



National Health and Nutrition Examination Survey (NHANES)

Respiratory Health ENO Procedures Manual



January 2008



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1. EXHALED NITRIC OXIDE OVERVIEW

1.1 Overview of the Exhaled Nitric Oxide Exam Component

Exhaled nitric oxide (ENO) provides a measure of airway inflammation, a factor in the causal pathway of asthma and possibly other lung diseases. A current estimate of the prevalence of asthma in the United States varies between 4-10 percent.^[1] Starting in 2007, NHANES will collect pulmonary function examination data to determine the prevalence of obstructive airway diseases in older children and adults. The new component, Respiratory Health (RH), will include an assessment of lung function testing, or spirometry, and a measurement of ENO. ENO is always performed before spirometry because spirometric maneuvers have been shown to transiently reduce exhaled NO levels.

The motivation for spirometry with bronchodilator and supplemental ENO testing is to evaluate airway inflammation among children and to help explain the unanticipated excess prevalence of undiagnosed pulmonary obstruction in the adult population that was previously identified in the NHANES III sample. Bronchodilator and ENO tests will allow improved estimation of asthma prevalence based on objective measurements and help analysts to discriminate asthmatics from otherwise healthy individuals who have episodes of wheezing.

Currently, there are no U.S. population-based estimates of ENO baseline levels for normal subjects or for those persons with asthma and chronic obstructive pulmonary disease (COPD). The goals of this study are to: (1) provide the first U.S. population-based estimates of ENO baseline levels for normal subjects as well as those with asthma and COPD; (2) allow estimation of the association of a marker for airway inflammation with other physical measurements of lung capacity and biologic correlates; (3) define the prevalence of undiagnosed airway inflammation; and (4) permit retrospective selection of a panel of questions and measures that would provide efficient screening for potentially treatable airflow limitation and obstruction in the general population.

All participants aged 6-79 years will be eligible to participate in the ENO component. There are safety exclusions for this test. ENO will be part of the Respiratory Health (RH), which will include Spirometry. Please refer to the *Spirometry Procedures Manual* for further details.

1.2 Exhaled Nitric Oxide (ENO)

Evaluation of airway inflammation, a precursor of asthma symptoms, is important in the investigation of underlying respiratory disease. ENO is a noninvasive marker of airway inflammation.^[2] Nitric Oxide (NO) is normally produced and detected in the exhaled breath from the respiratory tract where it plays important regulatory functions.^[3-6] NO concentrations often increase during the so-called late-phase reactions following exposures to an allergen, a phase that is characterized by the migration of inflammatory cells to the airways mucosa. There appears to be an association between NO in exhaled air and the number of eosinophils in sputum.

Data suggest that there are large differences in ENO between asthmatics and healthy controls; for example, ENO levels are 3 to 10 fold greater in asthmatics. These differences make the method sufficiently sensitive to detect cases of either mild asthma or incipient asthma, which are usually symptom-free. In addition, measurement of airway inflammation may reveal diseased airways not detectable by symptoms, clinical examination, questionnaire, baseline spirometry, or bronchodilator studies. In clinical studies, airway inflammation has been measured in secretions and biopsies obtained during bronchoscopy, but these methods are too invasive and not appropriate for use in epidemiological evaluations. NHANES is therefore proposing ENO testing to fulfill this need in data collection.

ENO has been previously measured in large epidemiological studies,^[7] but not on a national level. Data on ENO reference distributions for the U.S. general population are not currently available. For both ENO measurements and spirometry, standard protocols for testing have been established by the European Respiratory Society^[8] and the American Thoracic Society.^[9] The ENO measurement has been demonstrated to work well in conjunction with airway responsiveness tests to discriminate asthmatics.^[10]

1.3 ENO Measurements

The NIOX MINO™ monitor will be used to measure Fractional Exhaled Nitric Oxide (Fe_{NO}) in exhaled breath in NHANES participants. This device follows, in all essential aspects, the American Thoracic Society and European Respiratory Society 2005 equipment recommendations for measurement of exhaled nitric oxide. The test requires two acceptable or successful maneuvers, which will be averaged.

The ENO exhalation technique has several components, each of which is performed for a specific reason. In the first phase, the participant inhales air through the filter to fill up the lungs. The filter provides NO-free air for the subject to breathe, and therefore eliminates any background level of ENO in the room air from affecting the ENO testing. When the subject exhales, they must be coached to push out air at a standard rate. This is necessary because measured ENO levels are rate-dependent. For example, with a fixed amount of ENO in the bronchial tubes, a person breathing out forcefully will have a comparatively lower measured ENO level than a person breathing out slowly. The NIOX-MINO manufacturer has therefore designed the analyzer to accept test results only if the air flow rates are held constant at 50 ml per second. This way all participants have ENO measurements taken at a constant air flow rate, and their test results are strictly comparable.

The reason for requiring a 10-second exhalation for adults (6 seconds for children) is twofold. First, it is known that the nasal passages have much higher NO levels than do the bronchial tree or the lungs. Because nasal NO is highest in the first 2 seconds of expiration, the NIOX-MINO sensor will wait for 2 to 3 seconds before beginning to take readings. Following that, the NIOX-MINO sensor unit will look for a steady-state plateau in the NO measurements that lasts at least 2 seconds, taking that value as the reported measurement displayed on the NIOX-MINO display screen.

1.4 References

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4. Kharitonov, S.A., and Barnes, P.J. (2001). Exhaled markers of pulmonary disease. *American Journal of Respiratory and Critical Care Medicine*; 163(7):1693-1722.
5. Bates, C.A., and Silkoff, P.E. (2003). Exhaled nitric oxide in asthma: From bench to bedside. *Journal of Allergy and Clinical Immunology*; 111(2):256-262.
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8. Kharitonov, S., Alving, K., and Barnes, P.J. (1997). Exhaled and nasal nitric oxide measurements: Recommendations. *European Respiratory Journal*; 10(7):1683-1693.
9. American Thoracic Society. (1999). Recommendations for standardized procedures for the online and off-line measurement of exhaled lower respiratory nitric oxide and nasal nitric oxide in adults and children-1999. This official statement of the American Thoracic Society was adopted by the ATS Board of Directors, July 1999. *Am J Respir Crit Care Med*; 160(6):2104-2117.
10. Verleden, G.M., Dupont, L.J., Verpeut, A.C., and Demedts, M.G. (1999). The effect of cigarette smoking on exhaled nitric oxide in mild steroid-naïve asthmatics. *Chest*; 116(1):59-64.

2. EQUIPMENT AND SUPPLIES

The two components of Respiratory Health, Exhaled Nitric Oxide (ENO) testing and Spirometry, are conducted in an examination room in trailer 1 of the MEC. This chapter describes the ENO equipment and supplies and also explains the procedures for setup, operation, and packup of the ENO component.

2.1 List of Equipment and Supplies

A complete list of the equipment and supplies for this component is provided as follows:

Equipment	Supplies
■ NIOX MINO™ Monitor	■ NIOX™ Filters
■ NIOX MINO™ Sensor	■ Alcohol Preps
■ AC/DC Adapter	■ Tissues
■ Extension cord	■ Marker
■ Mesh bag	
■ Standard Test Card (Blue)	
■ 6-Second Special Test Card (Orange)	
■ NIOX™ QC Sensor	
■ Special NIOX™ QC Filter	
■ Mechanical counter	
■ Stadiometer	
■ Scale	
■ Stool	
■ Container for filters	
■ Mirror	

At the beginning and end of each stand, the health technologist will inventory all component-specific equipment and supplies. Supplies ordered from the warehouse by the previous team should be on site when the next examination staff arrives at the MEC. Technologists will check all newly received supplies against the associated packaging slips before incorporating them into the existing inventory. After reconciling the supplies, the technologist will stock the ENO exam room and store additional supplies in the MEC belly compartment. Any needed items should be noted on the inventory sheet, reported to the chief technologist and MEC manager, and documented in the Unusual Field Occurrence or UFO system. (Refer to *UFO Utility Manual* for details.)

2.2 Description of Equipment and Supplies

2.2.1 Equipment

- **NIOX MINO™ Monitor**

Used to measure Fractional Exhaled Nitric Oxide (Fe_{NO}) in a person's exhaled breath, this device is manufactured by Aerocrine Corp. The NIOX MINO™ monitor is currently in routine clinical use in Europe, although it is not yet approved by the FDA for use in the U.S. It is currently waiting FDA approval and thus will be used in NHANES for research purposes only. The NIOX MINO™ has a shelf life of 3.5 years from the date of manufacture or 1,500 measurements, whichever comes first. Two monitors will be housed per MEC, one for use and the other as a backup.

- **NIOX MINO™ Sensor**

Used to operate the NIOX MINO™ monitor, the sensor is located at the bottom of the monitor. **Important:** The sensors are extremely delicate and must always be handled with extreme care and must be in place before connecting the AC/DC adapter. Sensors used in NHANES will allow up to 300 tests and must be changed when 30 measurements remain. The maximum sensor cartridge shelf life (regardless of the amount of use) is 1 year from date of manufacture.

- **AC/DC Adapter**

The AC/DC adapter is the main power supply to the NIOX MINO™ monitor. It consists of the AC power plug at one end and a plastic modular connector plug at the other end. The modular connector plug is inserted into the lower right side of the monitor while the AC power plug is connected to the extension cord outlet as explained below.

- **Extension Cord**

An extension cord will be used with the AC/DC adapter. The extension cord must always be plugged into a power strip that is plugged into the electric outlet on the wall. The extension should never be plugged directly to the wall outlet.

- **Mesh Bag**

A mesh bag with a padded strap will be used to hold the NIOX MINO™ monitor. This will prevent the device from falling from the participant's hands during testing.

- **Test Cards**

Two different test cards are used for storing data: a standard test card (blue) and a 6-second special test card (orange). Although each card will store up to 2,000 measurements, new cards will be used at every stand.

 - Standard Test Card (Blue)**

 - This card is used for all participants 130 cm in height. The use of the card requires a 10-second exhalation.

 - 6-Second Special Test Card (Orange)**

 - This card is used for participants with heights less than 130 cm. Participants at this height may have difficulty with the longer exhalation time or a deep inhalation. The use of the card requires a 6-second exhalation.

- **NIOX™ QC Sensor**

The NIOX™ QC sensor will be used during weekly ENO QC checks. This makes it possible to verify two simulated levels of exhaled NO at 15 and 75 ppb. This permits verification that the NIOX-MINO™ monitor itself is functioning properly.

- **Special NIOX™ QC Filter**

The Special NIOX™ QC filter will be used during weekly ENO QC checks. The special QC filter allows the NIOX MINO™ monitor to check a “blank” sample using exhaled breath (zero ppb NO).

- **Container for Filters**

A plastic container will be available to hold unused filters.

- **Mechanical Counter**

A mechanical counter will be kept in the exam room to assist in counting the number of ENO trials conducted per participant.

- **Stadiometer**

A portable stadiometer will be used to measure the height of the participants when this data has not been previously captured in the MEC. Refer to Chapter 3, Section 3.4, Height and Weight Data Collection.

- **Scale**

A scale will be used to measure the SP's weight when this data has not been previously captured in the MEC. Refer to Chapter 3, Section 3.4, Height and Weight Data Collection.

- **Stool**

A stool without wheels will be kept in the ENO room. To promote the best results, participants should always perform the ENO testing in a sitting position, if possible.

- **Mirror**

A full-length mirror will be adhered to the door in the room to assist in the administration of the exam.

2.2.2 Supplies

- **NIOX™ Filter**

A disposable filter fits onto the monitor and will be used at the beginning of each exam. After the exam is completed, the filter is then discarded into the wastebasket.

