



# National Health and Nutrition Examination Survey (NHANES)

## Respiratory Health Bronchodilator Procedures Manual



January 2008

## TABLE OF CONTENTS

<u>Chapter</u>		<u>Page</u>
1	OVERVIEW: THE MEC PHYSICIAN’S ROLE IN THE NHANES SPIROMETRY EXAMINATION.....	1-1
2	BRONCHODILATOR ADMINISTRATION: INTRODUCTION.....	2-1
3	BRONCHODILATOR STUDY ELIGIBILITY.....	3-1
	3.1 Exclusion Criteria for Baseline Spirometry.....	3-1
	3.2 Overview of Exclusions from Bronchodilator Administration.....	3-2
	3.3 Specific Exclusion Criteria.....	3-2
	3.4 ISIS Automatic Bronchodilator Exclusions.....	3-3
	3.5 Bronchodilator Study Physician Evaluation.....	3-4
	3.5.1 Physician Screening Procedure.....	3-5
	3.5.1.1 BRONC_ Screen.....	3-5
	3.5.1.2 Spirometry Results.....	3-6
	3.5.1.3 SPABPPLS: Blood Pressure and Pulse for Age..	3-9
	3.5.1.4 SPAPREG: Pregnancy Status Evaluation.....	3-12
	3.5.1.5 Breastfeeding Evaluation (Women 12-59 years).	3-13
	3.5.1.6 Congenital Heart Disease Exclusion (Children 6-15 years).....	3-14
	3.5.1.7 Diagnosed Tachyarrhythmia Exclusion (All 6-79 years).....	3-15
	3.5.1.8 MEC Physician Medication Review (SI-RDQ & New Drug Data).....	3-16
	3.5.1.9 History of Epilepsy.....	3-21
	3.5.1.10 Exclusion for Previous Adverse Reaction to Albuterol.....	3-22
	3.5.1.11 Exclusion for Recent Use of Short- of Long- Acting Bronchodilator.....	3-24
	3.5.1.12 Bronchodilator Administration Message Screen.	3-26
	3.6 Bronchodilator Consent.....	3-28
	3.6.1 Bronchodilator Administration.....	3-29
	3.6.2 Level II Referral Evaluation for Participants with FEV1/ FVC% ≤ 50% Predicted.....	3-32
	3.6.3 Level II Referral Evaluation for Participants with FEV1/ FVC% ≤ Lower Limits of Normal.....	3-35
4	REFERENCES.....	4-1

## TABLE OF CONTENTS (continued)

### List of Appendixes

<u>Appendix</u>		<u>Page</u>
A	INFORMED CONSENT DOCUMENTS .....	A-1
B	MEDICATION LISTINGS FOR MEC PHYSICIAN'S DRUG REVIEW AND BRONCHODILATOR TYPE EVALUATION.....	B-1
C	SPIROMETRY REVIEW SCREEN .....	C-1

### List of Exhibits

<u>Exhibit</u>		
3-1	BRONC_ screen .....	3-6
3-2	Spirometry results screen.....	3-7
3-3	Blood pressure/pulse review screen.....	3-9
3-4	Dropped beats during pulse review screen .....	3-11
3-5	Pregnancy status review screen .....	3-12
3-6	Now breastfeeding a child screen .....	3-13
3-7	Congenital heart defect screen .....	3-14
3-8	SPs have a diagnosed tachyarrhythmia screen.....	3-15
3-9	Physician medication review (SPQME) screen .....	3-17
3-10	Epilepsy screen .....	3-22
3-11	Adverse reaction to albuterol screen.....	3-24
3-12	Bronchodilator within 12 hours screen .....	3-25
3-13	Bronchodilator within 4 hours screen .....	3-26
3-14	Please obtain informed consent screen .....	3-27
3-15	Participant/guardian informed consent .....	3-29

**TABLE OF CONTENTS (continued)**

List of Exhibits (continued)

<u>Exhibit</u>		<u>Page</u>
3-16	Administer bronchodilator screen.....	3-29
3-17	Bronchodilator administered screen .....	3-31
3-18	Physician end of subsection screen.....	3-32
3-19	Spirometry flow curves.....	3-34

## **1. OVERVIEW: THE MEC PHYSICIAN'S ROLE IN THE NHANES SPIROMETRY EXAMINATION**

Spirometry was previously performed in NHANES III and is being implemented again in the current NHANES (2007-8). Spirometry is the physical measurement of lung-expired air volumes and air flow rates. It is an adjunct diagnostic test, which aids in the diagnosis of chronic lung disease, but by itself, it is not sufficient to make a diagnosis of any specific condition. Spirometric data, however, is useful in population-based studies as an indirect indicator of chronic lung disease, and important knowledge of the natural history of chronic lung disease comes from studies such as NHANES III. For the current NHANES, the NHANES III spirometry protocol will again be implemented, however, with the addition of repeat spirometry after administration of a bronchodilator for selected participants. It should be recognized, however, that even with this enhancement, the screening version of spirometric testing employed in the current NHANES survey is a limited subset of the panel of lung function tests that would be routinely performed for diagnostic purposes in a hospital pulmonary function laboratory.

In the current NHANES, the MEC physician's role is four-fold:

1. Conduct pre-bronchodilator study safety exclusion evaluation and obtain informed consent;
2. Administer bronchodilator medication to selected, eligible participants;
3. Provide level II referrals for participants with abnormal baseline spirometry results; and
4. Perform emergency response according to NHANES protocols, if necessary.

## **2. BRONCHODILATOR ADMINISTRATION: INTRODUCTION**

Reversibility testing with a beta2-adrenergic bronchodilator is being used in the current NHANES to help distinguish between asthma and fixed chronic obstructive pulmonary disease (COPD). It is also being used to establish the best attainable lung function among sample persons who have airflow obstruction. For example, bronchodilator reversibility testing will help to determine the prevalence of poorly reversible airflow obstruction, which is a more objective measure of COPD than the simple reduction of airflow rates measured at baseline spirometry. It also permits estimation of prevalence of fully reversible airflow obstruction, which is usually caused by asthma. The health outcome measures obtained from combining pre- and post-bronchodilator spirometry results using the ATS and GOLD recommendations<sup>1,2</sup> will enable a more precise estimation of societal burden of COPD and asthma, which is of critical public health importance. Bronchodilator reversibility testing is a standard clinical pulmonary function test and is incorporated into many major survey studies of respiratory health.<sup>3,4,5</sup> It consists simply of a repeat baseline spirometry test after the administration of an inhaled dose of a beta2-agonist bronchodilator to open up the airways.

### 3. BRONCHODILATOR STUDY ELIGIBILITY

Participants will be screened for eligibility for bronchodilator studies automatically by the ISIS system after completion of baseline spirometry. Only participants with abnormal baseline spirometry values showing airflow obstruction defined as FEV1/FVC% equal to or less than the lower limit of normal (LLN), or an observed FEV1/FVC% equal to or less than 70 percent will be selected for bronchodilator reversibility testing. For sample persons aged 8-79 years, the FEV1/FVC% LLN is defined by NHANES III data<sup>6</sup> and for children aged 6-7 years it is the reference equations defined by the study of Wang et al.<sup>7</sup> When the ISIS system selects the participant for bronchodilator studies, the spirometry technologist will read the following script, which explains the reason for the referral to the MEC physician:

**“Your breathing test shows that you breathed out less air in one second than we expected. The doctor will talk to you; then if you agree, we’d like to repeat the test.”**

#### 3.1 Exclusion Criteria for Baseline Spirometry

The current NHANES spirometry protocol consists of baseline spirometry as performed in NHANES III, followed by repeat, post-bronchodilator spirometry for selected participants. Prior to baseline spirometry being performed, the following safety exclusions are applied:

	Age range (years)
Current painful ear infection	6-15
Eye, open chest, or abdominal surgery in preceding 3 months	6-79
SP or household member tuberculosis exposure	6-79
History of aneurysm or detached retina	16-79
History of collapsed lung	6-79
Stroke or heart attack in preceding 3 months	16-79
Breathing problem that requires supplemental oxygen	6-79
Physical problem that prevents SP from taking a deep breath	6-79
History of hemoptysis in previous month	6-79

### 3.2 Overview of Exclusions from Bronchodilator Administration

Bronchodilator exclusion criteria are based principally on safety concerns regarding the administration of albuterol. Beta 2-adrenergic bronchodilators have a well-described method of action, which is, in general, dose dependent. The most common transient side effects of beta 2-adrenergic bronchodilators include tachycardia, increased blood pressure, arrhythmia, and nervousness. These side effects are usually temporary; however, safety precautions are in place to exclude persons with pre-existing tachycardia, elevated blood pressure, or major arrhythmias from bronchodilator testing. Beta 2-adrenergic bronchodilators are thought to convey an increased risk of arrhythmia in persons taking medications such as MAO inhibitors, or tricyclic antidepressants. Beta 2-adrenergic bronchodilators also may cause hypokalemia, increasing the risk of arrhythmia. Persons taking certain types of diuretics who are not taking potassium supplements are excluded from bronchodilator testing.

The safety of albuterol in the setting of drug treatment for seizure disorders is uncertain; albuterol will not be administered when an SP is taking a medication for seizure disorder. Also, the safety of albuterol during pregnancy and lactation is uncertain, hence pregnant and breastfeeding women will be excluded from bronchodilator administration. Finally, participants who recently inhaled a dose of bronchodilator, and those with a history of adverse reaction to albuterol, will be excluded.

### 3.3 Specific Exclusion Criteria

#### ■ Reproductive Health Exclusions (Females 12-59 Years)

- Pregnancy\*      Positive urinary HCG test  
                                 A positive self-report of pregnancy
- Breastfeeding\*      MEC-SE Questionnaire  
                                 Physician questionnaire

#### ■ Physician Bronchodilator Questionnaire

- Congenital Heart Disease      6-15 years only
- Diagnosed Major Arrhythmia      6-79 years



- **Physician’s Exam Data**

- Elevated Blood Pressure for Age\*

Age group	Elevated blood pressure (exclude)
17-79 years	> 180 mmHg systolic or > 110 mmHg diastolic
12-16 years	≥ 132 mmHg systolic or ≥ 92 mmHg diastolic
8-11 years	≥ 124 mmHg systolic or ≥ 88 mmHg diastolic

- Resting Tachycardia\*      Age-specific cut points applied
- Irregular Pulse\*            2 or more dropped beats per 30 seconds

- **Medication/Therapy-Based Exclusions (SI-RDQ; SE; Physician’s Medication Review)**

Exclude all who take/use:

- A class 1 antiarrhythmic\*
- An implanted automatic defibrillator\*
- A monoamine oxidase inhibitor\*
- An anticonvulsant medication for epilepsy
- A tricyclic antidepressant; and age > 40, and has a listed medical condition
- Diuretic therapy without potassium supplementation/raising medication\*

### 3.4 **ISIS Automatic Bronchodilator Exclusions**

Immediately following baseline spirometry, at the time ISIS reviews spirometric data and selects a participant as potentially eligible for bronchodilator studies, the ISIS system will automatically screen the available data from the participant’s Household and MEC interviews, the MEC examination, and laboratory results to determine if any criteria exist that would make the participant ineligible for bronchodilator administration: i.e., ISIS determines, based on available data, if one of the safety exclusions listed above exists. If so, then the participant will be automatically excluded without having to see the physician for an evaluation. If no bronchodilator exclusion criteria are detected, the selected participant is then referred to the MEC physician for further evaluation.

---

\* An ISIS Automatic Exclusion, blood pressures are not measured for children aged 6 and 7 years.

It is anticipated that the majority of bronchodilator exclusions will be performed by the ISIS system itself, so the absolute number of physician evaluations will be minimized. The role of the MEC physician in bronchodilator eligibility evaluation for the remaining potentially eligible participants, therefore, is two-fold:

1. To review and verify the accuracy of the ISIS system results for these selected participants; and
2. To collect and assess selected additional information pertinent to bronchodilator exclusion criteria.

For example, the ISIS system has the ability to automatically assign Multum™ drug class codes to each drug listed in the participant's prescription medication data file, and does so in about 90 percent of cases. Experience has shown that when ISIS assigns a Multum™ drug class code to a participant's reported prescription drug, it does so with high fidelity. Accordingly, it is possible for ISIS to automatically perform prescription medication-based safety exclusion screenings for participants who have been selected for bronchodilator studies. On the other hand, some 10 percent of the participant's drug information is not codeable by ISIS, and participants may have begun taking new medications since the time of the household interview. The MEC physician must therefore collect information on new drugs started and review both these and any uncoded medications in the participant's data file to see if they belong to classes of drugs pertinent to bronchodilator exclusion decisionmaking.

