [ ] No [ ] Don’t know [ ]

If “YES”,

a. Did your natural father ever have asthma? Yes [ ] No [ ] Don’t know [ ]

b. Did your natural mother ever have asthma? [ ] [ ] [ ]

c. Do you have any children with asthma? [ ] [ ] [ ]

25. When you are near animals (such as cats, dogs, or horses), near feather pillows, quilts, or comforters, or in a dusty part of the house, do you ever: (check all that apply)

[ ] a. start to cough
[ ] b. start to wheeze
[ ] c. feel chest tightness
[ ] e. start to feel short of breath
[ ] f. get a itchy or stuffy nose
[ ] g. start to sneeze
[ ] h. get itchy or watery eyes
[ ] i. none

26. During the last 4 weeks, how often have asthma attacks awakened you at night or in the early morning? (Check one only)

[ ] 1 = never
[ ] 2 = less than once a week
[ ] 3 = one to four nights a week
[ ] 4 = almost every night
27. During the last 4 weeks, about how many days did you miss from work, or were your usual activities limited, because of your asthma?  
   [___]  
   [days]

28. Have you ever worked at a job which exposed you to vapors, gas, dust, or fumes?  
   Yes [___]  
   No [___]  
   Don’t know [___]

   If yes, what was the job?  

29. Have you ever had to leave a job because it affected your breathing?  
   Yes [___]  
   No [___]

30. Please list ALL the medicines or other remedies (including hand-held sprayers, inhalers, aerosols, or tablets) you have taken for asthma during the last 12 months.

   **Asthma Medications in the past 12 months**

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<th>When wheezing</th>
<th>Every day</th>
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   Which of these asthma medications do you take when you have an asthma episode (with wheezing and shortness of breath)? Check the “When wheezing” box after the medication.

31. Do you use an asthma inhaler every day even if you don’t feel short of breath? Check the “Every day” box after the medication in Q30.  
   Yes [___]  
   No [___]

32. Do you use a spacer tube with any of your asthma inhalers?  
   Yes [___]  
   No [___]

33. Do you ever use a nebulizer with an air compressor (electric pump) for your asthma?  
   Yes [___]  
   No [___]

34. Have you ever taken steroid pills (prednisone) for your asthma?  
   Yes [___]  
   No [___]  
   Don’t know [___]

35. Have you ever been given a peak flow meter to help manage your asthma?  
   Yes [___]  
   No [___]

   If yes, did you use it 5 days or more during the last month?  
   Yes [___]  
   No [___]
36. Have you ever visited an Emergency Room (ER), or been hospitalized because of asthma or other breathing problems?  
   Yes [1]  No [2]  
   If yes, how many times during the last 12 months? [__] times  

37. How many times during the last 12 months have you seen a health care provider for breathing problems or asthma? [__] times  

38. Do you seek care for your asthma from any other source (medicine man or alternative medicine)?  
   Yes [1]  No [2]  

39. Do you feel that you have been given enough information about what to do when your asthma gets worse?  
   Yes [1]  No [2]  

40. Have you been given written instructions for what to do when your asthma worsens? (an asthma action plan)?  
   Yes [1]  No [2]  

41. Please rate the quality of care that you receive for your asthma:  

42. Interviewer code [________]  

43. Interview date [____/____/____]摩 轭  轭  轭  轭