- **Alcohol Preps**

Alcohol preps will be used to clean the outside perimeter of the monitor. It will be cleaned only in the area where the participants would generally place their hands on the equipment. **Important: NEVER** attempt to clean the area where the sensor cartridge is attached on the bottom of the device, as this may damage the sensor unit.

- **Tissues**

Tissues should be readily available in the room during the exam.

- **Marker**

A Sharpie™ marker will be used to label the blue test card and the orange test card. Each card will be labeled with the stand number and date the card is installed.

2.3 Equipment Setup at Start of Stand

The following procedures describe how to set up the ENO equipment and supplies at the start of stand.

2.3.1 Equipment Setup Procedures

1. Remove the **NIOX MINO™ monitor** from its storage bag;
2. Place the **NIOX MINO™ sensor** in the device; see Section 2.4.2 for instructions;
3. Insert the plastic modular connector plug of the **AC/DC adapter** into the NIOX MINO™ monitor;
4. Plug the AC/DC adapter into the **extension cord** and then into its own power strip or wall outlet. Do NOT plug the machine in a power strip with other equipment;
5. Let monitor warm up (up to 30 minutes);
6. Place the NIOX MINO™ monitor in the **mesh bag**;
7. Label the **blue test card** with stand number and date and place into the NIOX MINO™ monitor;
8. Label the **orange test card** with stand number and date and place it in the container;
9. Unpack the backup **NIOX MINO™ monitor** to conduct SOS tests;
10. Turn on the computer and open RH application;
11. Unpack the **stadiometer**, insert the column in the base plate, and place this against the exam room wall opposite the door;
12. Unpack the **scale** and place it on the floor;
13. Place the **mechanical counter** on the counter top;
14. Unpack the **NIOX™ QC sensor** and Special NIOX™ **QC filter** and place them on the top shelf of the room;
15. Place the **stool** in the room; and
16. Ensure that a **wastebasket** is available in the exam room.

2.3.2 **Supplies Setup**

1. Fill the designated container with NIOX™ **filters** and make them accessible in the room;
2. Ensure that a box of **tissues** is available in the room; and
3. Check that **alcohol preps** and a **marker** are available.

2.4 **Equipment Care and Maintenance**

2.4.1 **NIOX MINO™ Monitor**

For infection control purposes, the NIOX MINO™ monitor must be cleaned weekly.

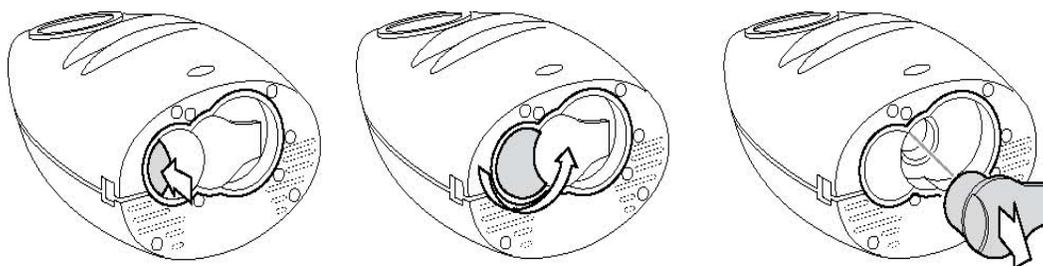
To clean the device:

1. Remove the NIOX MINO™ monitor from the mesh bag;
2. Unplug the AC adapter plug from the extension cord;
3. Remove the plastic modular connector plug from the device;
4. Wipe the outside perimeter of the device; only the areas where the participants generally place their hands; and
5. Do not wipe the bottom part of the device where the sensor is located.

2.4.2 NIOX MINO™ Sensor

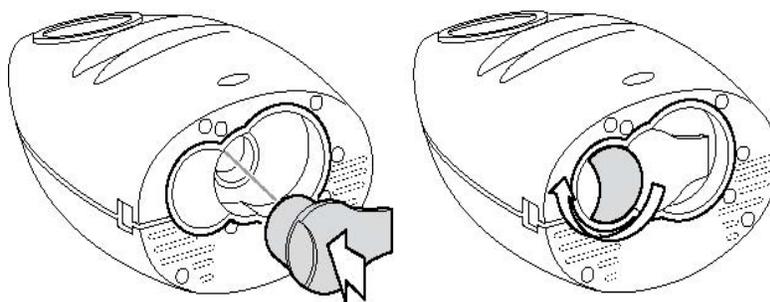
Sensors must be changed when the number of measurements displayed on the NIOX MINO™ monitor is at or before 30 measurements. To change sensors, make sure the AC/DC adapter is disconnected before the sensor exchange. Be careful when opening the sensor can. The inside of the opening has sharp edges. Follow these instructions:

Press and hold the blue part... ..while turning the orange part.. Remove the grey sensor.



Insert the new sensor.

Turn back the orange part until locked.



After the sensor is exchanged, place the used sensor in the sensor box labeled “Used.” It might take up to 30 minutes for the NIOX MINO™ monitor to warm up.

2.4.3 Test Cards

1. Keep the cards in the plastic storage container.

2.5 Equipment Pickup at End of Stand

At the end of the stand, follow the procedures listed below to pack up the NIOX MINO™ equipment for travel to the next stand.

2.5.1 Equipment Pickup Procedures

1. Retrieve the NIOX MINO™ storage bag;
2. Disconnect the NIOX MINO™ **AC/DC adapter cable** from the **extension cord**. Remove the extension cord from the power strip and then the power strip from the electrical outlet;
3. Unplug the plastic modular connector plug from the device;
4. Remove the **sensor** from the NIOX MINO™ monitor and place the sensor in the sensor box and ship all sensors (used and not used) to Westat;
5. Place the **NIOX MINO™ monitor** in the NIOX MINO™ storage bag;
6. Remove **test card** from the monitor;
7. Place **test cards (orange and blue)** in an envelope and ship to Westat;
8. Pack the **NIOX™ QC sensor** and **Special NIOX™ QC filter** in its box;
9. Pack the **mechanical counter**;
10. Remove the **stadiometer** column from the base plate and pack in its storage case/box;
11. Pack the **scale** from the room;
12. Ensure that the **filter container** is empty;
13. Leave the **stool** in the exam room; and
14. Discard any trash in the **wastebasket**.

2.5.2 Supplies Pickup

Pack the following exam supplies in the storage container: unused **filters, tissue, alcohol preps, and markers**.

3. EXAMINATION PROTOCOL

The accuracy of the ENO examination largely depends on a coordinated effort exerted by the examinee and the conscientiousness of the technologist. Consequently, it is crucial that the examination protocol be observed consistently, and that the examinee is prepared and “coached” for this examination. For most participants, two tests will be administered, although in approximately 20 percent of the examinees, additional tests (up to four) may be necessary. Each participant will be given ten attempts to achieve the number of successful tests required.

Note that while this protocol describes the exhaled nitric oxide examination, questions related to spirometry are interspersed between testing periods for the purpose of time efficiency.

3.1 Eligibility Criteria for ENO Component

Examinees aged 6-79 years are eligible for the ENO component. There are two safety exclusion questions for this exam. In addition, a set of questions are included in the component solely to support data analysis and interpretation. See Section 3.5.5 for a list of questions.

3.2 ENO Pre-examination Procedures

If possible, prepare the room for the examination before the participant enters the room. Confirm that all supplies needed for the exam are available and accessible: filters, test cards, and tissues. Introduce yourself when the participant enters the room and ask him or her to sit down in the stool. Use the following suggestive script:

“In this room we will conduct two tests. The first test will measure the level of nitric oxide in your breath using this machine. The second exam will be a lung function test and will be done with this machine. I will explain them in more detail as we go along but let me ask you a few questions before we start.”

Open the Respiratory Health (RH) component in ISIS and log onto the system. Wand the participant’s identification bracelet or else type in the participant’s ID number on the Sample Person Pickup screen (Exhibit 3-1) to log the participant into the component. Verify that the correct participant

name appears on the Sample Person Pickup screen and click “OK” to initiate the component. All Sample Person Pickup screen data is preloaded by ISIS, and you should not attempt to edit or change any displayed information. If the information ISIS displays appears incorrect, contact the MEC manager for assistance.

Exhibit 3-1. Sample Person Pickup screen

The screenshot shows a window titled "Sample Person Pickup". At the top, there are two fields: "Sample Person ID:" with the value "245515" and "Sample Person Select:" with a dropdown menu showing "245515 - JUNE". Below these is a larger form area containing several fields: "Last Name:" with "JUNE", "First Name:" with "ERIC", "Middle Name:" (empty), "Date of Birth:" with "6/28/1980", "Gender:" with "Male", and "Age at Interview:" with "24". At the bottom of this area is a "Special Considerations:" field with a scrollable text area. At the very bottom of the window are three buttons: "Ok", "Cancel", and "Message".

3.3 Safety Exclusion Questions

The first section of the ENO examination consists of asking two safety exclusion questions to all examinees. To view the individual screen shots of each question, see Appendix A. The questions are listed below:

ENQ010: {Do you/Does SP} currently have a breathing problem that requires {you/him/her} to use supplemental oxygen during the day? (This is air stored in a tank that you use to help you breathe. Do not include night treatments for sleep apnea.)

ENQ020: {Do you/Does SP} now have any pain or physical problem that may prevent {you/him/her} from taking a deep breath and exhaling forcefully?

Examinees will be excluded from the ENO exam and the Spirometry exam if they answer positively to any of the safety exclusion questions. The exam will end and the ENO End of Subsection, will be coded as “Not Done” with “Safety Exclusion” pre-filled in the comment section. See Exhibit 3-2. Click “next” and the screen will have a message stating that “SP is ineligible for Spirometry due to identified safety exclusion.” It will then take you to the Spirometry End of Subsection, coded as “Not Done” with “Safety Exclusion” pre-filled in the comment. The last screen will be the End of Exam screen. See Exhibit 3-3.

Exhibit 3-2. ENO End of Subsection

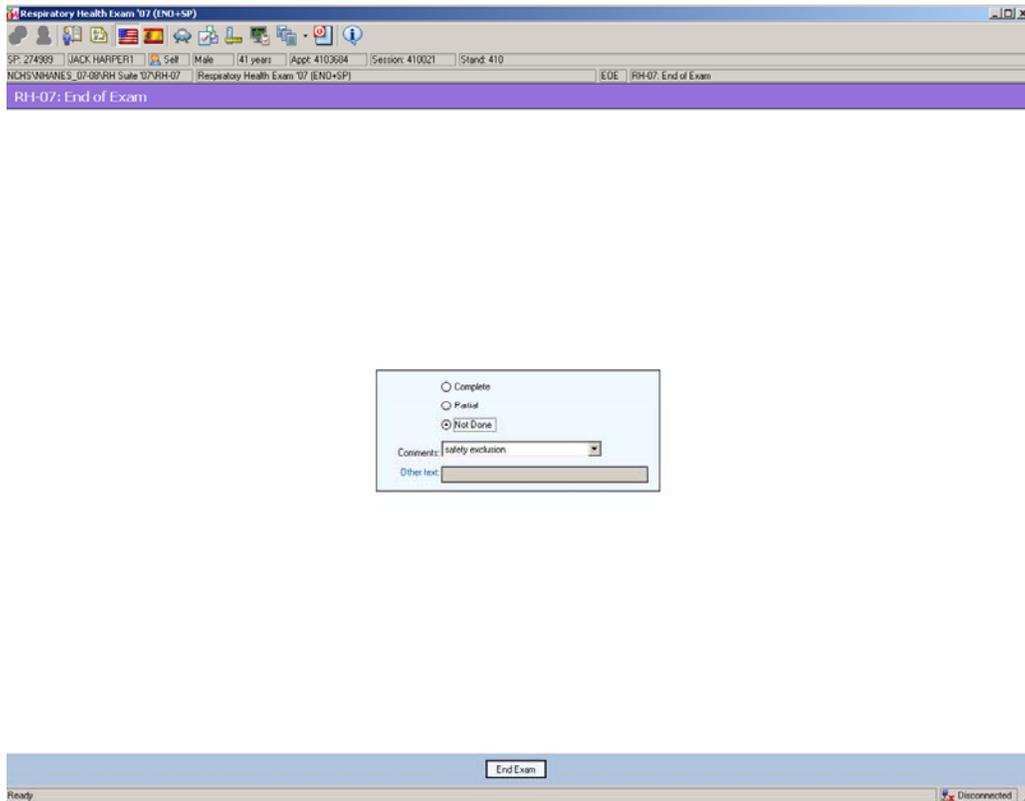
ExhaledNitrousOxide: End of Subsection

Complete
 Partial
 Not Done

Comments: Safety exclusion
Other text:

Begin Previous Next End

Exhibit 3-3. End of Exam



Alternatively if the technologist records “No” to any of the safety exclusion questions, the application will proceed with the exam.