### **3.5 Bronchodilator Study Physician Evaluation**

Bronchodilator testing will be performed using albuterol, a beta 2-adrenergic bronchodilator which is FDA approved for use in persons aged 4 years and above. Exclusion criteria based on contraindications to albuterol use have been developed based on standard criteria used in other pulmonary function survey research studies, and on product safety information. If the participant passes the initial automatic review of bronchodilator eligibility by the ISIS system, the participant will then be seen by the MEC physician who will evaluate the participant and make a final determination on bronchodilator eligibility based on study exclusion criteria. The physician evaluation consists of verification of the participant's status with respect to key examination data (pulse, blood pressure, pregnancy status) and additional interview questions. For the latter, proxy informants will be necessary for children 6-15 years of age. Additionally, at this time, the MEC physician may exclude any participant from bronchodilator testing if in their judgment the use of albuterol appears otherwise contraindicated. If the participant is

eligible and testing is indicated (the participant is not excluded), then specific written informed consent (see Appendix A) will be obtained. Then the physician will instruct the participant in the use of the spacer and albuterol inhaler. Once the medication is administered, the participant must wait for a minimum of 10 minutes for the medication to take effect before proceeding with repeat spirometry.

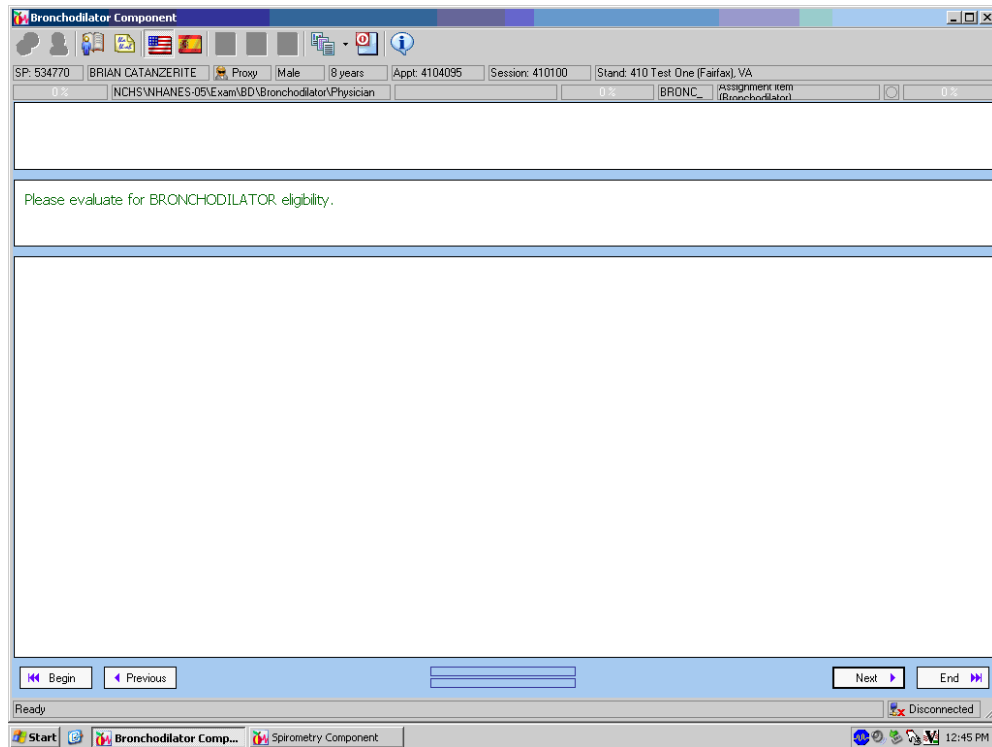
### **3.5.1 Physician Screening Procedure**

The MEC physician bronchodilator safety exclusion evaluation will be guided by the ISIS bronchodilator (BRONCH) section screens. As these are completed, they provide a guide for the evaluation of potential safety exclusions from bronchodilator testing. These are listed here in sequential order.

#### **3.5.1.1 BRONC\_ Screen**

This initial ISIS screen (Exhibit 3-1) is administrative in nature, prompts the physician to evaluate the participant for bronchodilator testing and for the spirometry pilot study, and identifies the participant as either eligible for a true bronchodilator test or for exclusion.

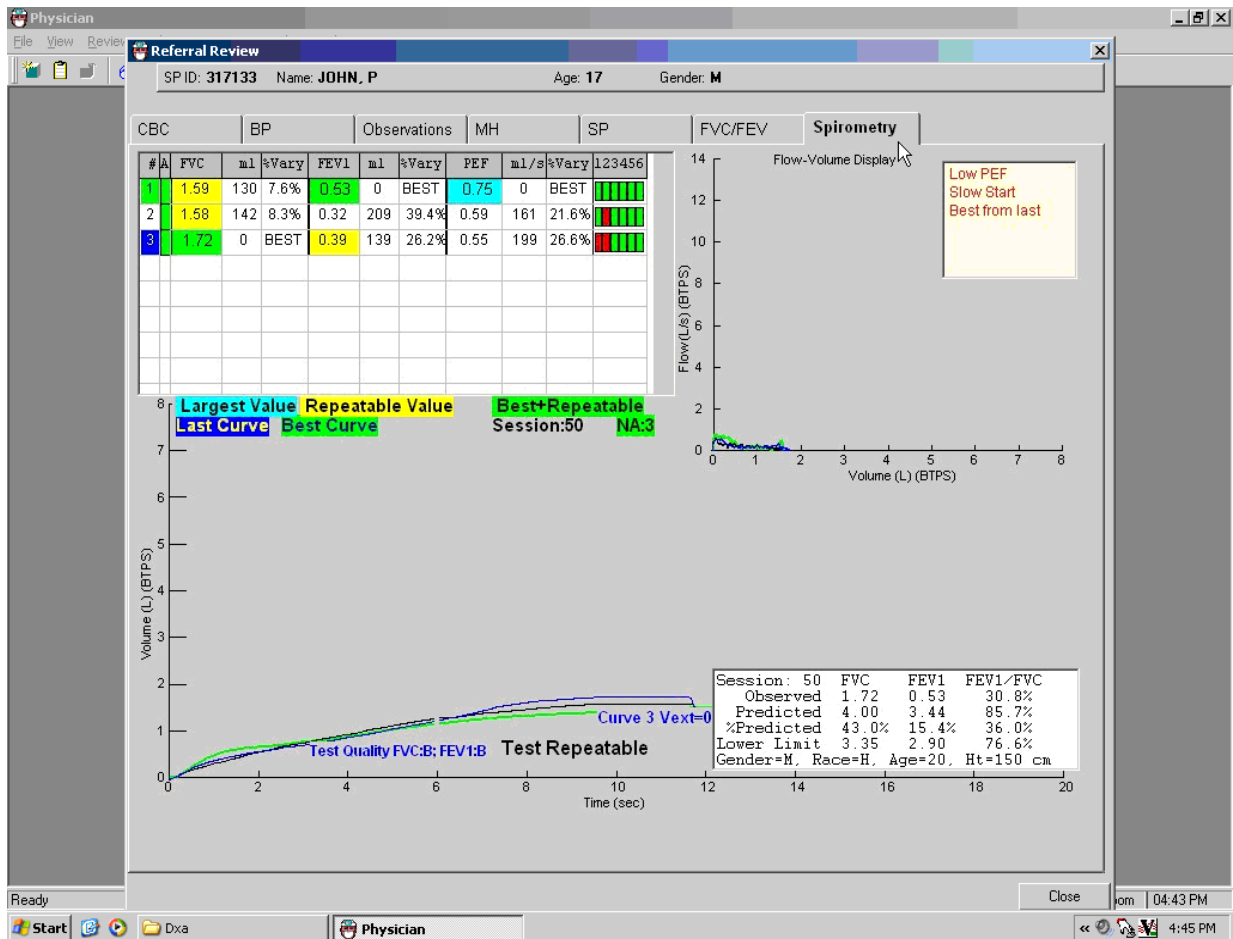
Exhibit 3-1. BRONC\_ screen



### 3.5.1.2 Spirometry Results

The Spirometry Results screen (Exhibit 3-2) shows the participant’s flow-volume and volume-time curves and two summary results tables. The purpose of the Spirometry Results screen is to allow the physician to exclude the occasional participant who may have been inappropriately selected for the bronchodilator component due to artifact or baseline spirograms of extremely poor quality. Such exclusion should be necessary only in a very small minority of cases. The Spirometry Results screen is organized as follows: the top left table includes the FVC, FEV1, and PEF readings, with the last column containing color-coded quality code indicators for each successive trial. The 6-item acceptability quality code box is displayed to the right of the results for each trial. The largest achieved values for the FVC, FEV1, and PEF are indicated by the entry “BEST” to the right of the selected value in the “%Vary” column. The milliliter differences and the percent differences between the individual values and the “best value” are also provided for your review. The bottom right table includes predicted values for the FVC, FEV1, and FEV1/FVC based on a normal reference population of persons in with similar age, gender, race, and height. The table also includes the predicted lower limits of normal for these parameters.

Exhibit 3-2. Spirometry results screen



The Spirometry Results Screen allows the physician to perform a brief overall quality check on the participant’s baseline spirometry test results that led to his or her selection for the bronchodilator study. As mentioned, in occasional instances, the participant may have been inappropriately selected for the bronchodilator study simply because of poor quality tracings that may mimic abnormal results. It is the physician’s responsibility to try to identify these instances and to exclude them from unnecessary testing. The input of the MEC technologist performing the baseline spirometry can be solicited to help clarify this point. As an example, a low FEV1 may simply result from poor effort, i.e., a slow start to the spirometric maneuver; or, an extra breath taken during a maneuver may artificially increase the FVC and therefore dramatically decrease the FEV1/FVC ratio. The physician should therefore check to see if the bronchodilator selection may have been on the basis of an artifact in the spirogram, rather than being based on an acceptable quality spirometric study.

Most baseline spirograms obtained in NHANES can be expected to be of high quality. These quality standards are described in the *Spirometry Procedures Manual*. Briefly, baseline spirometric testing aims to obtain at least three acceptable spirometric maneuvers, and among these at least two which are reproducible. Acceptable maneuvers are those in which there is no hesitation nor any false starts on the part of the participant, and no coughing or extra breaths taken. Also, the spirometric maneuver should last at least 6 seconds for adults (3 seconds for young children) to obtain a maximum FVC reading, and a visible plateau should be evident at the end of the spirometric tracing (indicating that no more air could be exhaled). Ideally, there should also be at least two reproducible spirometric curves, defined as two curves that have FVC values that agree within 150 ml, plus FEV1 values that agree within 150 ml.

In general, the great majority of baseline spirograms will have both acceptable and reproducible curves. Most other spirometric studies that are of less than this highest quality will still be of sufficient quality to be interpretable. For example, it is known that persons with Chronic Obstructive Pulmonary Disease (COPD), the target group for bronchodilator studies, may routinely have more difficulty performing the spirometric maneuvers than those persons with normal lung function. In particular, participants with COPD may have spirometric tracings with prolonged exhalation and never reach a true plateau. Nevertheless, their spirograms are interpretable and should be included in the NHANES study.

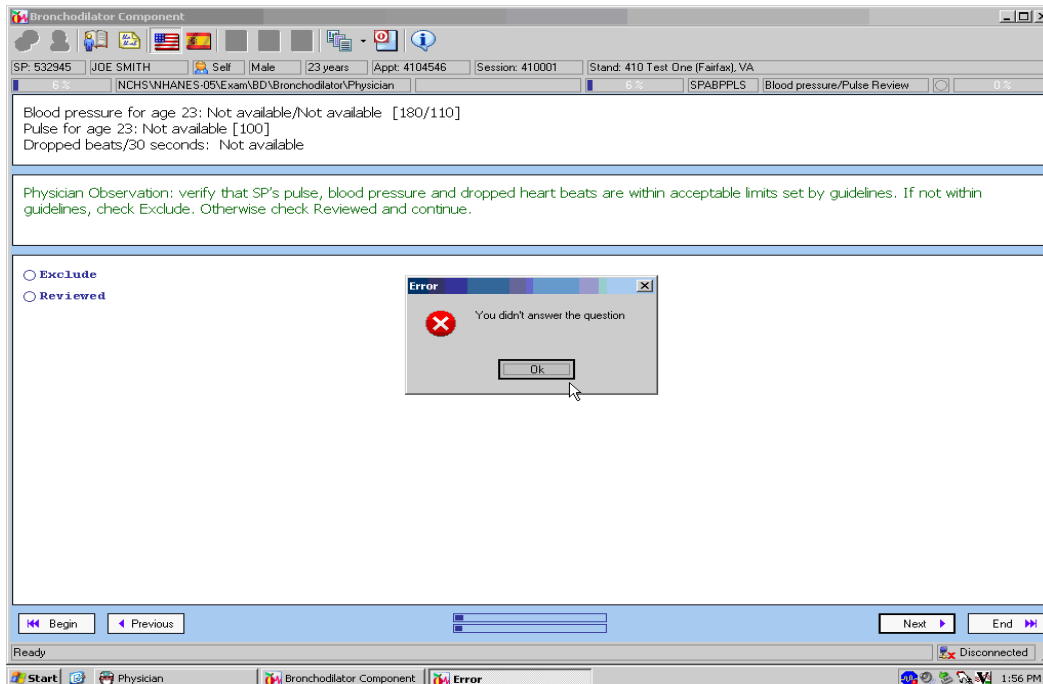
The MEC physician, with the advice of the MEC technologist when necessary, should therefore review the participant's baseline spirometric tracing. If the baseline tracing is acceptable, check "reviewed" and continue to the next ISIS screen. If the curves appear to be of poor quality or there are artifacts present such that the baseline spirometric study is not interpretable, check "exclude" and end the bronchodilator eligibility assessment.