3.4 Height and Weight Data Collection

After the safety exclusion questions are answered, it will prompt you to collect the participant’s height and weight (see Exhibit 3-4 and 3-5). While height only is necessary for ENO to largely estimate lung capacity, both height and weight are used for the calculation of spirometry reference values.

Exhibit 3-4. Participant height screen

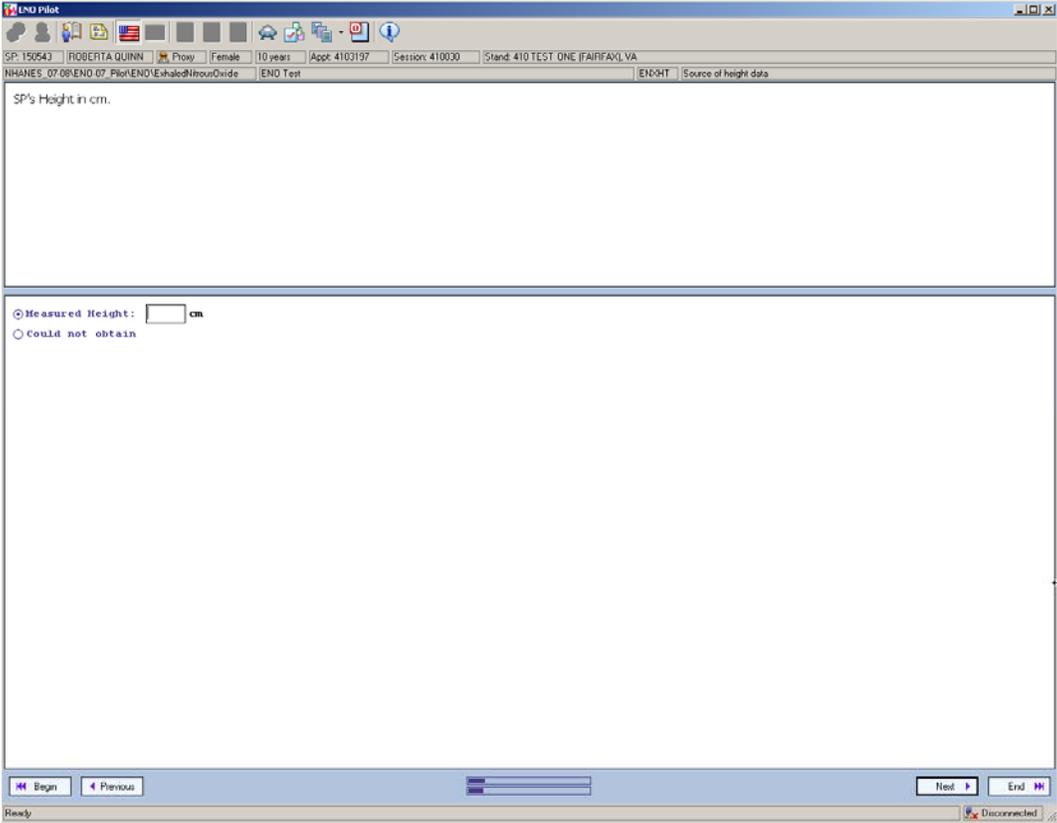
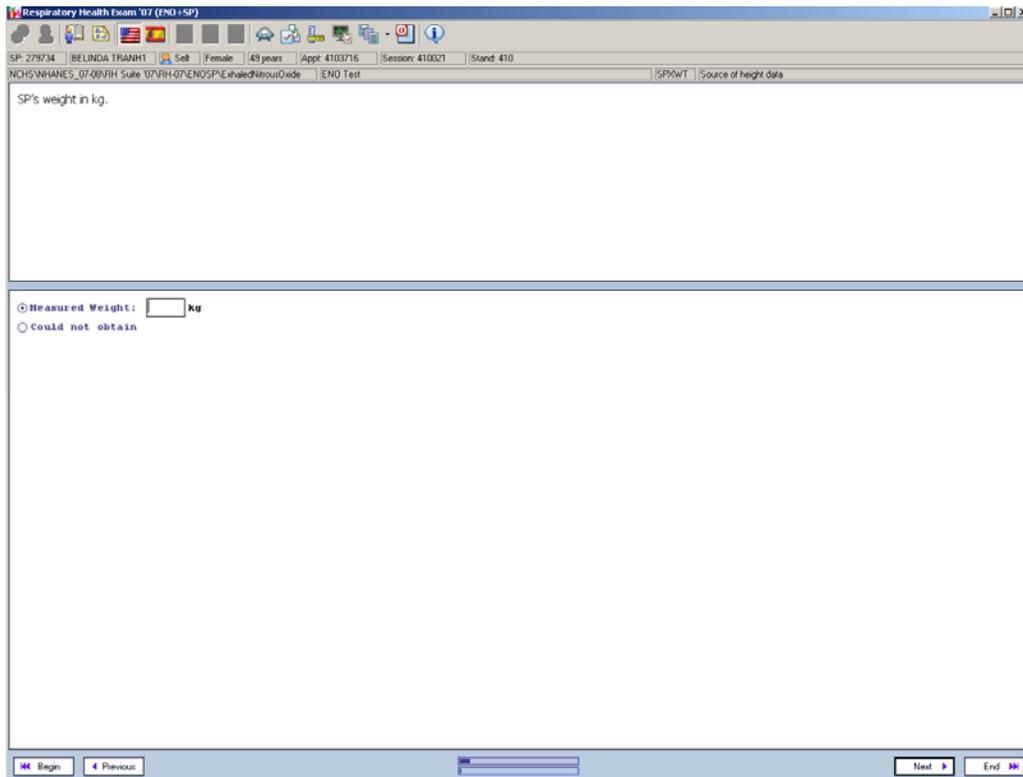


Exhibit 3-5. Participant weight screen



If height or weight was obtained before the participant was assigned to ENO (i.e., during either the anthropometry or DXA components), ISIS will automatically import this data into the ENO component, and the height or weight screen will appear completed. You will then continue the examination.

In the event that height or weight does not already appear on the screen, the technologist will measure and record the participant's height in centimeters and weight in kilograms using the stadiometer and scale in the room.

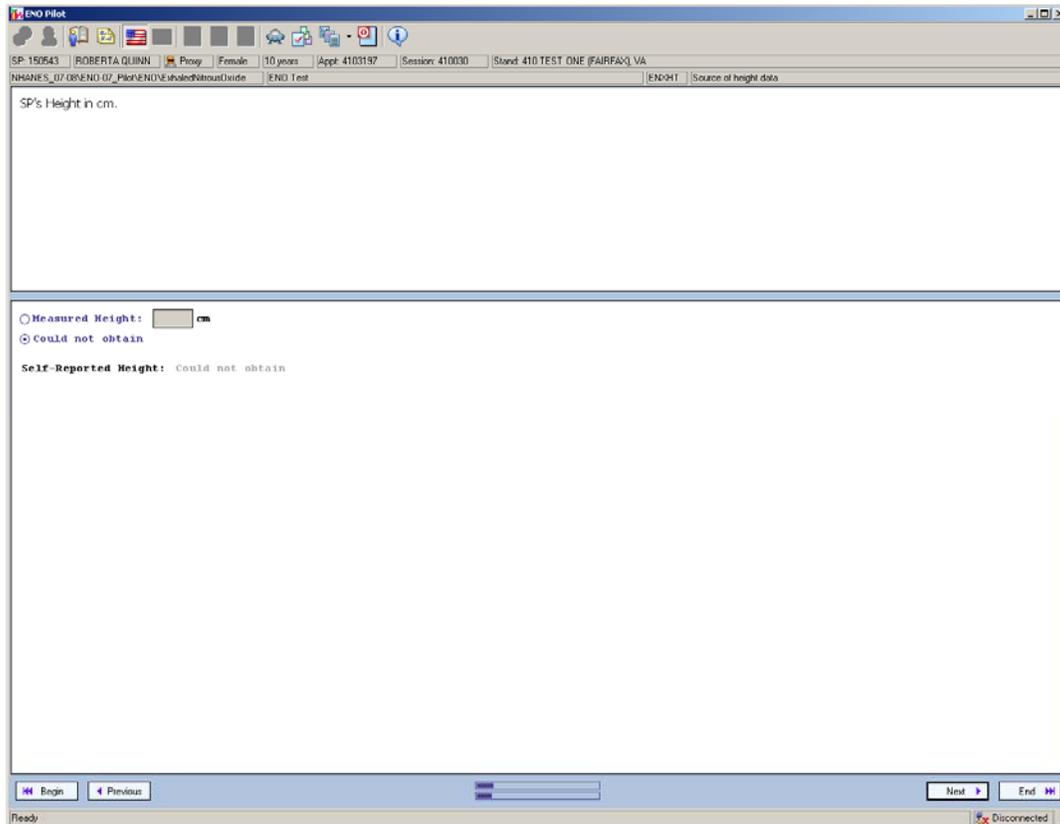
If the participant refuses or for some reason the technologist cannot obtain the participant's height or weight in the ENO component, click the "Could Not Obtain" radio button on the screen. This will trigger ISIS to import the corresponding self-reported data from the household interview into the ENO component. For example, Exhibit 3-6 shows height data imported from the household interview.

Exhibit 3-6. Height data from household interview screen

The screenshot displays the ENO Pilot software interface. At the top, a status bar shows the subject name "MICHAEL DREW PARKER", sex "Male", age "52 years", and session information. Below this, a large text area contains the prompt "SP's Height in cm.". Underneath, there are three radio button options: "Measured Height:" (unselected), "Could not obtain" (selected), and "Self-Reported Height:" (unselected). The "Self-Reported Height:" option has a text input field containing the value "175.3" followed by "cm". At the bottom of the window, there are navigation buttons: "Begin", "Previous", "Next", and "End".

However, if no data are available from the household interview, then the software will display “Could not obtain” beside the self-reported data label. Exhibit 3-7 shows this example for height data.

Exhibit 3-7. Could not obtain height data screen

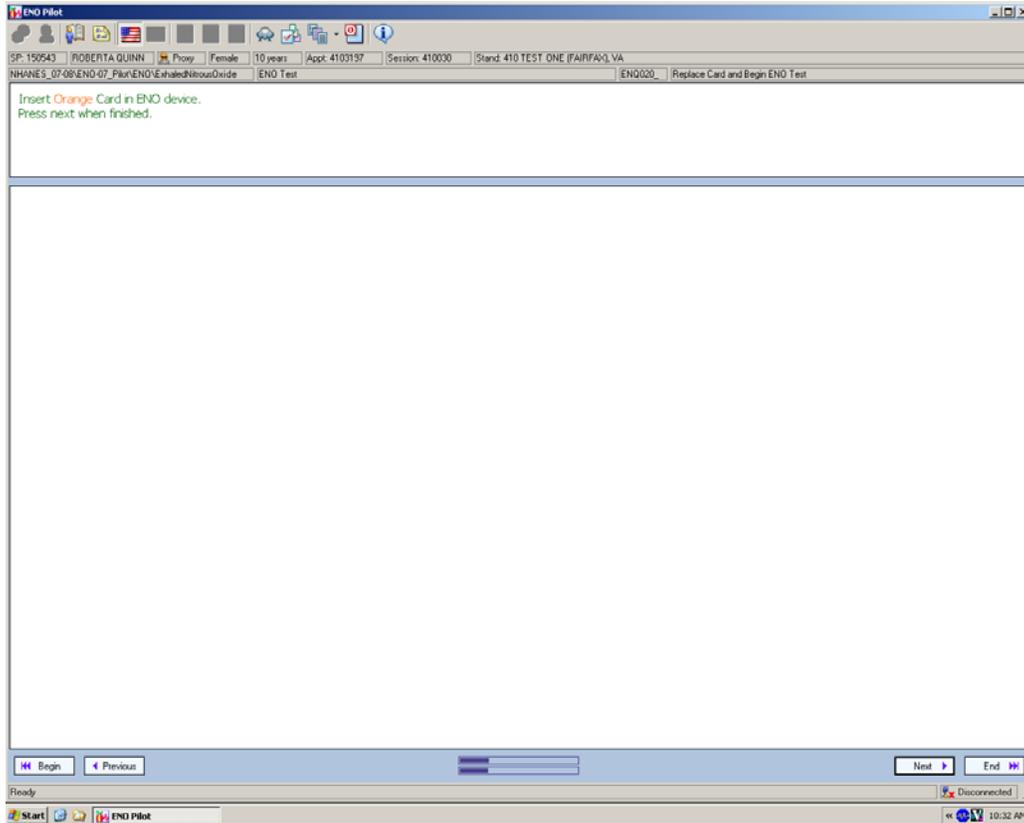


Finally, the component software will end the examination altogether if the height or weight data is ultimately missing. This is because ENO cannot be performed and interpreted without height and weight data, which are essential to the calculation of normal predicted values for the participant.

3.4.1 Test Cards

Two test cards are available to capture the ENO measurement data based on height of the participant. The blue standard test card, the default card, is used for participants 130 cm (4'3") and taller and requires an exhalation of 10 seconds. The orange 6-second special test card is used for participants (mostly children) with heights less than 130 cm and who may be unable to sustain a longer exhalation time or deep inhalation. The blue test card should be inserted in the NIOX MINO™ monitor at all times unless it is replaced with the orange test card. ISIS will instruct you about replacing the different cards based on height of the participants. See Exhibit 3-8.

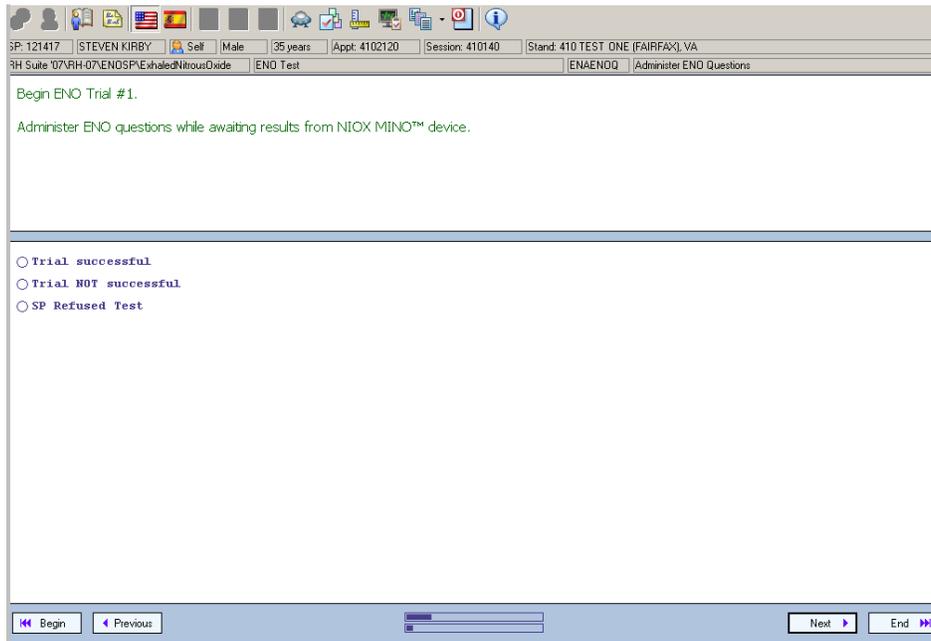
Exhibit 3-8. Insert orange card screen



3.5 ENO Examination Procedures

After the height and weight have been entered, the next screen will prompt you to “Begin ENO trial #1.” See Exhibit 3-9.

Exhibit 3-9. Begin ENO trial #1



At this point introduce the ENO test. Use the following suggestive script:

“We would like to measure the nitric oxide level in your breath using this device. Nitric oxide is a normal part of what you breathe. First you will face the mirror. Empty your lungs by breathing away from the machine. Then put your mouth over the new filter and seal your lips tightly around it. Take a deep breath until you fill up your lungs and then breathe out at a normal rate through the filter.”

Have the digital counter within reach to assist on counting the number of attempts it takes to achieve a successful trial.

3.5.1 Summary of Flow of Testing Procedures

1. Follow the prompts from the ENO application to access testing screens.
2. Make sure the proper card is in the device.
3. Introduce the ENO test.
4. Demonstrate test display screen including sounds and use of mirror.
5. Prepare NIOX MINO™ monitor.

6. Initiate test.
7. Continue coaching until successful test is conducted.
8. Administer ENO-related questions during Test #1 waiting period.
9. Enter ENO Test #1 results.
10. Conduct ENO Test #2.
11. Administer Spirometry-related questions during Test #2 waiting period.
12. Enter ENO Test #2 results.
13. If needed, administer Test #3 and/or Test #4.
14. Exit ENO software and complete End of Subsection screens.

3.5.2 Instructions on Conducting the Test

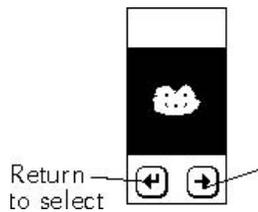
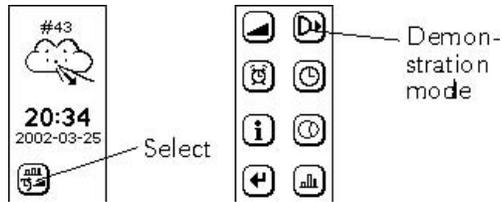
Open the bag with the plastic filter mouthpiece and using the plastic bag to grasp the filter, securely attach the filter to the NIOX MINO™ monitor. Ensure that the participant is sitting and facing the wall mirror in order to clearly see the image displayed on the monitor. If needed, have participant move closer to the mirror. Make sure the correct test card is inserted into the monitor

Briefly explain to the participant that he or she will empty his or her lungs, inhale deeply through the filter first, and then exhale slowly without removing his or her mouth from the unit. The SP will use the cloud pictures and sound cues to guide him or her through the exhalation, which will be 6 (orange card) or 10 (blue card) seconds.

Use the Demonstration mode in the NIOX MINO™ monitor to show the participant the different steps during the test with display of audiovisual feedback. While in the demo mode use the following suggestive script:

“When you breathe into the machine, you see the cloud getting bigger. Once the cloud is big, you can breathe out. As you breathe out, the machine will display a cloud that you will see in the mirror and you will hear a beeping sound. When the cloud is centered within the black box and you hear a constant sound, it means that you are breathing out at the right rate. When the cloud is under the black box and you hear a low-pitched sound, this means that you are breathing too slowly. When the cloud is above the black box and you hear a high-pitched sound, it means that you are breathing too hard.”

Touch the display screen to go to Demonstration mode. To move from screen to screen press the arrow key. To exit the Demonstration mode, press on the arrow key twice.



Inhalation: the cloud is growing during the inhalation sequence and the top light is turned off.



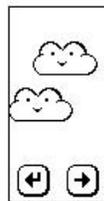
Correct Exhalation Pressure: the cloud is in a steady centered position, the top light is lit, and the audio emits a constant sound.



Too Weak Exhalation Pressure: the cloud is partly below the valid exhalation pressure area, the top light is flickering, and the audio emits a low intermittent sound.



Too Strong Exhalation Pressure: the cloud is partly above the valid exhalation pressure area, the top light is flickering, and the audio emits a high intermittent sound.



Measurement Processing: a scrolling image of clouds is shown during the analysis phase after a correct exhalation, and before a measurement value is shown.

3.5.3 Initiate Test

Prior to beginning the test, ensure that the participant is seated. Make sure the monitor is in the Ready for Measurement mode. Touch the smiling cloud on the NIOX MINO™ monitor. The screen will change to show the cloud with arrows pointing in and out of the cloud. The top blue light should be lit.

The top light is lit



Unit is ready for measurement

Please note that if the test is performed using the orange test card, two clouds with arrows pointing in and out should be displayed on the screen.

When the monitor is ready, begin the ENO test by having the participant first breathe out and then raise the NIOX MINO™ monitor to a position where he or she can place his or her mouth with a tight seal on the filter mouthpiece. When the SP takes a deep breath in through the mouthpiece filter he or she is simply breathing in air and nothing else. Then the SP will begin to breathe out.

Active coaching during each trial is essential to achieving a successful test. Face the participant and the monitor screen (or mirror) to assist with your coaching. When the trial is not successful, the NIOX MINO™ monitor quickly cuts off. Reset the monitor by touching the display screen and begin again coaching the examinee with the audio and visual cues. It is not unusual for the participant to need several tries before he or she has a successful test. Be patient and calm so as to minimize SP's frustration when he or she is having difficulty. Use the mechanical counter to keep track of the number of trials attempted. If needed, provide short breaks in between maneuvers, for some participants might become lightheaded.

Each participant is given **10 attempts** to achieve a successful trial. An attempt will be constituted when a participant inhales and exhales into the machine and the visual and auditory signals appear regardless of the outcome. In situations where instead of a result, the ENO machine produces an error message (E2101-2120), that maneuver will be **counted as an attempt**. The only exception to the 10 attempts rule will be in the case when an error message instead of a result appears on the 10th attempt. **One more attempt** will then be tried to achieve a successful ENO test; that is, 11 attempts will be tried. In addition, when the ENO machine is stabilizing or when spinning circles appear while trying to conduct the exam, it does not count as an attempt. However, even when a participant has a difficult time producing a successful trial, the 10 attempts rule will apply.

Observe to see if the participant does any breath holding at any time during the procedure. If this should occur, the test should be repeated. Breath-hold results in NO accumulation in the nasal cavity, lower airway, and probably in the oropharynx, which causes NO peaks in the exhalation profiles of NO versus time. For this reason, the use of breath hold is discouraged in the ENO standardized testing technique. Also observe to see that the participant does not remove his or her mouth from the filter during the exam.