Following the spirometry curve results screen, two additional administrative/physician observation screens will be presented for physician review. These are SPABPPLS, the blood pressure and pulse for age screen (Exhibit 3-2); and SPAPREG, the pregnancy test results screen (Exhibit 3-4). These present the participant's data from previous interview, examination, and laboratory tests. ISIS should have previously reviewed this data and automatically excluded the participant from bronchodilator testing if the established safety exclusion criteria were met. The physician's role for these two screens is to review the presented data and perform a cross-check on the ISIS system to verify that the participant's values are within acceptable ranges for bronchodilator testing. If the displayed data is within the acceptable range, then check the "Reviewed" box and continue; otherwise check "Exclude."

### 3.5.1.3 SPABPPLS: Blood Pressure and Pulse for Age

Use this screen (Exhibit 3-3) to review the participant's status with respect to blood pressure and pulse rate measurement, and the number of dropped beats observed in the pulse rate examination.

Exhibit 3-3. Blood pressure/pulse review screen



■ **Blood Pressure**

Because albuterol may potentially elevate blood pressure, this medication should not be administered to participants whose blood pressure is already markedly elevated. Note that this blood pressure evaluation is performed only for participants aged 8-79, as blood pressure is not obtained for child SPs aged 6-7 years. The ISIS screen displays the mean blood pressure previously obtained during the physician’s examination. Verify that the blood pressure displayed for the selected participant is below the guideline values. For this purpose, the following age-specific guidelines will be used and will be displayed in parentheses on the blood pressure/pulse review screen:

Age group	Elevated blood pressure (exclude)
7-79 years	> 180 mmHg systolic or > 110 mmHg diastolic
12-16 years	≥ 132 mmHg systolic or ≥ 92 mmHg diastolic
8-11 years	≥ 124 mmHg systolic or ≥ 88 mmHg diastolic

■ **Pulse Rate**

Because albuterol may potentially increase the heart rate, this medication should not be administered to participants whose heart rate is already markedly elevated. The ISIS screen displays the heart rate previously obtained during the physician’s examination. Verify that the heart rate displayed for the selected participant is below the guideline values. For this purpose, the following age-specific guidelines will be used and will be displayed in parentheses on the blood pressure/pulse review screen:

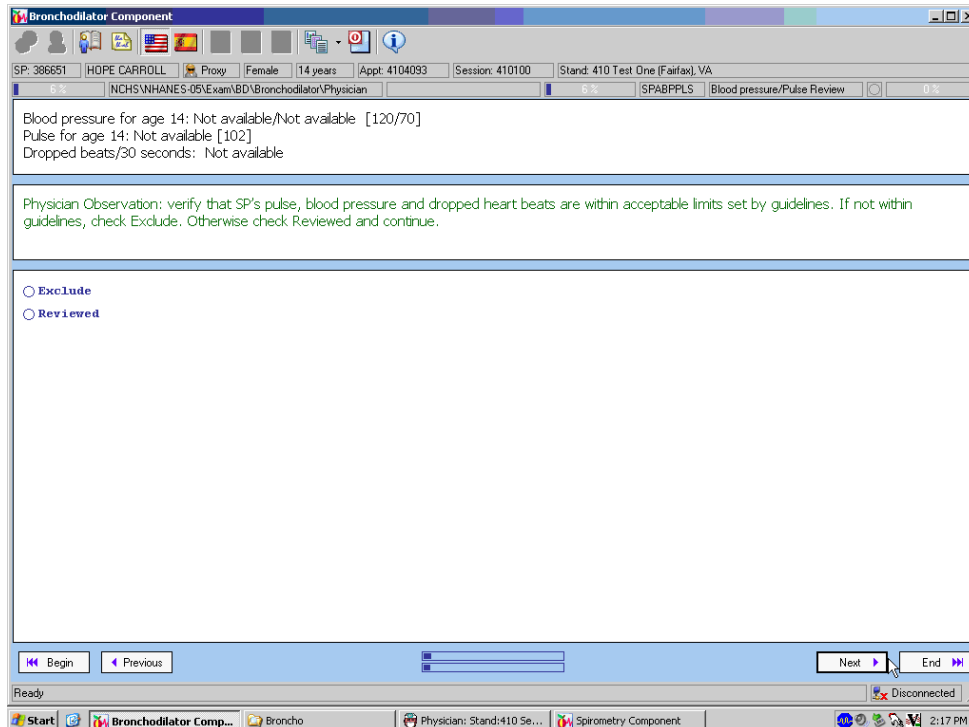
Age group	Elevated pulse (exclude)
16-79 years	exclude if > 100 beats per minute
12-15 years	exclude if > 102 beats per minute
8-11 years	exclude if > 104 beats per minute
6-7 years	exclude if > 108 beats per minute



## ■ **Dropped Beats Observed During Pulse Determination**

Because albuterol may potentially cause arrhythmias, this medication will not be administered to participants whose heart rhythm is already irregular. The regularity of the participant's pulse will be determined at the physician's exam. Verify that the displayed data on this screen for the number of dropped beats (Exhibit 3-4) is below the guideline value of 2 per 30-second exam period. If the number of dropped beats is 2 or more, check the "Exclude" box. Otherwise, check "Reviewed" and continue. Please note that the presence of a sinus arrhythmia (a normal variant which is especially common in children and adolescents) will not exclude participants from bronchodilator testing.

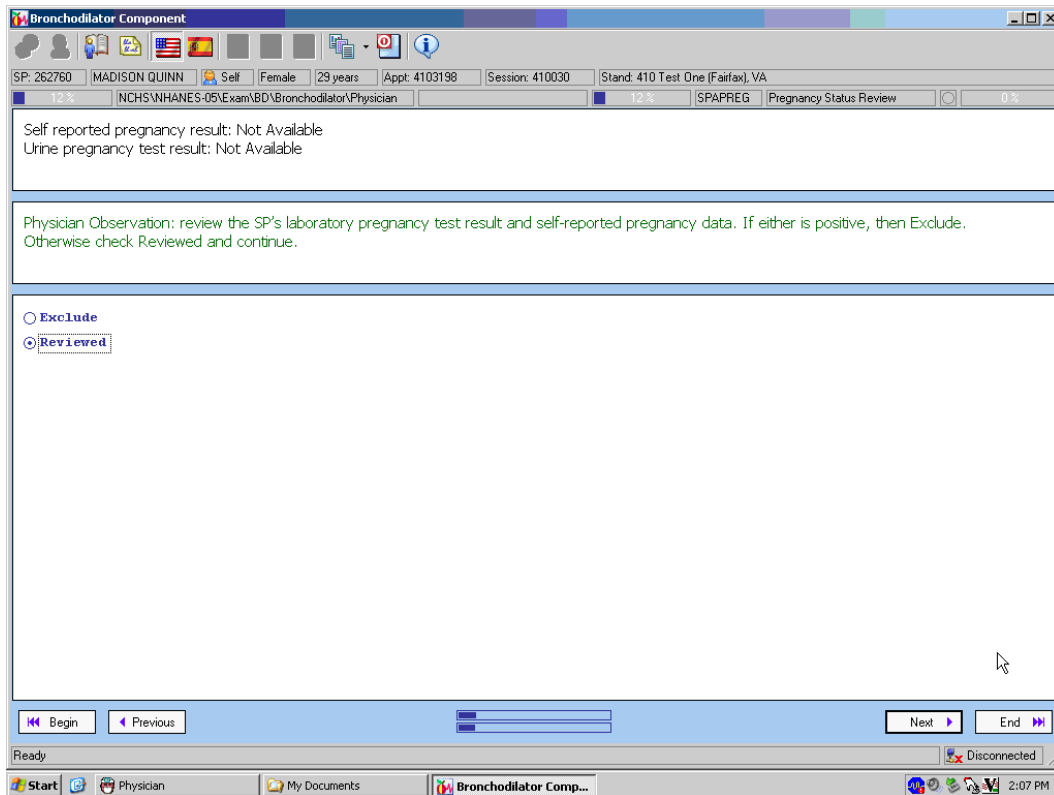
Exhibit 3-4. Dropped beats during pulse review screen



### 3.5.1.4 SPAPREG: Pregnancy Status Evaluation

In this screen (Exhibit 3-5), the physician is asked to verify the displayed data regarding the participant's pregnancy status. If the participant is a female of reproductive age (8-59 years), the SPAPREG screen will appear displaying the participant's urine pregnancy test result, and the participant's self-reported pregnancy status. Verify that the participant's urine pregnancy (HCG) test is negative. If for any reason it is not possible to obtain a urine pregnancy test, then data from the self-report of pregnancy data field can be used to assess the participant's exclusion status. The participant's pregnancy status should be verified as negative before proceeding with the bronchodilator evaluation and administration. In all cases, if **either** the urine pregnancy test or the self-report of pregnancy is positive, the participant should be excluded from bronchodilator testing by checking the "Exclude" option; otherwise, designate the participant's nonexcluded status by checking "Reviewed" and continue with the next screen.

Exhibit 3-5. Pregnancy status review screen



### 3.5.1.5 Breastfeeding Evaluation (Women 12-59 years)

This screen (Exhibit 3-6) prompts the physician to ask women about current breastfeeding. Participants who are breastfeeding a child should not be administered albuterol. Use the following question: “{Are you/Is SP} now breastfeeding a child?” Mark the appropriate response: if it is “Yes,” “Refused,” or Don’t Know,” the participant is excluded from bronchodilator testing. If the response is “No,” then the participant passes this screen and the bronchodilator evaluation continues.

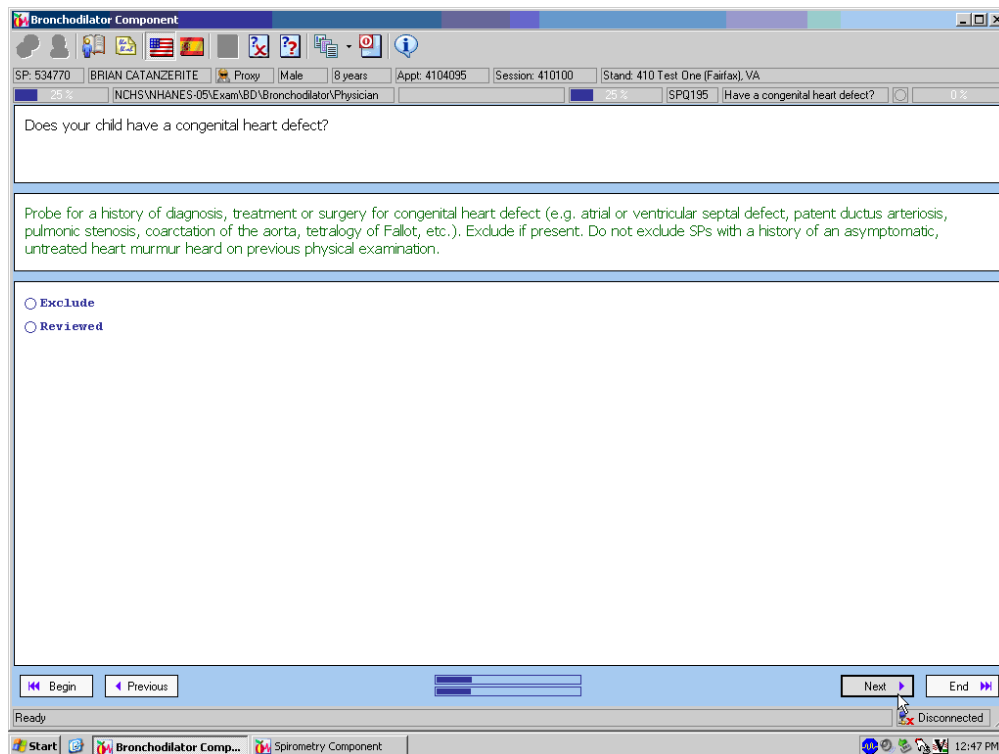
Exhibit 3-6. Now breastfeeding a child screen

The screenshot displays the 'Bronchodilator Component' software window. The title bar reads 'Bronchodilator Component'. The interface includes a patient information header with fields for SP: 262760, MADISON QUINN, Self, Female, 29 years, Appt: 4103198, Session: 410030, and Stand: 410 Test One (Fairfax, VA). Below this is a progress bar showing 18% completion for 'NCHS\NHANES-05\Exam\BD\Bronchodilator\Physician' and 0% for 'Now breastfeeding a child?'. The main content area contains the question: 'Are you now breastfeeding a child?'. Below the question are two radio button options: 'Yes' and 'No'. At the bottom of the window, there are navigation buttons: 'Begin', 'Previous', 'Next', and 'End'. The Windows taskbar at the bottom shows the Start button, 'Physician' folder, 'My Documents' folder, and the 'Bronchodilator Comp...' application icon. The system tray on the right shows a 'Disconnected' status and the time '2:08 PM'.

### 3.5.1.6 Congenital Heart Disease Exclusion (Children 6-15 years)

This screen (Exhibit 3-7) prompts the physician to ask child participants about congenital heart disease, which is a bronchodilator exclusion. Use the following question: “Does your child have a congenital heart defect?” If the response is affirmative, probe to determine whether there is a history of a diagnosis of, treatment for, or surgery for a recognized congenital heart defect (atrial or ventricular septal defect, patent ductus arteriosus, pulmonic stenosis, coarctation of the aorta, and tetralogy of Fallot, or other defect). If there is such a history or the informant does not know or refuses to answer the question, exclude the participant from bronchodilator testing. This evaluation segment is intended to be interview-based, and if after the initial interview, there is uncertainty as to the participant’s status with respect to this exclusion criterion, then the participant should be excluded. Participants with a history of an asymptomatic, untreated heart murmur heard on prior physical examinations, but without a diagnosis of or treatment for heart disease, should not be excluded. Record the participant’s status on the following ISIS screen.

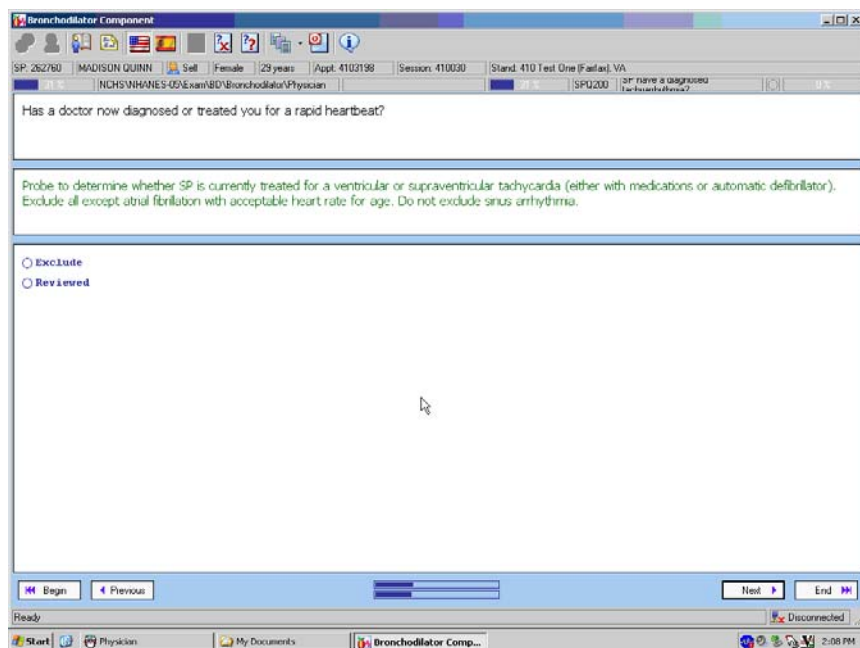
Exhibit 3-7. Congenital heart defect screen



### 3.5.1.7 Diagnosed Tachyarrhythmia Exclusion (All 6-79 years)

This screen (Exhibit 3-8) prompts the physician to ask participants about the current diagnosis and treatment of tachyarrhythmias, which are a bronchodilator exclusions. Beta 2-agonist bronchodilators such as albuterol should not be administered to persons currently being treated for tachyarrhythmias, for example supraventricular or ventricular tachycardia. Use the following question to ask the participant whether they are currently diagnosed or treated for a rapid heart beat (tachyarrhythmia): “Has a doctor now diagnosed or treated {you/your child} for a rapid heartbeat?” If there is such a history or the informant does not know or refuses to answer the question, exclude the participant from bronchodilator testing. This evaluation segment is intended to be interview-based, and if after probing, there is uncertainty as to the participant’s status with respect to this exclusion criterion, the participant should be excluded. Please note that treatment for such conditions may include either drug therapy, or implanted automatic defibrillators. A prior history of surgery that successfully corrected a tachyarrhythmia should not necessarily exclude a participant from bronchodilator testing. If the participant has a history of treatment for atrial fibrillation, and a regular heart rhythm, they may undergo bronchodilator testing if their heart rate is in an acceptable range for age based on NHANES criteria. Otherwise, they should be excluded. Use the following ISIS screen to check the participant’s status with respect to this criterion.

Exhibit 3-8. SPs have a diagnosed tachyarrhythmia screen



### **3.5.1.8 MEC Physician Medication Review (SI-RDQ & New Drug Data)**

A number of bronchodilator medication exclusion criteria relate to prescription medications that the participant may currently be taking. A particular class of drugs may in and of itself constitute an exclusion criterion; or the use of certain prescription drugs in persons with certain co-morbidities may constitute an exclusion criterion. Prescription medication data for each participant is collected in the household interview (SI-RXQ) and is automatically coded according to Multum™ drug class by the ISIS system in about 90 percent of cases. In these cases the ISIS will automatically exclude participants from bronchodilator testing if they are taking certain classes of medications.

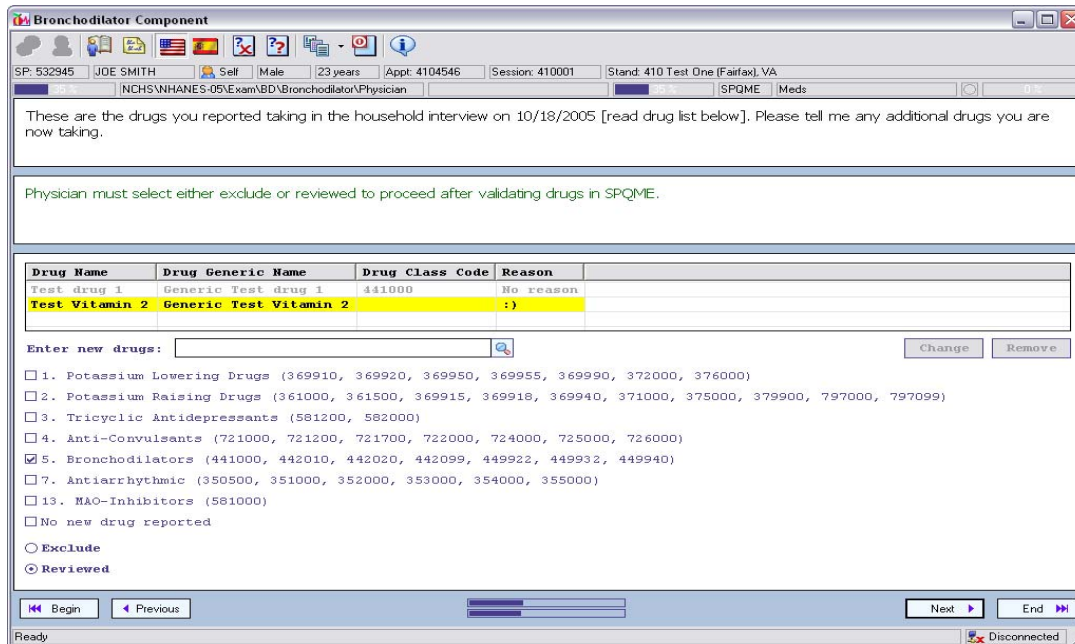
In about 10 percent of prescription drugs listed in the participant's NHANES data file, ISIS will not be able to assign a Multum™ drug class code. Also bronchodilator-eligible participants may have started taking new medications in the interval between their household interview and the time of spirometry examination in the MEC. In both these cases, it is necessary for the physician to perform an additional evaluation using the Physician Medication Review screen.

The physician's role here is two-fold:

1. To review the uncoded medications in the household interview prescription medication data and if applicable, assign each of these medications to one of the special drug type categories that are relevant to bronchodilator safety exclusions.
2. To ask the participant whether they have started taking any new prescription medications since the time of the household interview; to record these new medications (if any) in the "Enter New Drugs" text box; and to determine whether they belong to a drug class relevant to bronchodilator safety exclusions.

The physician will be assisted in these processes by a special "multiple look-up" drug coding software utility provided by ISIS. Once the uncoded drugs from the household interview and any new drugs started have been assigned to their classes, the ISIS software is programmed to automatically determine whether a safety exclusion exists and if so, to automatically check the "Exclude" box at the bottom of the Physician Medication Review Screen (Exhibit 3-9).

Exhibit 3-9. Physician medication review (SPQME) screen



In the Physician Medication Review Screen, the primary drug information box lists all the prescription drugs reported by the participant in the household interview and categorizes them by Drug Name, Drug Generic Name, Multum™ Drug Class Code, and a stated Reason for Use. If a drug is unable to be coded by the Multum™ software, the verbatim text description of the drug collected by the household interviewer will be displayed in highlighted mode on the screen. By double-clicking on the highlighted (uncoded) drug, the automated look-up table will open and the physician can employ this utility to identify the actual name of the drug and provide a Multum™ Drug Class Code. When the actual drug name is identified in the look-up utility, simply click on the specific entry to code the drug. This code is then automatically entered into the system. ISIS will then automatically check any applicable drug class code box, and if the drug's class code is pertinent to the NHANES exclusion criteria, it will check the participant as excluded from bronchodilator testing.

The ISIS software system will always automatically evaluate the participant against study exclusion criteria based on available data or whenever any new information is entered into the system. When the Physician Medication Review screen is first opened, previously coded drugs are evaluated and the appropriate drug class check boxes will be prechecked. Also, as mentioned, if the physician using the drug look-up utility checks a code for a previously uncoded drug, ISIS will automatically check the appropriate drug class box and mark the participant as excluded, if applicable. If the physician cannot

assign a drug name and class code using the look-up utility, or is uncertain about which coding choice to pick, the drug may be left uncoded. However, if the physician either knows the drug based on previous experience or can identify it by looking it up in another reference source, then one of the seven general medication categories pertinent to the NHANES safety exclusions may be manually checked, if applicable. ISIS will then automatically determine whether the participant should be excluded. If the physician cannot identify a drug using the utilities provided, from prior knowledge or from any other available reference source, that participant should be excluded from bronchodilator testing by checking the “Exclude” box.

There are seven general drug classes that are pertinent to bronchodilator safety exclusions. These include the following:

1. Potassium Lowering Drugs;
2. Potassium Raising Drugs;
3. Tricyclic Antidepressants;
4. Anticonvulsants;
5. Bronchodilators;
6. MAO Inhibitors; and
7. Class I Antiarrhythmics.

The specific drugs currently contained in each of these seven categories are listed in Appendix B of this manual, the contents of which are also provided as an ISIS “help” screen for the Physician Medication Review screen. This will be updated on a periodic basis during the progress of the survey. For individual drugs, detailed information including exact chemical name, brand name, and drug coding may be accessed by using the “multiple look-up” drug coding software utility provided in the Physician Medication Review screen. A review of the seven different drug classes and their importance for bronchodilator safety exclusions includes the following:

**Potassium Raising and Lowering Drugs.** Beta 2-agonist adrenergic bronchodilators have a physiological effect of lowering serum potassium levels, especially with chronic administration. This may be less of a concern with short-term administration; however, when albuterol is administered in the setting of pre-existing hypokalemia, there can be an increased likelihood of arrhythmias, which are an exclusion



for bronchodilator testing. It is desirable therefore to exclude from beta 2-agonist bronchodilator testing persons who may potentially have some degree of pre-existing hypokalemia. In the general population, the principle cause of hypokalemia is as a side effect of diuretic therapy.

To evaluate this exclusion, it is first necessary to determine whether the participant is currently taking a diuretic medication (for example, hydrochlorothiazide, chlorthaladone, furosemide, xaroxolyn, etc.) that could predispose to hypokalemia. If the participant is taking this type of diuretic, then in the Physician Medication Review screen check the box “Potassium Lowering Drug.” Next, determine whether any of the prescription medications the participant is taking is a potassium raising drug. Potassium raising drugs are prescription potassium supplements, or another concurrent medication that has the physiological effect of raising the serum potassium (for example, an ACE inhibitor, an Angiotensin II Receptor Antagonist, amiloride, acetazolamide, spironolactone, triamterine etc.). Participants taking combination drugs designed to prevent hypokalemia (Dyazide, Maxizide, and Moduretic) should be classified as taking both a potassium lowering and a potassium raising drug. Use the look-up utility to code the drug correctly, or manually check either the “Potassium Lowering” or “Potassium Raising” check box as appropriate. Once the potassium raising or lowering boxes are checked, ISIS will determine whether to exclude the participant from bronchodilator testing based on the following criteria: if a potassium lowering drug is checked but no potassium raising drug is checked, then the participant will be excluded; if a potassium lowering drug is checked and a potassium raising drug is also checked, then the participant will not be excluded; participants taking solely a potassium raising drug will not be excluded. As a practical matter, in completing this screen, if a participant has been identified as taking a potassium raising drug, they should not be excluded. Therefore in this special case, it is not necessary for the physician to determine whether the participant is also taking a potassium lowering drug.