3.5.4 Trial Successful or Not Successful

When the participant has completed the test successfully, ask the SP to let the monitor hang from his or her neck. On the “Begin ENO trial #1” screen (see Exhibit 3-10), click on “Trial successful,” “Trial NOT successful,” Or “SP refused test.” If the participant is unable to conduct a successful test after 10 attempts, click “Trial NOT successful” and it will prompt to “Administer Spirometry exclusion questions.” Once all the questions are answered, the next screen will ask you to “Enter total number of ENO attempts” and enter if a translator was used. It will take you to the “ENO: End of Subsection” screen, coded as “Not Done” with the pre-filled comment “SP failed test(s).” The next screen will prompt you to begin spirometry. See *Spirometry Procedures Manual*, Section 3.3, to begin the test. If a participant refuses the ENO test, the same procedure described will be followed; however, the test will be coded as “Not Done” with the pre-filled comment of “SP refused.”

If the participant is able to conduct a successful trial, click on “Trial Successful” and administer ENO questions while waiting for results.

3.5.5 ENO Questions

A series of questions will be asked while waiting for the first test results. These questions are included in the component solely to support data analysis and interpretation. Read the questions exactly as they appear on the screen. The questions will be administered to all age-eligible participants (aged 6-79 years) however there are age criteria for some of the questions vary as listed below. Examinees 12 and older will answer all of the questions for him or herself (except the smoking question), while the questions on steroid use and respiratory illness will be included in the proxy questions for all 6-11 year olds and generally asked prior to the exam to a parent or guardian. Questions answered during proxy will be grayed out. Table 3-1 summarizes the question items and applicable age ranges within each category.

Table 3-1 ENO questions

Screening item by category	Age range eligibility (years)
Smoked in the last hour	16-79
Exercised strenuously in the last hour	12-79
Had anything to eat or drink	12-79
Eaten nitric rich vegetables	12-79
Eaten nitric rich meats	12-79
Used oral or inhaled steroids	6-79
Had a respiratory illness in last 7 days	6-79

The complete questions for ENO are listed below. Response options for these questions are in the form of radio buttons for “Yes” and “No.” Also, the toolbar menu at the top of the screen contains response options for “Refused” and “Don’t Know.” To view the individual screen shots of each question, see Appendix B.

- ENQ.040 Within the **last hour** {have you/has SP} smoked a cigarette, cigar, pipe, or used any other tobacco product?
- ENQ.050 [Within the last hour] have you exercised strenuously?
- ENQ.060 [Within the last hour] have you had anything to eat or drink?
- ENQ.070 Within the last **three** hours have you eaten beets, broccoli, cabbage, celery, lettuce, spinach, or radishes?
- ENQ.080 Within the last **three** hours have you eaten bacon, ham, hot dogs, or smoked fish?

ENQ.090 Within the last two days {have you/has SP} used any oral or inhaled steroids? This list provides some examples (show hand card).

ENQ100 In the past 7 days, {have you/has SP} had a cough, cold, phlegm, runny nose, or other respiratory illness? Do not count allergies or hay fever.

3.5.6 Enter ENO Trial #1 Result

The wait time for results is 1 minute and 45 seconds. The Monitor screen will display clouds and countdown to zero.



Once results for ENO trial #1 are ready, the NIOX MINO™ monitor will beep and display the results. Enter the results for the trial (Exhibit 3-10). Possible values range from 5 to 300 ppb. The options for data entry are:

- **Enter Reading:** the application will prompt you to enter the results again in the next screen (Exhibit 3-11). If the entries do not match, it will prompt you to correct them.
- **<5pp:** no double entry needed.
- **>300 ppb:** no double entry needed.
- **Could not obtain:** no double entry needed.

Exhibit 3-10. Entry of ENO trial #1 screen

Respiratory Health Exam '07 (ENO+SP)

SP: 395140 MIGUEL MARCOSZ Salt Male 14 years Appt: 4103772 Session: 410021 Stand: 410

NICH5\NHANES_07-08\RH Suite 07\RH-07\ENOSP\ExhaledNitrousOxide ENO Test ENO-TRI1 Value or Could Not Obtain Trial #1

ENO Trial #1

Enter the Result displayed on the NIOX MINO™ device.

Enter Reading

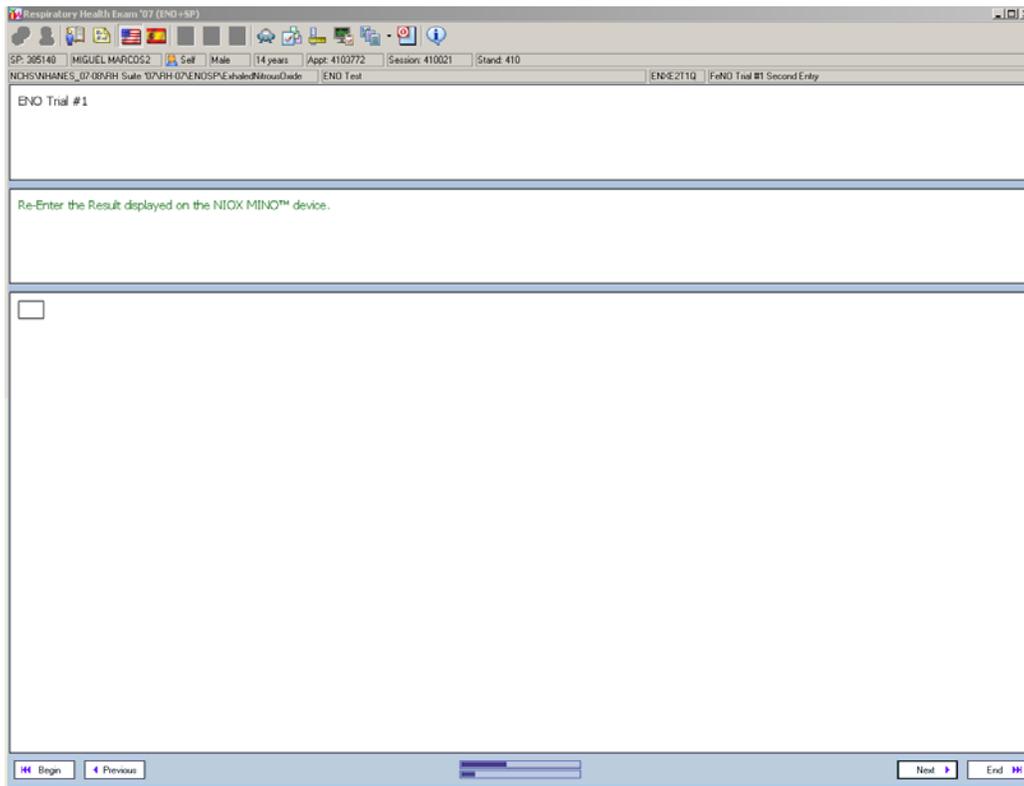
< 5 ppb

> 300 ppb

Could Not Obtain

Begin Previous Next End

Exhibit 3-11. Second entry of ENO trial #1 screen

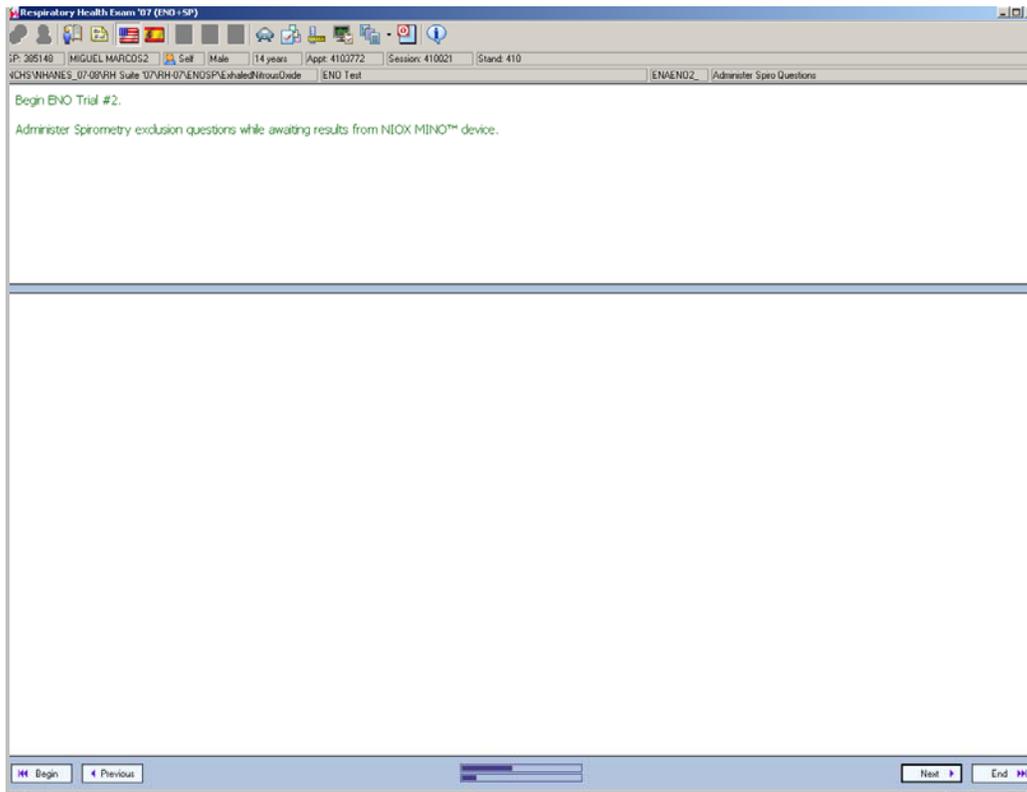


Once the results are displayed, touch the arrow key once and it will prompt you to be ready for the Measurement screen.

3.5.7 Conduct ENO Trial # 2

Once ENO trial #1 has been successfully conducted and results entered, ISIS will prompt you to conduct ENO trial #2 (Exhibit 3-12). Coach the participant to conduct the test correctly. See Section 3.5.2 for instructions on conducting the test. Continue using the mechanical counter to assist the technologist in keeping track on the number of attempts made to achieve a successful test.

Exhibit 3-12. ENO trial #2



A series of safety exclusion questions for spirometry will be asked while waiting for ENO trial #2 results. To view the questions, please refer to Section 3.2 of the *Spirometry Procedures Manual*. Once all the spirometry questions are asked, ISIS will prompt you to enter the results for ENO trial #2. Enter the results displayed on the monitor in the same manner as ENO trial #1.

3.5.8 Conduct ENO Trial #3 and/or #4

Participants whose reading between the first and second trial are not within the limited precision range, will have to perform a third and perhaps a fourth trial. If the third ENO trial is not within precision, they will be asked to conduct a fourth ENO trial. See Exhibit 3-13. Also, before conducting the third ENO trial, a new filter should be placed in the ENO monitor. ISIS will remind you to change the filter (see Exhibit 3-13). There will be no questions asked while waiting for results of trials #3 and #4.

Exhibit 3.13. ENO trial #3

Respiratory Health Exam TDF (ENO+SP)

SP: 285148 MIGUEL MARCOSZ Self Male 14 years Appt: 4103772 Sesión: 410021 Stand: 410

NIOX: NIOX_07_08_VH Suite: 107_VH 07ENOSP-E-shield@hrou.edu ENO Test ENO TR3 Value or Could Not Obtain Trial #3

Results were not within precision limits.
PLEASE REPLACE FILTER BEFORE BEGINNING.
Begin ENO Trial #3.

Enter the Result displayed on the NIOX MINO™ device.

Enter Reading

< 5 ppb

> 300 ppb

Could Not Obtain

Begin Previous Next End

Ready Disconnected

Please note that participants will be given a total of ten attempts to achieve all of the successful maneuvers. If they have exceeded ten trials prior to achieving the number of successful tests requested, then code it as “Could not obtain” in the ENO Trial Data Entry screen.

3.5.9 Finish ENO Exam

After the required number of successful trials has been achieved, the ISIS application will prompt you to enter the number of ENO attempts. See Exhibit 3-14. Record the number indicated on the mechanical counter on this screen. If the technologist enters more than 10 attempts, an error message will appear.

Exhibit 3-14. Enter ENO attempts

Respiratory Health Exam '07 (ENO+SP)

SP: 385148 MIGUEL MARCOS2 Male 14 years Appt: 4103772 Session: 410021 Stand: 410

NOHSUNHANS_07-08VRH Suite 107VRH-07ENOSP.EvaldedkznouDxds ENO Test ENMATMPT Total Number of ENO Attempts

Enter total number of ENO attempts

Begin Previous Next End

Ready Disconnected

After the last trial is completed and recorded, assist the participant in removing the strap from around his or her neck and place the NIOX MINO™ monitor on the counter. Click “Next” to advance to where it asks if an interpreter was used. See Exhibit 3-15. The next screen is the End of Subsection screen with the code of “Complete.” See Exhibit 3-16.

Exhibit 3-15. Interpreter used

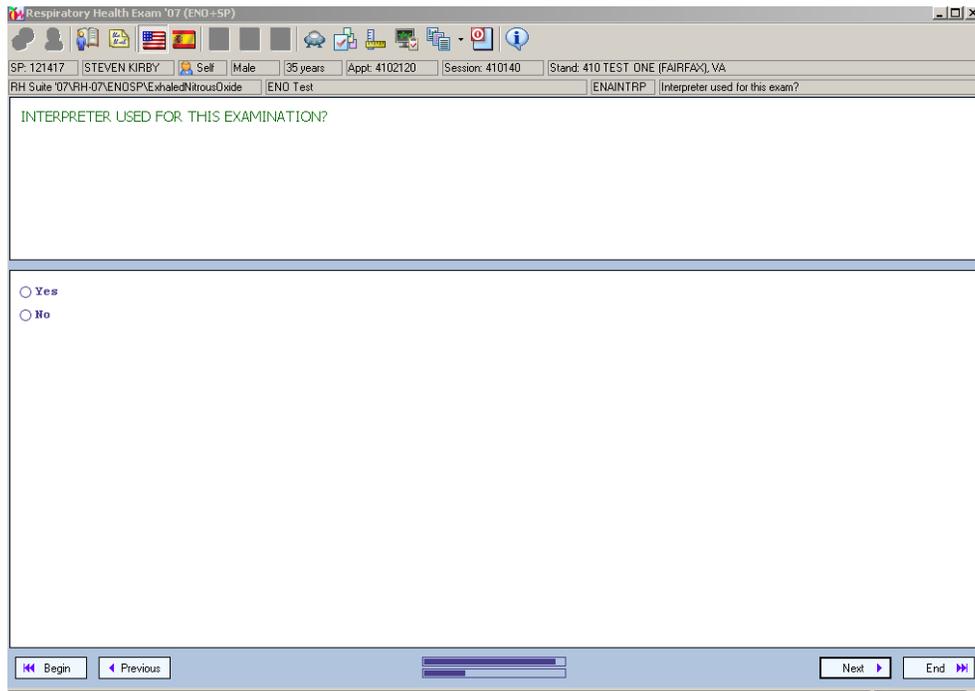
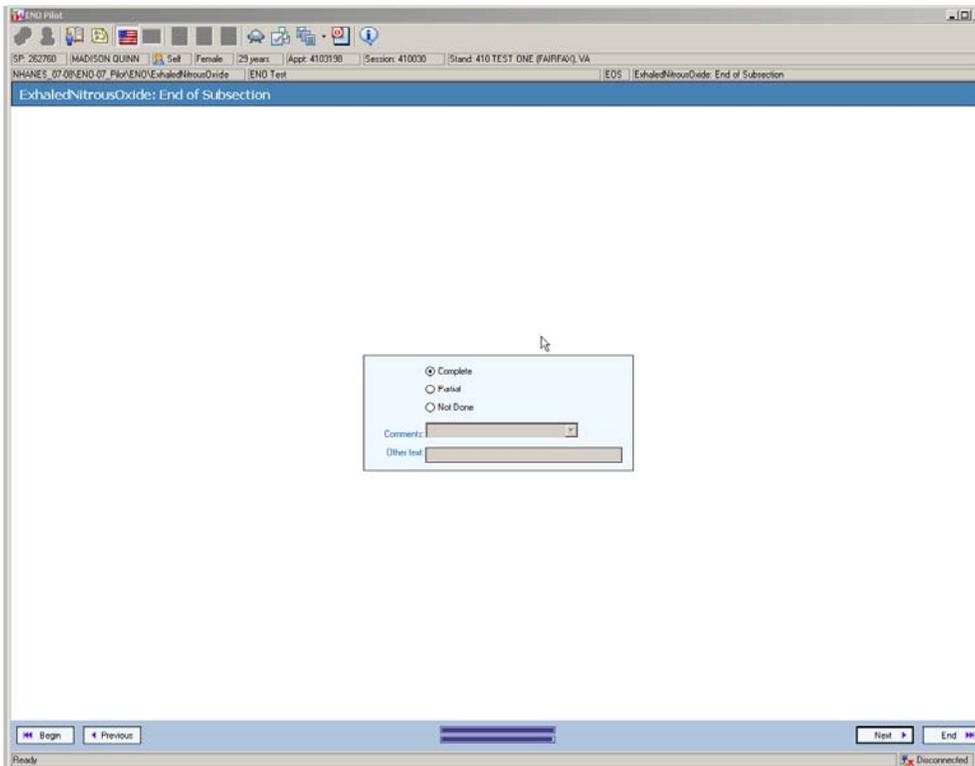


Exhibit 3-16. End of Subsection – complete screen



After the End of Subsection, the application will prompt you to begin the Spirometry test. See Exhibit 3-17. Please refer to the *Spirometry Procedures Manual* for test procedures. The End of Exam screen will appear after the Spirometry test has been completed. The purpose of this screen is to document the overall status of the ENO examination: Complete, Partial, or Not Done. As with all other MEC exam components, ISIS will automatically fill in the applicable component status for each exam. For Partial and Not Done exams, select the appropriate reason using the drop-down menu of the Comments field; or choose Other, specify and enter a brief explanation for the Partial or Not Done status (Exhibit 3-18).

Exhibit 3-17. Begin spirometry exam

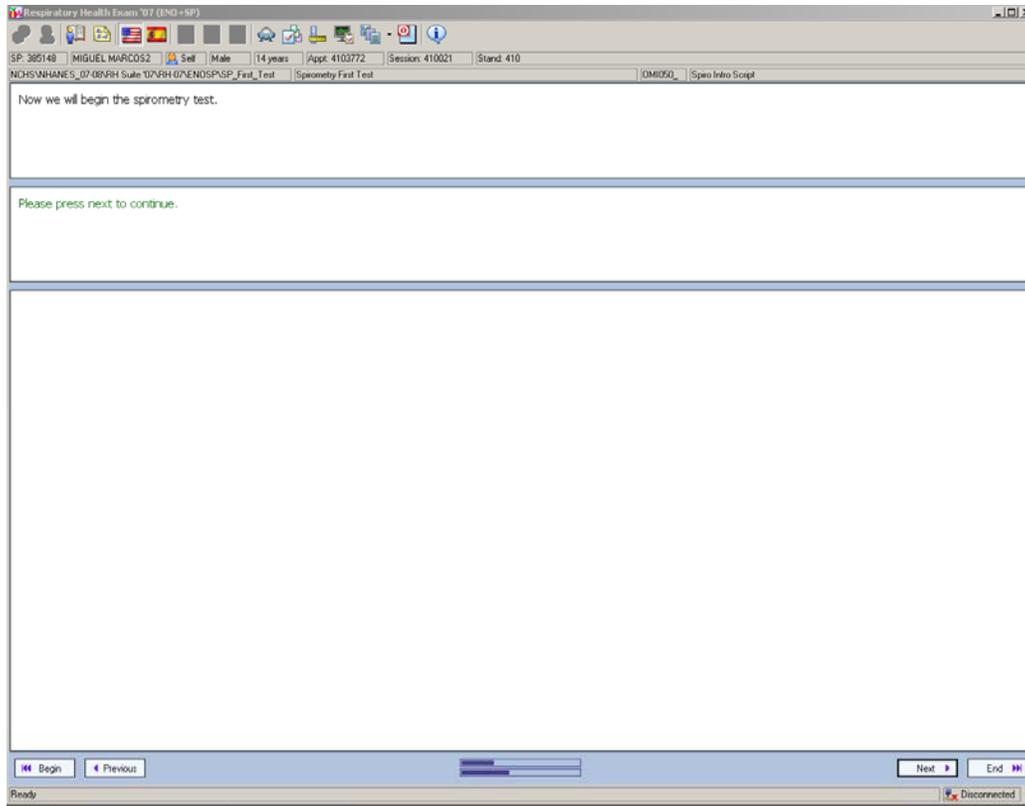
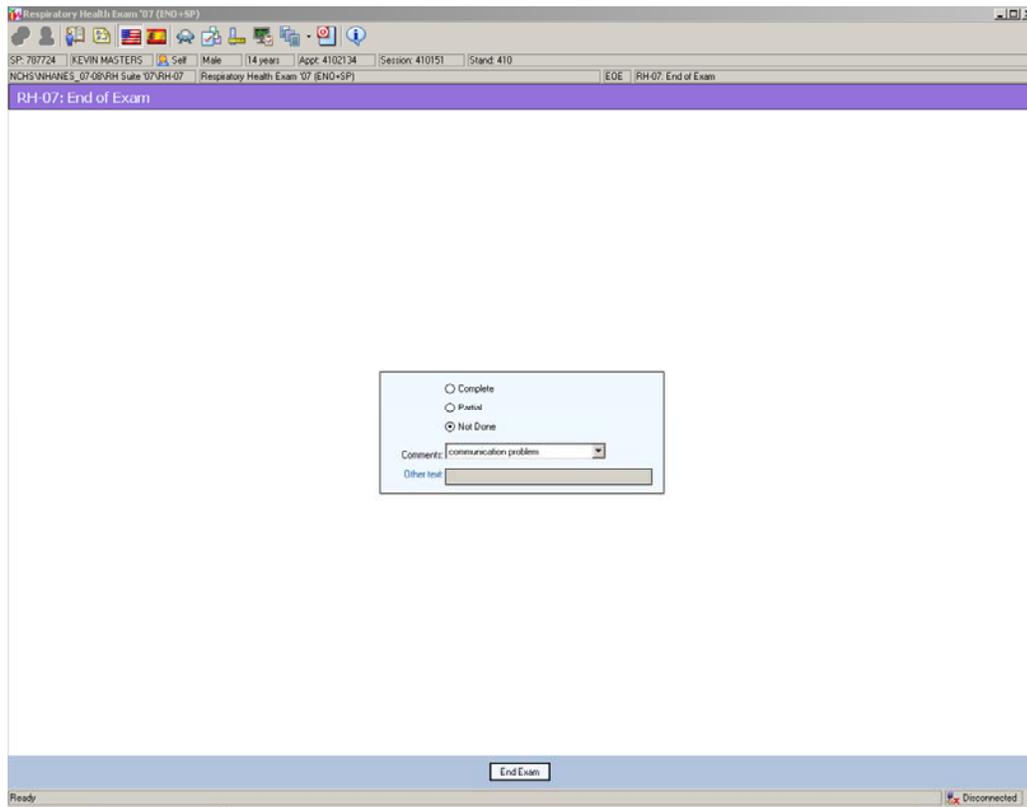


Exhibit 3-18. End of Exam



3.6 Troubleshooting ENO Examinations

Report all ENO equipment malfunctions promptly to the chief technologist, MEC manager, and Westat component specialist. If the issue is computer-related and cannot be resolved by the chief technologist and/or MEC manager, contact the home office ISIS support staff for assistance. Document the issue in the Unusual Field Occurrence (UFO) system and/or Equipment Tracking System (ETS) as appropriate (refer to the *UFO Utility Manual* and *ETS User Guide* for details).