**Tricyclic Antidepressants.** Tricyclic antidepressants are prescription medications used primarily to treat depression, but are also commonly used to treat migraine headache, pain from peripheral neuropathy, and other chronic pain syndromes. The commonly used tricyclic antidepressant medications are listed in Appendix B. Review the participant’s uncoded and new medications, and if they are taking a medication in this class, use the look-up utility to code the drug as an antidepressant or manually check the “Tricyclic Antidepressants” box. When this box is checked, ISIS will automatically review demographic and co-morbidity data from the participant’s household interview data file to determine whether they should be excluded from bronchodilator administration. If the participant is currently taking a tricyclic antidepressant, is over 40 years of age, and states that he or she is currently

being treated for heart disease (angina, myocardial infarction, congestive heart failure, and arrhythmia), kidney disease, or a thyroid disorder, they will be excluded.

**Anticonvulsants.** Beta 2-adrenergic bronchodilators may lower the seizure threshold and potentially precipitate seizures in persons taking anticonvulsants for epilepsy. Therefore, the participant's uncoded or newly started medications should be reviewed, and if they are taking an anticonvulsant, the look-up utility should be used to appropriately code the drug, or the "Anticonvulsants" box can be manually checked. When this box is checked (either automatically by ISIS or manually), the participant is not automatically excluded from bronchodilator administration. This is because anticonvulsants may be taken for a variety of reasons (therapy of migraine headache, peripheral neuropathy, etc.). The increased seizure risk is limited to those with a history of epilepsy. Accordingly, checking the "Anticonvulsant" box in the Physician Medication Review screen flags the ISIS system to prompt you to ask an additional question regarding the participant's history of epilepsy. This question is administered later after the Physician Medication Review screen is completed and closed.

**Bronchodilators.** Beta 2-adrenergic and other bronchodilators should only be administered in FDA/manufacturer recommended doses. If a participant has recently taken a dose of a bronchodilator, they should be excluded from bronchodilator administration because administering an additional bronchodilator in this setting would result in exceeding the FDA/manufacturer recommended dose level. In the Physician Medication Review screen, it is therefore necessary to classify whether the participant is currently taking a bronchodilator of any type (either a short- or a long-acting preparation). If the participant is taking a bronchodilator, use the look-up utility to code the drug or manually check the appropriate box in the Physician Medication Review screen. This will flag the ISIS system to prompt you to ask additional questions regarding the participant's recent history of bronchodilator use. These questions are administered later after the Physician Medication Review Screen is completed and closed.

**Monoamine Oxidase (MAO) Inhibitors.** Because of their potential to engender arrhythmias, participants taking monoamine oxidase inhibitors will be excluded from bronchodilator testing. These drugs are most typically used to treat depression, but are not commonly used by physicians today. MAO inhibitors in use currently are: Isocarboxazid (Marplan), Phenelzine (Nardil), and Tranylcypromine (Parnate).

An ISIS help screen also provides this list of MAO inhibitors. Review the participant's drug lists, including uncoded and newly started drugs to verify whether or not the participant is currently

taking an MAO inhibitor. If the participant is taking a MAO inhibitor, use the look-up utility to code the drug or manually check the appropriate entry in the ISIS screen. The participant will then be excluded from bronchodilator administration.

**Class I Antiarrhythmics.** If the participant is currently taking a listed Class I antiarrhythmic, they should be excluded from bronchodilator administration. This class of drugs is used only for major cardiac rhythm disorders, typically the more serious life-threatening tachyarrhythmias. Persons with these medical conditions should not have bronchodilator administration. Verify the participant's status with regard to this important class of medications. If the participant is taking a drug in this class, either use the look-up utility to code the drug or manually check the category "Class I Antiarrhythmics." ISIS will then exclude the participant from bronchodilator administration.

**Physician's Discretionary Exclusion.** During completion of the Physician's Medication Review screen, the physician may chose to exclude the participant from bronchodilator administration if in his or her judgment there is a valid reason for doing so. For example, the Physician's Medication Review screen process provides the physician with a comprehensive view of the participant's current medications (including the opportunity to assess possible drug interactions) and some insight into the participant's current health condition. If based on this information, bronchodilator administration seems contra-indicated, then the physician may choose to exclude the participant by using the "Exclude" check box. ISIS will then open the examination status screen where "Not Done" should be checked. The reason for the exclusion should be documented in a text note utility on this screen.

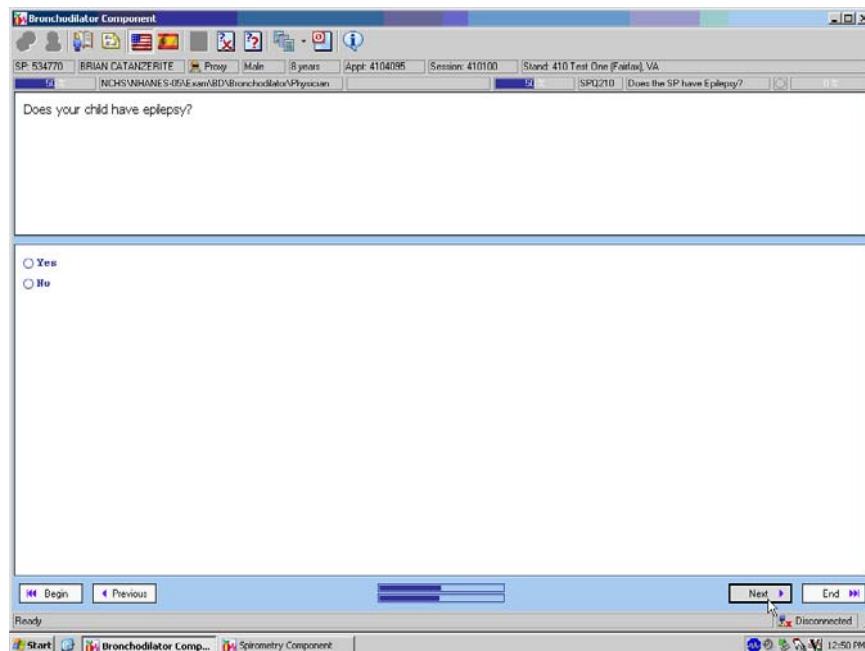
### **3.5.1.9 History of Epilepsy**

If in the physician medication review, the participant is classified as currently using an anticonvulsant, the following screen will appear to prompt you to ask the participant whether they have a history of epilepsy or seizures. Beta 2-adrenergic bronchodilators may lower the seizure threshold and potentially precipitate seizures in persons taking anticonvulsants for epilepsy. Therefore, this class of persons will be screened and excluded from bronchodilator administration.

Epilepsy is a disorder involving repeated seizures of any type. Seizures are episodes of disturbed brain function that cause changes in attention and/or behavior. They are caused by abnormal electrical excitation in the brain. A history of previous seizures does not necessarily mean that the SP has

epilepsy. For example, many young children have convulsions from fevers. A history of a febrile convulsion does not constitute a diagnosis of epilepsy. Nor does a history of a single, nonrecurrent seizure in the past mean that the person has epilepsy. Other types of seizures not classified as epilepsy include those caused by an imbalance of body fluids or chemicals or by alcohol or drug withdrawal. Record the participant's status with respect to epilepsy on the following ISIS screen (Exhibit 3-10).

Exhibit 3-10. Epilepsy screen



If a participant has a history of epilepsy checked in the previous screen, or their status is “Refused” or “Don’t Know,” then check the appropriate box and they will be excluded from bronchodilator testing. Otherwise check “No” and continue.

### 3.5.1.10 Exclusion for Previous Adverse Reaction to Albuterol

Albuterol is the inhaled bronchodilator being used in this study. If an SP has had a previous adverse reaction to albuterol, then do not administer the drug. Use the following question to ask about a history of such adverse reactions:

*“{Have you/Has your child} ever had an adverse reaction to albuterol?”*

If there is uncertainty on the part of the informant, then read the explanatory text provided in parentheses “[Albuterol is a medication used to treat asthma and other breathing problems. Product brand names are Proventil, Ventolin, Combivent, and Accuneb.]”

The principal adverse effects of albuterol include the following:

- Tremor/nervousness
- Dizziness
- Headache
- Insomnia
- Upset stomach
- Palpitations/tachyarrhythmia
- Hypertension
- Lightheadedness/fainting
- Skin rash/allergic reactions

Albuterol is also available in oral form as pills or liquid. Oral forms of beta 2-agonists tend to have more side effects because they are in higher doses and are absorbed throughout the bloodstream to get to the lungs. If the participant has had an adverse reaction to albuterol, refuses to answer, or does not know, then check the appropriate box in the ISIS screen shown below (Exhibit 3-11) to exclude the person from bronchodilator testing. Otherwise check “No” and continue.

Exhibit 3-11. Adverse reaction to albuterol screen

SP: 438452 DONALD NOEL Self Male 47 years Appt: 4104113 Session: 410102 Stand: 410 Test One (Fairfax), VA

56 NCHS\NHANES-05\Exam\BD\Bronchodilator\Physician 56 SPQ230 Adverse reaction to albuterol? 0%

Have you ever had an adverse reaction to albuterol? [Albuterol is an inhaled medication used to treat asthma and other breathing problems. Brand names are Proventil, Ventolin, Combivent and Accuneb.]

If an SP has had a previous adverse reaction to albuterol, do not administer the drug. The principle adverse effects of albuterol include the following: tremor/nervousness, dizziness, headache, insomnia, upset stomach, palpitations, rapid or irregular heart beat, hypertension, lightheadedness/fainting, and skin rash/allergic reactions.

Yes  
 No

Begin Previous Next End

Ready Disconnected 3:44 PM

### 3.5.1.11 Exclusion for Recent Use of Short- of Long-Acting Bronchodilator

These two physician evaluation screens only appear if during the completion of the Physician Medication Review screen, the participant was previously coded as currently taking a beta 2-adrenergic bronchodilator or anticholinergic bronchodilator. It is the intention of NHANES not to administer beta 2-adrenergic bronchodilators to participants if the dose can be anticipated to exceed current maximum FDA/manufacturer recommended dosages. This means that if a participant has recently already taken a bronchodilator, another dose should not be administered, and they should therefore be excluded from NHANES bronchodilator administration. Specifically, for a short-acting bronchodilator, the participant should be excluded if they have taken a dose of a short-acting beta 2-adrenergic bronchodilator or anticholinergic bronchodilator within the previous 4 hours; for a long-acting bronchodilator, they should be excluded if they have taken a dose within the previous 12 hours. (Please note that the current use of a β-blocker medication by the participant is not a reason to exclude the participant from testing.)

Note that the classification of the bronchodilators employed in the Physician Medication Review screen is a general one and does not distinguish between short- and long-acting formulations. To expedite completion of these two screens, the physician will be asked to complete the screen for long acting bronchodilators first. This is because there are relatively few long-acting bronchodilators currently approved for use in the U.S. It is anticipated that it will be relatively straightforward to determine whether an individual participant currently takes a long-acting bronchodilator, and whether they have taken a dose within the previous 12 hours. All other bronchodilators the participant may be taking may then be considered to be short-acting ones. Therefore, to complete the following screen, all bronchodilators other than the ones identified as long acting in the previous screen may be considered short-acting preparations. To complete this screen, therefore, it is only necessary to ask whether the participant has taken a dose within the previous 4 hours. As with previous exclusion questions, if the participant's answer is "Refused" or "Don't Know," they should be excluded.

Use the following two ISIS screens (Exhibits 3-12 and 3-13) to record exclusion status for recent bronchodilator use.