See Appendix C for a list of troubleshooting warning messages and a list of error message codes that could appear on the NIOX MINO™ monitor screen.

3.7 Report of Findings

Participants may ask how they did on this test. Assure that this is currently being used for research only and that many factors affect their results such as what they last ate, whether or not they smoke, and their respiratory health in general. We will not provide results to the ENO test.

4. QUALITY CONTROL

Quality control procedures ensure the accurate and reliable collection and documentation of data. In this chapter, quality control procedures for the ENO component are described. To view spirometry quality control procedures, please refer to Chapter 4 of the *Spirometry Procedures Manual*.

4.1 Equipment Cleaning and Calibration

Routine cleaning and calibration of the ENO equipment are essential quality control measures in order to ensure that the equipment produces accurate results. The NIOX MINO™ monitor must be cleaned and calibrated according to the schedule outlined in this section. The technologist will complete these procedures using the Quality Control Checks dialog box, which contains designated tabs for the Start of Stand, Daily, Weekly, and End of Stand. To access this dialog box, select the Quality Control Checks option from the toolbar menu at the top of the screen. Click the “Done” box beside each of the checked items listed to record completion of the procedure.

4.1.1 Quality Control Checks Screens

The schedule for equipment cleaning and calibrations is provided in the following screens of the Quality Control Checks dialog box.

- Start of Stand (Exhibit 4-1 and 4-2)
 - ENO: Label stand # and date on a new blue card and insert card in device;
 - ENO: Label stand # and date on orange card;
 - ENO: Enter ambient air – backup machine;
 - ENO: Enter 15ppb QC sensor reading – backup machine;
 - ENO: Enter 75 ppb QC sensor reading – backup machine
 - ENO: Enter QC filter reading – backup machine; and
 - ENO: Enter measurement result – backup machine.

Exhibit 4-1. Quality Control Checks – Start of Stand QC

QC Check	D	Result	Comment
SPIRO: Clean/disinfect spirometer.	<input type="checkbox"/>		
SPIRO: Calibrate spirometer/perform leak check with syringe.	<input type="checkbox"/>		
ENO: Label Stand # and date on a new blue card and insert card in device.	<input type="checkbox"/>		
ENO: Label Stand # and date on a new orange card.	<input type="checkbox"/>		
Calibrate scale - Full	<input type="checkbox"/>		
Calibrate stadiometer	<input type="checkbox"/>		
ENO: Enter ambient air - backup machine.	<input type="checkbox"/>		

Buttons: Ok, Cancel

Exhibit 4-2. Quality Control Checks – Start of Stand QC (cont)

QC Check	D	Result	Comment
Calibrate scale - Full	<input type="checkbox"/>		
Calibrate stadiometer	<input type="checkbox"/>		
ENO: Enter ambient air - backup machine.	<input type="checkbox"/>		
ENO: Enter 15 ppb QC sensor reading - backup machine.	<input type="checkbox"/>		
ENO: Enter 75 ppb QC sensor reading - backup machine.	<input type="checkbox"/>		
ENO: Enter QC filter reading - backup machine.	<input type="checkbox"/>		
ENO: Enter measurement result - backup machine.	<input type="checkbox"/>		

Buttons: Ok, Cancel

- Daily (Exhibit 4-3)
 - ENO: Enter ambient air NO in result field.
 - ENO: Enter # of measurements displayed on ENO machine—MUST CHANGE SENSOR AT OR BEFORE 30 MEASUREMENTS.

Exhibit 4-3. Quality Control Checks – Daily QC

QC Check	D	Result	Comment
SPIRO: Change hose.	<input type="checkbox"/>	<input type="text"/>	<input type="text"/>
ENO: Enter ambient air NO in the result field.	<input type="checkbox"/>	<input type="text"/>	<input type="text"/>
ENO: Enter # of measurements displayed on ENO machine. - MUST CHANGE SENSOR AT OR BEFORE 30 MEASUREMENTS.	<input type="checkbox"/>	<input type="text"/>	<input type="text"/>

Buttons: Ok, Cancel

- Weekly (Exhibit 4-4)
 - ENO: Wipe device with alcohol prep pad.
 - ENO: Enter 15 ppb QC sensor reading.
 - ENO: Enter 75 ppb QC sensor reading.
 - ENO: Enter QC Filter reading.

Exhibit 4-4. Quality Control Checks – Weekly QC

QC Check	D	Result	Comment
SPIRO: Clean/disinfect spirometer.	<input type="checkbox"/>		
ENO: Wipe ENO device with alcohol prep.	<input type="checkbox"/>		
ENO: Enter 15 ppb QC sensor reading.	<input type="checkbox"/>		
ENO: Enter 75 ppb QC sensor reading.	<input type="checkbox"/>		
ENO: Enter QC filter reading.	<input type="checkbox"/>		
SPIRO: Conduct weather check.	<input type="checkbox"/>		

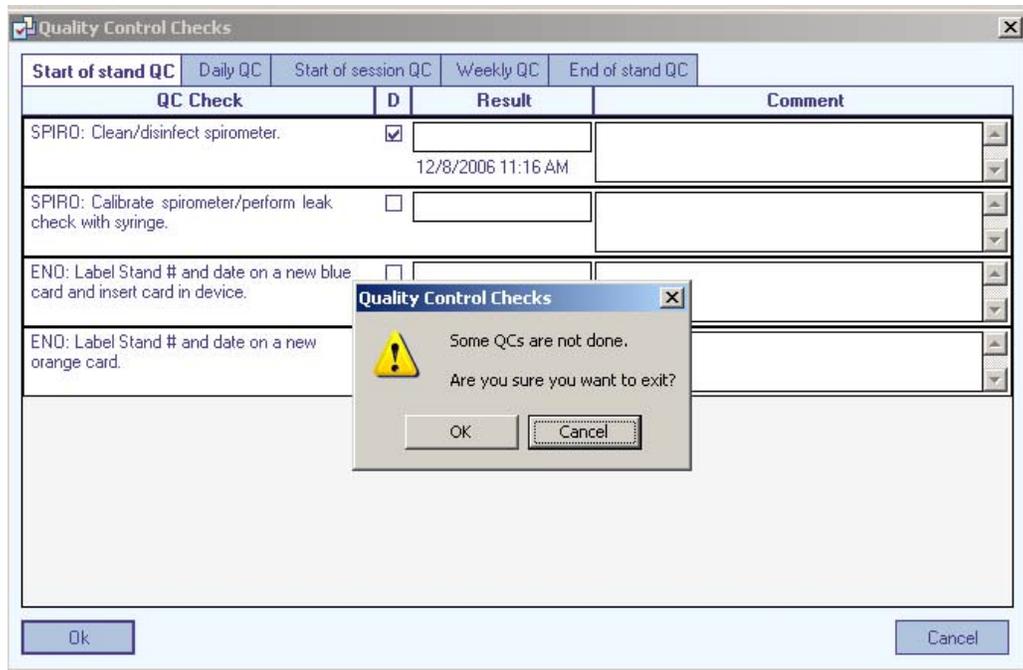
- End of Stand (Exhibit 4-5)
 - ENO: Ship used blue and orange cards to Westat.
 - ENO: Ship all sensors to Westat.

Exhibit 4-5. Quality Control Checks – End of Stand QC

QC Check	D	Result	Comment
SPIRO: Clean/disinfect spirometer.	<input type="checkbox"/>		
SPIRO: Ship used hoses and hose adaptors to NIOSH.	<input type="checkbox"/>		
ENO: Ship used blue and orange test cards to Westat.	<input type="checkbox"/>		
ENO: Ship all sensors to Westat.	<input type="checkbox"/>		

When finished completing the required Quality Control Checks, click “OK” to exit the dialog box and return to the main Respiratory Health Component screen. However, if you have not checked the “Done” box beside all of the required checks, clicking “OK” will open the following pop-up window (Exhibit 4-6).

Exhibit 4-6. Quality Control Checks – Not Done QC



To return to the QC Checks dialog box and complete the remaining checks, click “Cancel.” Alternatively, if you need to close out of the dialog box without completing all of the checks at this time, click “OK” to the above window to return to the main Respiratory Health Component screen.

4.1.2 Equipment Cleaning

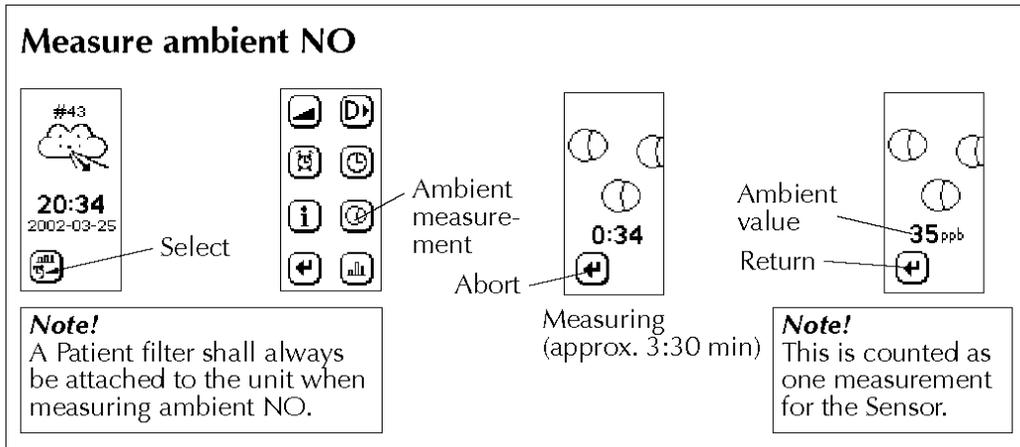
For infection control purposes, the NIOX MINO™ monitor must be cleaned with alcohol pads “Weekly.” Wipe the surface of the device with an alcohol prep pad, but do **not** wipe the bottom of the device where the sensor cartridge is located as alcohol can damage the sensor.

On a daily basis, the technologist will also inspect the external surfaces of the monitor and wipe them clean with disinfectant wipes as needed.

4.1.3 Ambient Air Testing and Equipment Calibration

NIOX MINO™ monitor ambient air testing and calibration will be conducted “Daily.” This is performed on a daily basis so data analysts can examine the possible effects of background ambient air NO on test results. This testing is not performed for calibration purposes. A standard filter must be attached to the monitor when measuring ambient air and the blue standard test card always needs to be placed in the unit.

- The procedures for performing the ambient air testing are outlined below:
 1. On the NIOX MINO™ monitor, touch the menu screen. Select the ambient measurement icon (looks like an eyeball). The monitor screen will display floating eyeballs with a clock counting down. It takes 3 minutes and 30 seconds to perform the calibration. At the end of the calibration, the results will be displayed in parts per billion (ppb).
 2. In the Quality Control Checks screen under the appropriate tab (Daily), click the “D” box and enter the results displayed on the monitor in “Enter ambient air NO in result field.”



4.1.4 NIOX™ QC Sensor and Special NIOX™ QC Filter Checks

Three quality control procedures will be conducted “Weekly” to check the accuracy of the NIOX MINO™ monitor’s reading. A NIOX filter will be attached to the monitor when conducting the QC checks. For the NIOX™ QC Sensor check procedure, a new NIOX filter will be used; for the Special NIOX™ QC Filter check, both a special NIOX™ QC filter and a NIOX filter will be used. For both the NIOX™ QC Sensor check and the Special NIOX™ QC Filter check, the standard blue test card needs to be placed in the unit.