Exhibit 3-12. Bronchodilator within 12 hours screen

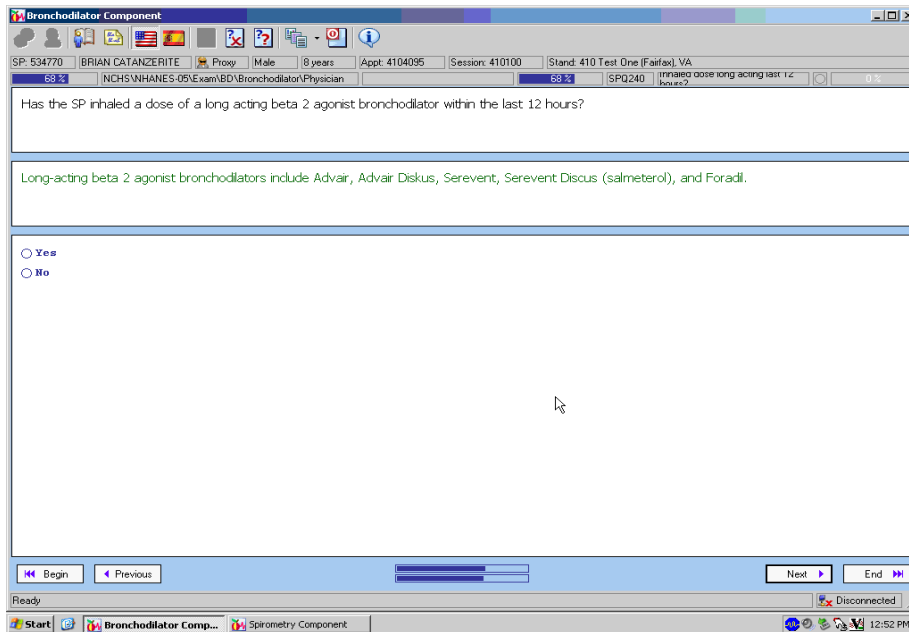
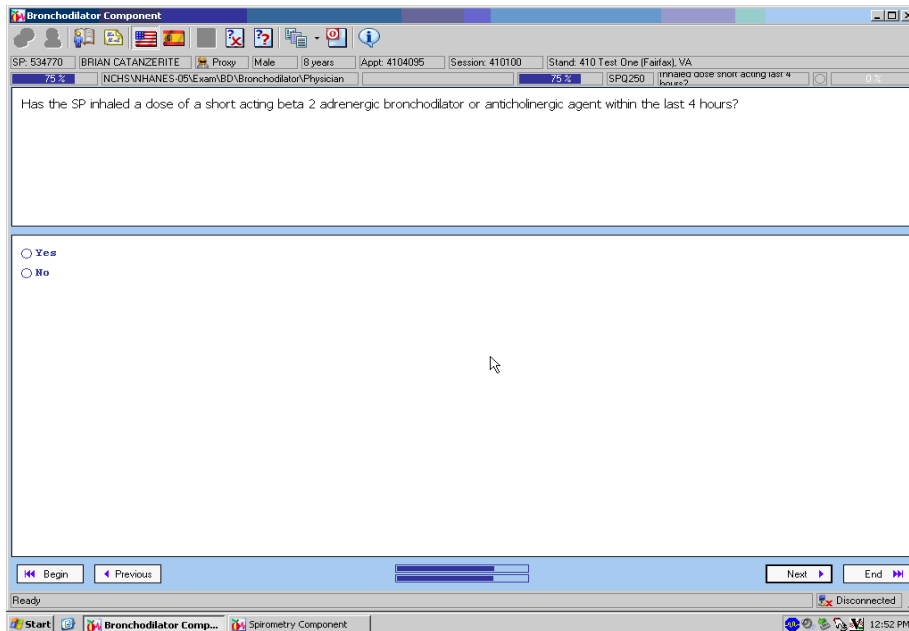


Exhibit 3-13. Bronchodilator within 4 hours screen

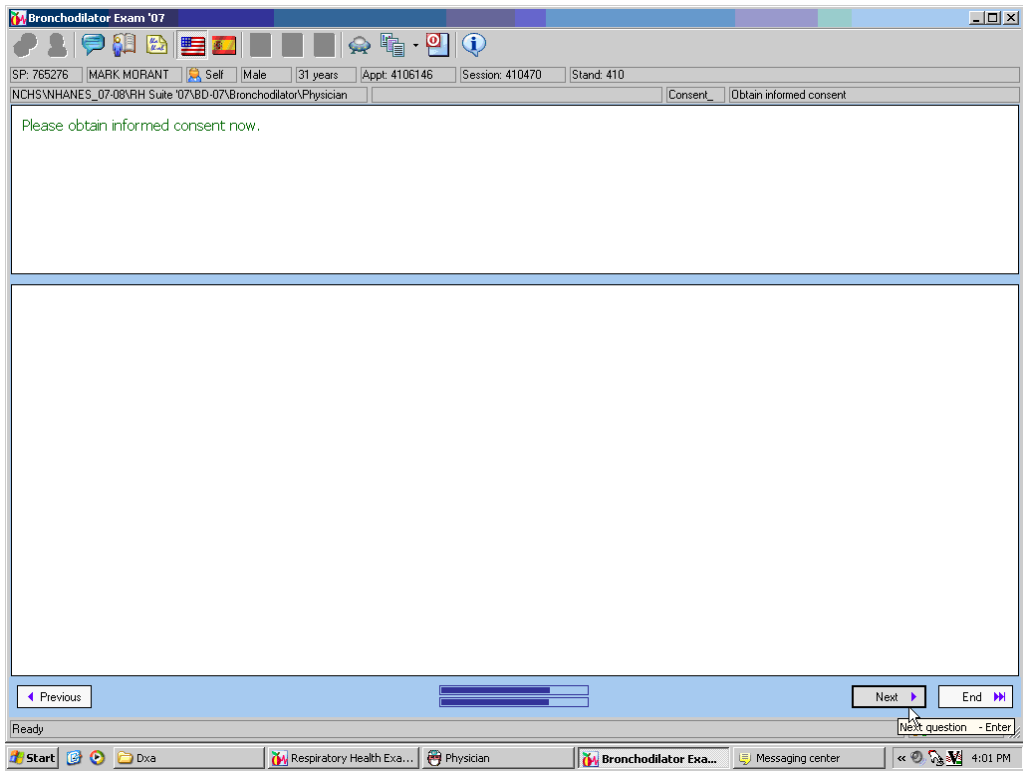


### 3.5.1.12 Bronchodilator Administration Message Screen

If, following the MEC physician safety exclusion evaluation, the participant is eligible for bronchodilator testing, the following ISIS screen (Exhibit 3-14) will appear to prompt you to obtain informed consent for albuterol bronchodilator administration.



Exhibit 3-14. Please obtain informed consent screen



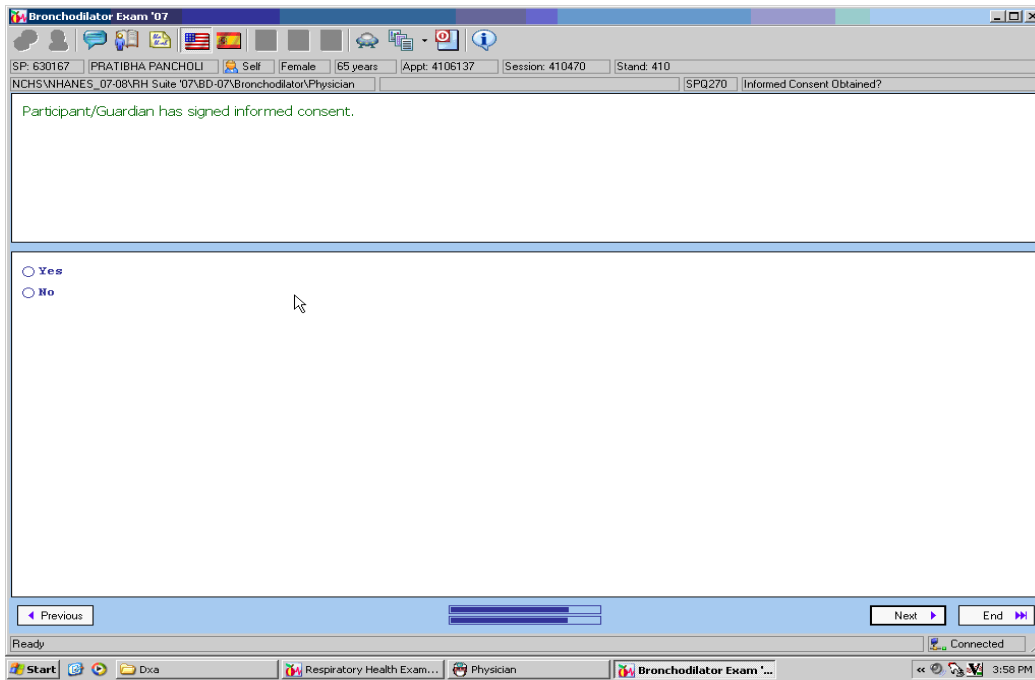
### 3.6 **Bronchodilator Consent**

When the SP becomes eligible for the bronchodilator the physician is responsible for informing the SP about the known risks of the use of albuterol, and obtaining the SPs signature signifying that they have been adequately informed about the risks of taking albuterol. Specifically, the physician:

- Gives the SP the informed consent form (Appendix A) to read;
- Informs the SP that the albuterol may, in a small percentage of cases, cause an allergic reaction, and how the allergic reaction would be treated;
- Informs the SP of the side affects that sometimes occurs with the use of albuterol: fast heart beat, chest pain, nervousness, or tremor;
- Assures that the SP understands that taking the albuterol is voluntary, and that refusing to take the albuterol will not negatively affect any remuneration that the SP was promised;
- Assures that the SP understands that she or he can stop taking the albuterol at any time;
- Answers any questions the SP has about the use of the albuterol;
- Asks the SP to read the consent form and signs it; and
- Administers the albuterol only after informed consent is provided to the SP, and the consent form has been signed by the SP and the physician.

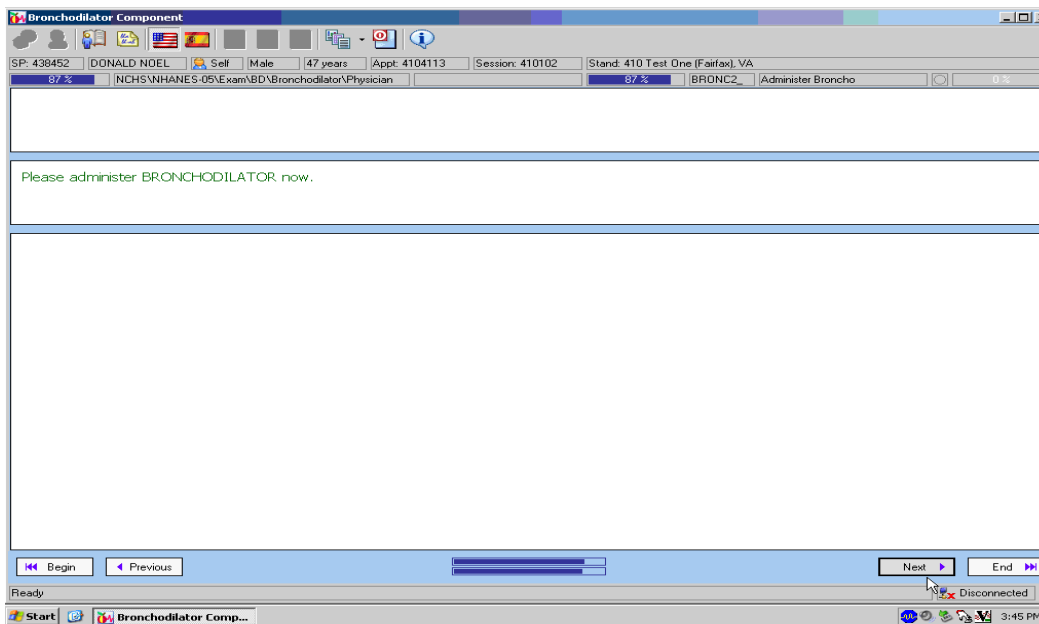
The bronchodilator application will display a second informed consent screen, which confirms that the consent was signed by the participant or guardian, as shown in Exhibit 3-15.

Exhibit 3-15. Participant/guardian informed consent



### 3.6.1 Bronchodilator Administration

Exhibit 3-16. Administer bronchodilator screen



When the MEC physician evaluates the participant for bronchodilator safety exclusions (see above), and the participant is found eligible and consents, the physician will then show the participant how to use the metered-dose albuterol inhaler (MDI) through a spacer. The following procedure will be used.

**Physician Instructions:**  
**How participants should use the albuterol with the AeroChamber MAX™ spacer:**

1. Check the expiration date on the albuterol before using it.  
(Discard it if it has expired and get a new canister.)
2. Remove the cap from the albuterol MDI.
3. Shake the canister.
4. Prime the MDI once by depressing the canister.
5. Insert the MDI into the back piece of the AeroChamber MAX chamber.
6. Ask the participant to put his or her lips around the AeroChamber MAX mouthpiece.
7. Have the participant exhale completely, then ask the participant to start breathing in. As the participant begins to inhale, depress the inhaler to release the medication into the spacer.
8. Have the participant breathe in slowly and deeply through his or her mouth (3-5 seconds).
9. Have the participant hold his or her breath and count to 10.
10. Have the participant exhale and breathe comfortably.
11. Rest for 1 minute. Repeat items 5-9.
12. Remove the MDI and discard the AeroChamber MAX.
13. Put the cap back on the albuterol MDI.

After completing the bronchodilator administration, record the status of the bronchodilator administration using the following ISIS screen (Exhibit 3-17).

Exhibit 3-17. Bronchodilator administered screen

SP: 280141 B TEST Proxy Female 15 years Appt: 4103175 Session: 410211 Stand: 410 Test One (Fairfax), VA

90 % NCHS\NHANES-05\Exam\BD\Bronchodilator\Physician 90 % SPQBDA Bronchodilator administered? 0 %

BRONCHODILATOR administered successfully?

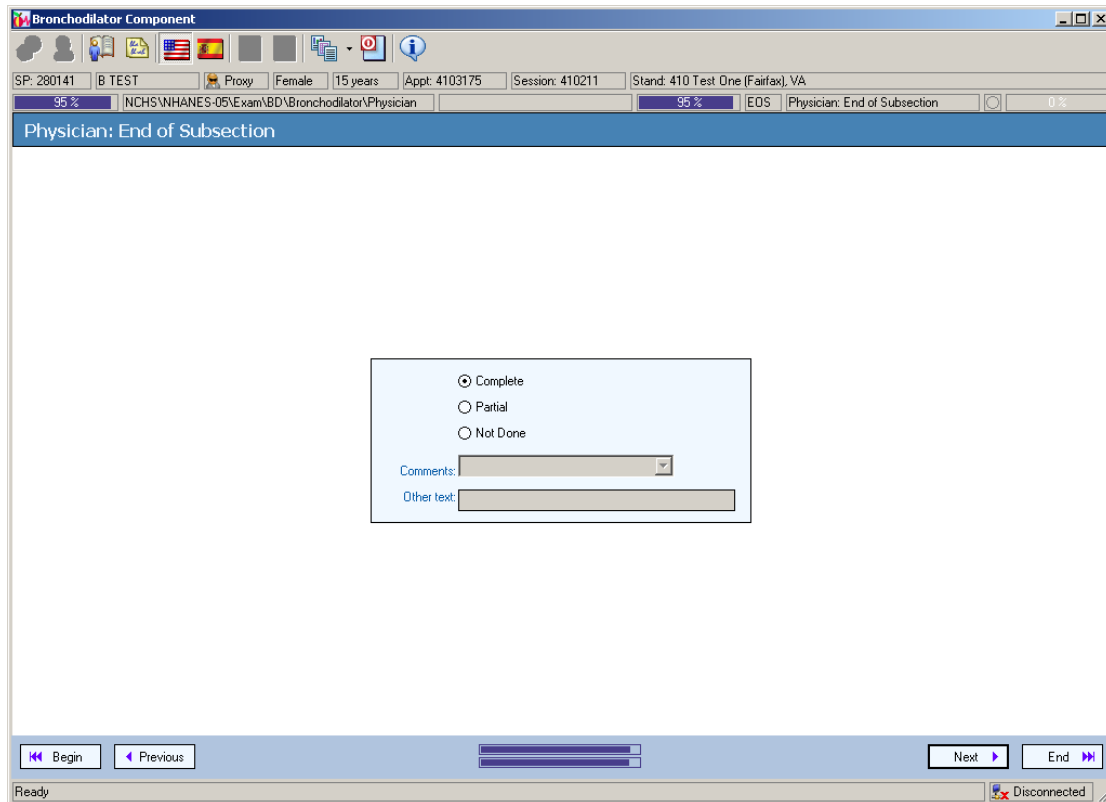
Yes  
 No

Begin Previous Next End

Ready Disconnected

Then complete the following screen (Exhibit 3-18) to indicate the status of the Bronchodilator administration subcomponent.

Exhibit 3-18. Physician end of subsection screen



ISIS will then prompt you to send the SP to the next exam or back to the MEC coordinator to schedule repeat spirometry, ensuring that a minimum of at least 10 minutes has passed prior to retesting to allow the medication to take effect.

### 3.6.2 Level II Referral Evaluation for Participants with $FEV1/FVC\% \leq 50\%$ Predicted

There is an obligation to inform participants of abnormal results from the examinations and to refer participants to local medical providers when appropriate. MEC physicians are responsible for such referrals. All participants completing spirometry will routinely be sent a summary of their examination findings by mail. In these reports, abnormal results will be highlighted. In addition, all spirometry examination participants with an  $FEV1/FVC\% \leq 50\%$  of predicted **in baseline spirometry testing regardless of whether they are eligible for bronchodilator testing** will be referred to the MEC physician for counseling and evaluation for Level II Referral. Persons with an  $FEV1/FVC\% \leq 50\%$

predicted have an increased likelihood of severe obstructive lung disease, and constitute the group that may benefit most from physician counseling and Level II referral.

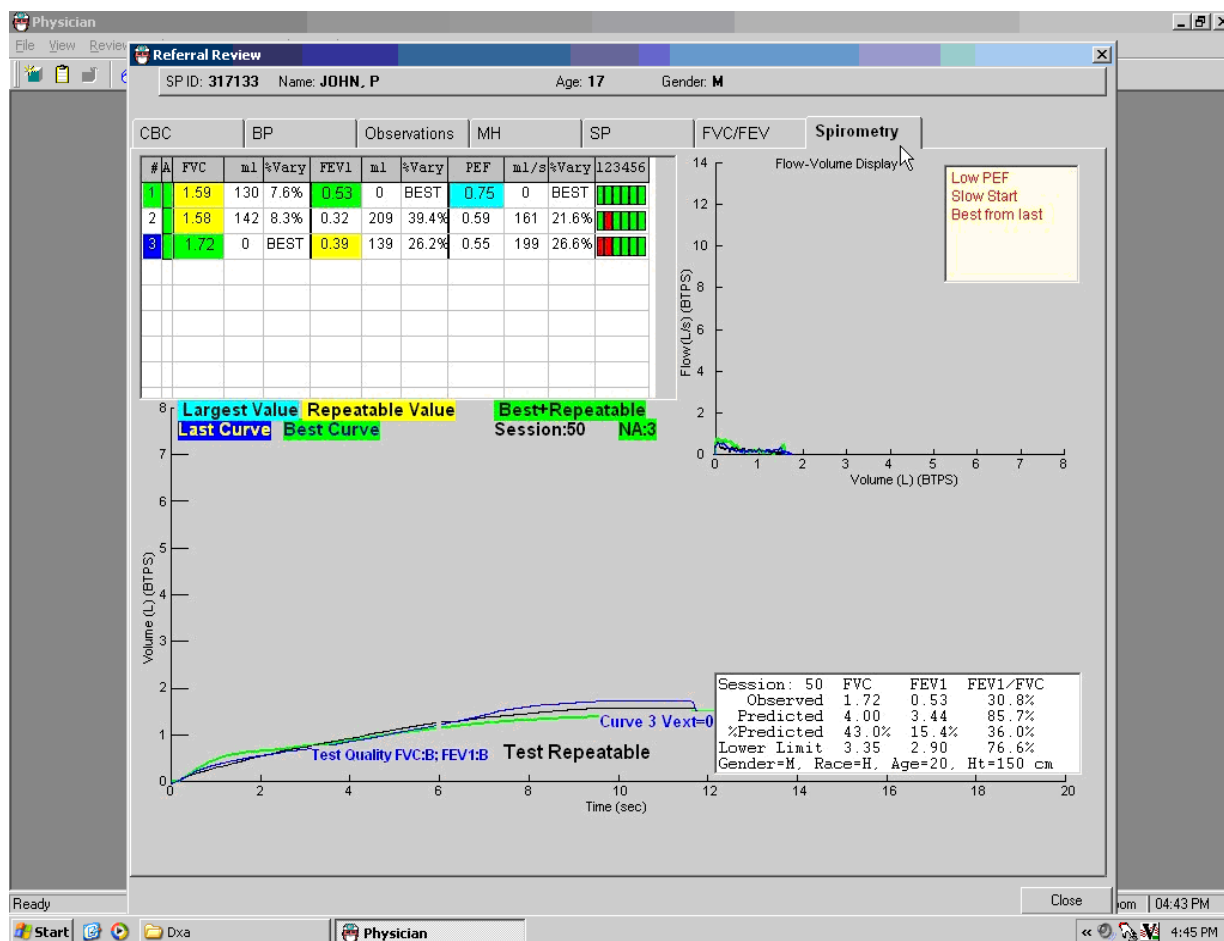
At the completion of baseline spirometry, the ISIS software will compare the participant's results to the values for the standard prediction equations to determine whether the participant's  $FEV_1/FVC\% \leq 50\%$  of predicted. If this is the case, then a physician observation message will be generated by the ISIS system. The MEC physician will receive the following message:

“The baseline Spirometry results for this participant indicate the possibility of severe obstructive lung disease (asthma or chronic bronchitis). The  $FEV_1/FEV\%$  is  $\leq 50\%$  of predicted. A referral to the MEC physician is being made.”

The MEC physician will then see the participant in followup. Generally speaking, it is not necessary to delay the Level II referral evaluation until after all spirometry studies are complete: i.e., it is not necessary to wait to see the results of the post-bronchodilator studies. This is because the finding of such abnormal results at baseline spirometry is a potentially significant finding in and of itself: such a finding would result from either severe obstructive lung disease (fixed COPD), or from more severe cases of asthma (i.e., either undiagnosed or untreated, severe cases or cases under the case of a physician but with loss of treatment control). The MEC physician, however, has the option to counsel these participants either at the time baseline spirometry is completed or at the completion of bronchodilator testing, at his or her discretion. (Typically all participants with obstructive airflow limitation of this magnitude would be eligible for post-bronchodilator spirometry, however some may be excluded for safety reasons.)

The MEC physician should speak with the participant and review the spirometry results. The possibility that the abnormal findings could result from poor participant effort or poor quality tracings should be evaluated, and the SP's spirometry test results summary and the graphic display of the spirometry curves can be reviewed (Exhibit 3-19). The MEC physician can also consult with the spirometry technologist who performed the test. If the observed abnormality appears simply due to a poor quality effort or tracing, then a Level II referral is not necessary. However, it should be kept in mind that persons with severe obstructive lung disease can often have a more difficult time performing spirometry, and in general are less likely to produce high quality tracings.

Exhibit 3-19. Spirometry flow curves



The following guidelines can be used by the MEC physician as a basis for Level II referrals:

- If the participant is **not** under the care of a physician, a Level II referral should be made. In this case, the participant may have either asthma or COPD, or both, and requires expedited medical evaluation to determine the diagnosis and therapy that may be indicated.
- If the participant is known to have fixed COPD (chronic bronchitis or emphysema), **and** is currently under the regular care of a physician, then a Level II referral is not generally necessary. The results of the spirometry test should be reviewed with the participant and the participant should be instructed to give a copy of these to his or her medical provider at their next office visit.
- If the participant is known to have COPD, and is **not** currently under the care of a physician, then a Level II referral **is** generally necessary. This potential degree of airways obstruction requires regular medical monitoring.



- If the participant shows significant improvement from the abnormal baseline after bronchodilator administration, then this is an indication of poorly controlled asthma, and the participant **should** have a Level II referral to see their treating physician for re-evaluation of therapy.

Generally speaking, the MEC physician should counsel the participant selected for Level II referral evaluations that their NHANES spirometry test results were abnormal as compared to national standards. The participant should be informed that this finding raises the question of whether a participant has potentially serious degree of lung disease such as asthma or COPD. However, because it is primarily a screening test, the NHANES spirometry examination cannot by itself diagnose any disease. The participant's spirometry test result makes it very likely there is a problem, but as a research evaluation, NHANES testing cannot say for certain whether a problem exists, or how severe it is. Occasionally, screening tests may give abnormal results even when there is not an actual problem; however, NHANES sets its criteria such that this possibility is minimized, so it is important to get further, proper medical evaluation.

The participant should be counseled that in order to make a diagnosis of a disease such as asthma or COPD, a physician must be consulted and take a more extensive history, perform a physical examination, additional laboratory tests, and possibly x-rays. A more complete lung function test should be done of the type available in hospitals. This type of evaluation is the only way the participant can learn their true status. It is important for the participant to make sure to follow through and get a medical evaluation, because if asthma or COPD was actually present, it is potentially a serious health problem, and could cause major health problems if ignored or not properly treated.

Level II referrals should be made to the participant's own personal treating physician, if they have one. If not, the MEC physician would advise on a new referral.

### **3.6.3 Level II Referral Evaluation for Participants with FEV1/FVC% $\leq$ Lower Limits of Normal**

All participants with an FEV1/FVC% less than or equal to the lower limits of normal are referred to the physician for the bronchodilator. The physician can at that point review the flow curves for all participants referred. Those participants who have abnormal pulmonary function testing who are not currently under the care of a physician specifically for their breathing problem should be referred to a

community provider on an elective basis for evaluation and treatment. Also, those participants who are currently under medical treatment for asthma who also have a low FEV1/FVC% should be referred to their treating physicians because their asthma may not be properly controlled on their current therapy. Finally, at their discretion, the MEC physician may also refer other participants whose FEV1/FVC% is very low if they feel there is a medical need, based on the participant's information.

#### 4. REFERENCES

1. American Thoracic Society. (1995). Standards for the diagnosis and care of patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*, 152, S77-S120.
2. Pauwels, RA, Buist AS, Calverley PMA, Jenkins CR, Hurd SS. (2001). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. NHLBI/WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD) Workshop Summary. *Am J Respir Crit Care Med*, 163, 1256-1276.
3. Taussig LM, Wright AL, Holberg CJ, Halonen M, Morgan WJ, Martinez FD. (2003, Apr). Tucson Children's Respiratory Study: 1980 to present. *J Allergy Clin Immunol*, 111(4), 661-75.
4. Burney PG, Luczynska C, Chinn S, Jarvis D. (1994, May). The European Community Respiratory Health Survey. *Eur Respir J*, 7(5), 954-60.
5. Menezes AM, Victora CG, Perez-Padilla R; The PLATINO Team. (2004, Jun). The Platino project: methodology of a multicenter prevalence survey of chronic obstructive pulmonary disease in major Latin American cities. *BMC Med Res Methodol*, 17;4,15.
6. Hankinson JL, Odencrantz JR, Fedan KB. (1999). Spirometric reference values from a sample of the general US population. *Am J Respir Crit Care Med*, 159, 179-187.
7. Wang X, Dockery DW, Wypij D, Fay ME, Ferris BG Jr. (1993, Feb). Pulmonary function between 6 and 18 years of age. *Pediatr Pulmonol*, 15(2), 75-88.

## Appendix A

### Informed Consent Documents

**A. BRONCHODILATOR AND REPEAT SPIROMETRY INFORMED CONSENT  
NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY  
LUNG FUNCTION TESTING WITH MEDICATION**

Your lung function test results were outside the normal range. The amount of air you breathed out in one second was less than expected for someone your age and sex. One reason could be narrowing of the small breathing tubes leading to your lungs.

The NHANES survey is asking you to take a medicine and do another breathing test. The results will show if you have a reversible breathing problem like asthma.

- You will be given medicine called albuterol to inhale that works to open your lungs.
- Although rare, the medication can briefly cause a fast heart beat, chest pain, nervousness or tremor.
- The Food and Drug Administration (FDA) could review your personal survey data since they monitor the safety of all medications. The FDA has approved the use of this medication for people aged 4 years and older.
- You will be asked to do another breathing test.
- The doctor will ask you questions about your health. The breathing medicine will not be given to people with certain types of health problems. If you have any of these health problems, you will not be asked to take the medicine or have another breathing test.
- Participation is voluntary.

I have read the information above. I freely choose /permit my child/ to have the medication and another lung function test.

\_\_\_\_\_  
Signature of the participant (aged 6 years and older)

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature of the parent or guardian  
(required if the participant is a minor)

\_\_\_\_\_  
Date

Print the name  
of the participant:

\_\_\_\_\_ - \_\_\_\_\_ - \_\_\_\_\_  
First Middle Last

Name of staff member present when this form was signed: \_\_\_\_\_

**B. REPEAT SPIROMETRY WITH PLACEBO INFORMED CONSENT  
NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY  
LUNG FUNCTION TESTING WITH PLACEBO**

The NHANES survey is asking you to inhale a placebo and do another breathing test.

- The placebo is air without any medication delivered through an inhaler.
- The purpose is to see how well our doctor can teach participants about inhaler use. We are also learning how long it takes.
- You will be asked to inhale the placebo through a spacer device. Then you will be asked to do another breathing test.
- Before you are offered the placebo, the doctor will ask you questions about your health. These questions are designed to protect people who might take breathing medicines. If you have any of these health problems, you will not be asked to take the placebo or have another breathing test.
- Your participation is voluntary.

I have read the information above. I freely choose /permit my child/ to have the placebo and another lung function test.

\_\_\_\_\_  
Signature of the participant (aged 6 years and older)

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature of the parent or guardian  
(required if the participant is a minor)

\_\_\_\_\_  
Date

Print the name  
of the participant:

\_\_\_\_\_ - \_\_\_\_\_ - \_\_\_\_\_  
First Middle Last

Name of staff member present when this form was signed: \_\_\_\_\_

## Appendix B

### Medication Listings for MEC Physician's Drug Review and Bronchodilator Type Evaluation

Potassium Lowering Drugs:

These include the Loop Diuretics, Thiazides and Derivatives.

Loop Diuretics:

Bumetanide  
Ethacrynate Sodium  
Ethacrynic Acid  
Torsemide

Thiazide Diuretics and Derivatives:

Bendroflumethiazide  
Chlorothiazide  
Chlorthalidone  
Hydrochlorothiazide  
Hydroflumethiazide  
Indapamide  
Methyclothiazide  
Metolazone  
Polythiazide,  
Trichlormethiazide

Potassium Raising Drugs:

These include Potassium Supplements, Angiotensin Converting Enzyme Inhibitors, Angiotensin II Receptor Antagonists, Potassium Sparing Diuretics, and Combination drugs of which contain a potassium raising drug:

Angiotensin Converting Enzyme Inhibitors:

Benazepril HCl  
Captopril  
Enalapril Maleate  
Fosinopril Sodium  
Lisinopril  
Moexipril HCl  
Perindopril Erbumine  
Quinapril HCl  
Ramipril  
Trandolapril

Angiotensin II Receptor Antagonists

Candesartan Cilexetil  
Eprosartan Mesylate  
Irbesartan  
Losartan Potassium  
Olmesartan Medoxomil  
Telmisartan, Valsartan



Potassium Sparing Diuretics:

Amiloride  
Acetazolamide  
Dichlorphenamide  
Methazolamide  
Sironolactone  
Tiamterine

Combination Diuretics Designed to be Potassium Sparing:

Dyazide  
Maxizide  
Moduretic

Tricyclic Antidepressants:

<u>Generic Name</u>	<u>Brand Name</u>
Amoxapine	Asendin
Amitriptyline	Elavil
Clomipramine HCl	Anafranil
Desipramine	Pertofrane
Doxepin	Sinequan
Imipramine	Norfranil
Nefazodone	Nefazodone
Nortriptyline	Pamelor
Protriptyline	Vivactil
Trimipramine	Surmontil

Anticonvulsants:

Carbamazepine  
Clonazepam  
Divalproex Sodium EC  
Diazepam  
Ethosuximide  
Ethotoin  
Felbamate  
Fosphenytoin Sodium  
Gabapentin  
Levetiracetam  
Lamotrigine  
Methsuximide  
Oxcarbazepine  
Phenacemide  
Phenytoin  
Primidone  
Tiagabine HCl  
Topiramate  
Valproic Acid  
Zonisamide

Long Acting  $\beta$ 2-Agonist Bronchodilators:

Advair  
Advair Diskus (combines Serevent and an anti-inflammatory drug)  
Serevent  
Serevent discus (salmeterol)  
Foradil

(These drugs take longer to begin to work, but their benefits last longer, even up to 12 hours. Serevent and Foradil are the only inhaled, long-acting beta 2-agonists available. They are used twice a day to maintain open airways for long term-control. Serevent and Foradil are available in dry powder inhaler (DPI) form.)

Short Acting  $\beta$ 2-Agonist Bronchodilators:

Albuterol (Proventil HFA, Ventolin HFA, Accuneb)  
Alupent  
Combivent (combines a beta 2-agonist and an anticholinergic)  
Duoneb (combines a beta 2-agonist and an anticholinergic)  
Maxair  
Xopenex  
Bitolterol Mesylate  
Clenbuterol HCl  
Formoterol Fumarate  
Isoetharine HCl Nebulizer Solution  
Isoproterenol HCl  
Levalbuterol HCl Nebulizer Solution  
Levalbuterol HCl Nebulizer Solution  
Metaproterenol Sulfate  
Pirbuterol  
Terbutaline Sulfate

Short Acting Anti-Cholinergic Inhalers:

Atrovent (ipratropium)  
Tiotropium (Spiriva)

(Short-acting beta 2-agonists or anticholinergics are also called “quick acting,” “reliever,” or “rescue” medications because they relieve asthma symptoms very quickly by opening the airways. These inhalers are the best for treating sudden and severe or new asthma symptoms. They work within 20 minutes and last four to six hours).

MAO Inhibitors:

Isocarboxazid (Marplan)  
Phenelzine Sulfate (Nardil)  
Tranlycypromine Sulfate (Parnate)

Class I Antiarrhythmics:

Amiodarone (Cordarone)  
Bretylium (Bretylol)  
Bretylol (Bretylium)  
Cardioquin (Quinidine, Quinalan, Quinidex, Quinaglute)  
Cordarone (Amiodarone)  
Disopyramide (Norpace)  
Dofetilide  
Enkaid (Encainide)  
Ethmozine (Moricizine)  
Flecainide (Tambocor)  
Ibutilide  
Lidocaine (Xylocaine, Xylocard)  
Mexiletine (Mexitil) Mexitil (Mexilitine)  
Moricizine (Ethmozine)  
Norpace (Disopyramide)  
Procainamide (Pronestyl, Procan SR)  
Procan SP (Procainamide, Pronestyl)  
Pronestyl (Procan SP, Procainamide)  
Propafenone (Rhythmol)  
Rhythmol (Propafenone)  
Tambocore (Flecainide)  
Tocainide (Tonocard)  
Tonocard (Tocainide)  
Quinaglute (Cardioquin, Quinidine, Quinora, Quinalan, Quinidex)  
Quinidine (Quinora, Quinalan, Cardioquin, Quinidex, Quinaglute)  
Quinalan (Quinora, Cardioquin, Quinidex, Quinaglute, Quinidine)  
Quinora (Quinidine, Quinalan, Cardioquin, Quinidex, Quinaglute)  
Xylocaine (Lidocaine, Xylocard)  
Xylocard (Lidocaine, Xylocaine)

**Long-acting Beta 2-agonists:**

- Advair, Advair Diskus (combines Serevent and an anti-inflammatory drug)
- Serevent, Serevent discus (salmeterol)
- Foradil

(These drugs take longer to begin to work, but their benefits last longer, even up to 12 hours. Serevent and Foradil are the only inhaled, long-acting beta 2-agonists available. They are used twice a day to maintain open airways for long term-control. Serevent and Foradil are available in dry powder inhaler (DPI) form.)

**Short-acting Beta 2-agonists include:**

- Albuterol (Proventil HFA, Ventolin HFA, Accuneb)
- Alupent
- Combivent (combines a beta 2-agonist and an anticholinergic, see below)
- Duoneb (combines a beta 2-agonist and an anticholinergic, see below)
- Maxair
- Xopenex

**Short-Acting Anti-Cholinergic Inhalers Include:**

- Atrovent (ipratropium)

(Short-acting beta 2-agonists or anticholinergics are also called “quick acting,” “reliever,” or “rescue” medications because they relieve asthma symptoms very quickly by opening the airways. These inhalers are the best for treating sudden and severe or new asthma symptoms. They work within 20 minutes and last 4 to 6 hours.)

## Appendix C

### Spirometry Review Screen

## BRONCHODILATOR COMPONENT, SPIROMETRY REVIEW SCREEN

Quality Code Box in the OMI Spirometry Results Review Screen

1	2	3	4	5	6
PEF Time	Low PEF	< 6 s	Plateau	Cough	Vext
Red	Red	Green	Green	Green	Green

Override Acceptable UnAcceptable Help

Reject Curve UnReject Curve Clear Overrides Set Cough Clear Cough

Enter Curve Comments Below OK

**Quality Code Box:** The results table contains a 6-item acceptability quality code box that is displayed to the right of the results for each trial. During the exam, the OMI/NIOSH software will automatically evaluate the quality of each curve. The HTs will only reject a curve in circumstances where it is believed that the software may not have recognized a defective curve—for example, the presence of a small progressive leak, or an undetected cough or extra breath being taken. Otherwise, the software will guide the HT as to how to achieve an acceptable and reproducible spirogram.

### **Box 1: PEF Time**

Indicates a slow start to the test; the time required to reach the peak of the flow-volume curve was too long. This is not a fatal error. The HT will coach the SP to blow harder and faster when this error occurs.

### **Box 2: Low PEF**

This stands for low peak expiratory flow. If the peak flow for a specific maneuver is more than 20% lower than the best peak flow recorded for that session, then the box will turn red. Sometimes a maneuver will have all green boxes and after a subsequent maneuver, box #2 for that maneuver may turn to red. In this instance the SP blasted harder on the latter maneuver. This is not a fatal error. The HT will coach the SP to blast the air out more forcefully.

**Box 3: < 6 S**

The SP failed to continue the maneuver for at least 6 seconds. The HT will coach the SP to keep blowing until told to stop. Note that the 6 second criterion applies to adults and adolescents. In young children, the standard is to expect them to continue for a minimum of 3 seconds (because young children typically empty their lungs much more quickly than adults).

**Box 4: Plateau**

A plateau in the volume-time curve is defined as no change (< 25 ml increase) in volume for at least 1 second at the end of the expiratory maneuver. Most healthy test subjects will reach an acceptable plateau. In cases of obstructive lung disease, a longer expiratory time is usually required to reach a plateau. Many persons with obstructive lung disease may not be able to reach a plateau at all. Therefore, failure to reach plateau is not a fatal quality control error.

<p><i>The two fatal error boxes:</i></p>
--

**Box 5: Cough**

The SP coughed during the first second of the maneuver. This invalidates the test. Coughing can artificially increase or decrease the FEV1.

**Box 6: Vext**

This refers to a high extrapolated volume. A high Vext occurs when there is hesitation or a slow start at the beginning of the maneuver. This will invalidate the test because it will make the FEV1 appear much smaller than it actually is.