4.1.5 NIOX™ QC Sensor checks

The QC sensor makes it possible to verify two simulated levels of exhaled NO at 15 and 75 ppb. This permits verification that the NIOX-MINO™ monitor itself is functioning properly. Two QC checks will be performed with the NIOX™ QC sensor, one set at 15 ppb and the other set at 75 ppb. Prior to conducting the QC sensor checks, visually inspect the NIOX™ QC sensor for any damages. Do not touch the top gray area of the sensor or drop it.

- The procedures for performing the NIOX™ QC sensor check for **15** ppb are outlined below:
 1. Disconnect the power supply to the NIOX MINO™ monitor.
 2. Remove the standard NIOX MINO™ sensor according to Section 2.4.2.
 3. Set NIOX™ QC sensor switch to 15.

4. Place the NIOX™ QC sensor face up (gray side up) and insert into the monitor according to Section 2.4.2.
5. Re-connect the power supply and check that the NIOX™ QC sensor indicator light turns on when power is connected. It might take a few minutes for the monitor to warm up.
6. Set the monitor to be in the Ready for Measurement mode and check that the top blue light is lit.
7. Place a new filter on the monitor.
8. Check that the NIOX™ QC sensor indicator light turns OFF and stays OFF. When the NIOX™ QC Sensor light is OFF, it indicates that it is ready for QC testing (if QC testing is performed with the QC Sensor light ON, an error message will occur).
9. Perform the ENO test. Use a mirror to assist you in achieving a correct maneuver.
10. Within 5 seconds of completing a successful maneuver, press the white or blue button on the QC sensor and check that the indicator light turns ON.
11. Wait for the results (1.45 minutes).
12. Results should be between 10-20 ppb. If the reading is not in that range or an error message is displayed, QC did not pass. Another trial must be conducted.
 - a. If after three trials, the reading is not between 10-20 ppb, QC did not pass.
 - b. Disconnect the current NIOX MINO™ monitor.
 - c. Use the back-up NIOX-MINO unit for all further QCs and testing.
 - d. Send UFO of the failed QC check.
 - e. Notify Westat component specialist that the unit failed to meet QC specifications.
13. In the Quality Control Checks screen under the appropriate tab (Weekly), check the “D” box and enter the results displayed on the monitor in the “ENO: Enter 15 ppb QC sensor reading” field.

- The procedures for performing a QC sensor check for **75** ppb are outlined below:
 1. Set the QC sensor switch to 75.
 2. Check that the QC sensor indicator light is OFF.
 3. Set the monitor in the Ready for Measurement mode and ensure that the top blue light is lit.
 4. Perform the ENO test using a new NIOX filter. Use a mirror to assist you in achieving a correct maneuver.
 5. Within 5 seconds of completing a successful maneuver, press the white or blue button on the QC sensor and check that the indicator then turns ON.
 6. Wait for the results (1.45 minutes).
 7. Results should be between 67-83 ppb. If the reading is not in that range or an error message is displayed, QC did not pass. Another trial must be conducted.
 - a. If after three trials, the reading is not between 67-83 ppb, QC did not pass.
 - b. Disconnect the current NIOX MINO™ monitor.
 - c. Use the back-up NIOX MINO™ monitor for all further QCs and testing.
 - d. Send UFO of the failed QC check.
 - e. Notify Westat component specialist that the unit failed to meet QC specifications.
 8. In the Quality Control Checks screen under the appropriate tab (Weekly), check the “D” box and enter the results displayed on the monitor in the “ENO: Enter 75 ppb QC sensor reading” field.
 9. Disconnect the power supply to the NIOX MINO™ monitor.
 10. Remove the NIOX™ QC sensor and store in the assigned box.
 11. Insert original standard NIOX MINO™ sensor back into the monitor unit.
 12. Connect the power supply to the NIOX MINO™ monitor.

4.1.6 Special NIOX™ QC Filter Check

The special NIOX™ QC filter allows the NIOX MINO™ monitor to check a “Blank” sample using exhaled breath (zero ppb NO). Prior to conducting the QC Filter check, visually inspect the Special NIOX™ QC filter for any damages. Ensure that the blue standard test card is in the monitor.

- The procedures for performing the Special NIOX™ QC Filter check are outlined below:
 1. Attach the Special NIOX™ QC filter to the NIOX MINO™ monitor opening.
 2. Attach a new NIOX filter to the Special NIOX™ QC filter.
 3. Set the monitor in the Ready for Measurement mode and ensure the top blue light is lit.
 4. Perform the ENO test. Use a mirror to assist you in achieving a valid measurement.
 5. Remove the NIOX filter and the Special NIOX™ QC filter after completing the test.
 6. Wait for reading of results (1.45 minutes).
 7. Results should be less than 5 ppb (shown as <5 ppb).
 8. If the reading is higher than 5 ppb or an error message for a negative result (E2120) is displayed, repeat the test one more time.
 - a. If the reading from a repeated test is 5ppb or lower (shown as <5ppb) then the QC has passed.
 - b. If the reading from repeated test is higher than 5ppb or an error message for negative results (E2120) is displayed, QC did not pass.
 - c. Disconnect the current NIOX MINO™ monitor and replace it with the back-up NIOX MINO™ monitor. Perform all further QCs and testing on the back-up NIOX MINO™ monitor.
 - d. Send UFO of the failed QC check.
 - e. Notify Westat component specialist that the unit failed to meet QC specifications.
 9. In the Quality Control Checks screen under the appropriate tab (Weekly), check the “D” box and enter the results displayed on the monitor in the “ENO: Enter QC Filter reading” field.

4.1.7 Storing NIOX™ QC Sensors and Special NIOX™ QC Filter

QC sensors should be handled with careful attention. Always hold the sensor by the blue plastic part. Do NOT touch the gray part of the sensor. When storing the NIOX™ QC sensor, place it in the padded box, labeled QC sensor. Place the sensor sideways, gray part on the side. Never pack the sensor with the gray part facing up. Keep the sensor box in the Respiratory Health component room at all times.

Handle the Special NIOX™ QC filter with care. Keep filter in the assigned box and keep it in the Respiratory Health component room at all times.

4.2 Equipment Maintenance

One NIOX MINO™ monitor will be used at each MEC. A backup monitor will also be kept at each MEC and used if the main monitor becomes disabled or expires. If the main monitor in the field becomes disabled or expires, document the problem in the UFO system and contact the chief technologist, MEC manager, and Westat component specialist immediately. Use the backup monitor for further testing. The NIOX MINO™ monitor has an expiration date; either 3.5 years from date of manufacture or 1,500 measurements. In NHANES we will most always meet the measurement limit not the expiration date. When the monitor is close to its expiration date or permitted measurements, an error code of “E9000” will be displayed on the monitor. This code indicates that 50 measurements are left on the monitor. When this occurs, replace this monitor with the backup monitor and follow the procedures described above. See Appendix C for error messages.

The NIOX MINO™ sensor also has a measurement limit. The sensors are allowed 300 measurements and must be changed when 30 measurements remain. The number of measurements left is displayed on the monitor above the cloud with the “#” sign and the number of measurements. When the expiration date approaches, a warning message will be displayed on the monitor screen. To change sensors see Section 2.4.2.

4.3 Observation

Staff from Westat, NCHS, and Aerocrine will observe the ENO component at regular intervals. These observations will serve to verify that the protocol is being implemented correctly and consistently and that standard procedures and techniques are being followed. Problems or deviations will be noted and feedback will be provided to the technicians as necessary.

4.4 Review of Exam Status

To further monitor the quality of data collection, component staff will generate reports from the ISIS intraweb. The number of ENO examinations and examination times: cumulative and sorted by session, by age group, and by technician, as well as the reasons for not done and partial examinations, will be monitored by stand.

4.5 ENO Safety Precautions

The major safety precautions taken in the ENO component are prevention of dropping the NIOX MINO™ monitor, prevention of electrical shock during the procedure, and prevention of infection transmission among participants and exam staff.

4.5.1 Infection Control Measures

The transmission of infections between participants or from the participant to the technologist is a remote possibility. The following measures are taken to minimize the least risk of infection transmission among participants and MEC staff:

- After each exam, the technologist will have the participant discard the disposable filter used during ENO testing; and
- If a participant has a cold, wipe the device with alcohol pads prior to the next participant's test.

4.6 Comprehension or Language Difficulties

Some participants may have difficulty understanding the examination instructions. The technologist should use extreme caution when attempting to conduct the ENO component on these participants.

For many participants, language barriers are a common cause of difficulty in understanding examination instructions. Participants who are able to communicate in English and Spanish will be recruited to participate in the ENO exam. If the technologist is not English-Spanish bilingual, a Spanish interpreter will be assigned to interpret for the participant and the technologist during the exam. If the participant speaks a language other than English or Spanish, arrangements will be made ahead of the ENO exam to identify an appropriate interpreter. Otherwise, as in the case of other forms of comprehension difficulties, if the participant cannot understand your directions enough to provide valid responses, then end the component and code the status as “Not Done” due to “Communication Problem.”

4.7 Emergency Procedures

Ordinarily, the ENO examination should pose little risk to the safety of the participant. In rare cases, the participant may hyperventilate and become dizzy during ENO testing. Any participant who feels faint should be guided onto the chair with his or her head down toward the knees, and encouraged to breathe slowly and deeply until he or she recovers.

If the participant fails to recover normal breathing, faints, or reports feeling ill, the technologist should summon the MEC manager and physician immediately. The physician will assume command of the emergency response. The physician should always be consulted if there is any question regarding the participant’s safety status during the exam. The NHANES mobile examination center has a well-developed emergency response protocol that will be implemented in the event of any emergency. Refer to the *NHANES Safety Issues and Emergency Procedures Manual* for complete details.

Appendix A

Respiratory Health Safety Exclusion Questions

ENQ010

The screenshot shows a software window titled "Respiratory Health Exam '07 (END+SP)". The patient information bar includes: SP: 121417, STEVEN KIRBY, Self, Male, 35 years, Appt: 4102120, Session: 410140, Stand: 410 TEST ONE (FAIRFAX), VA. The question ID is ENQ010 and the question text is "Breathing problem require oxygen?".

Do you currently have a breathing problem that requires you to use supplemental oxygen **during the day**? [This is air stored in a tank that you use to help you breathe. Do not include night treatments for sleep apnea.]

Yes
 No

Navigation buttons: Begin, Previous, Next, End. Status: Ready, Disconnected.

ENQ020

The screenshot shows a software window titled "Respiratory Health Exam '07 (END+SP)". The patient information bar includes: SP: 385148, MIGUEL MURCOSZ, Self, Male, 14 years, Appt: 4103772, Session: 410021, Stand: 410. The question ID is ENQ020 and the question text is "Problem taking deep breath?".

Do you now have any pain or physical problem that may prevent you from taking a deep breath and exhaling forcefully?

Yes
 No

Navigation buttons: Begin, Previous, Next, End. Status: Ready, Disconnected.

Appendix B

ENO Questions

ENQ040

Respiratory Health Exam '07 (END+SP)

SP: 279734 BELINDA TRANH1 Female 49 years Appr: 4103716 Session: 410021 Stand: 410
NCHS\NHANES_07\04\NH Suite 07\RH-07\END\SP\ExhaledNitrouDate END Test ENQ040 Smoked last hour?

Within the **last hour** have you smoked a cigarette, cigar, pipe, or used any other tobacco product?

Yes
 No

Begin Previous Next End
Ready Disconnected

ENQ050

Respiratory Health Exam '07 (END+SP)

SP: 385140 MIGUEL MARIOS2 Male 14 years Appr: 4103772 Session: 410021 Stand: 410
NCHS\NHANES_07\04\NH Suite 07\RH-07\END\SP\ExhaledNitrouDate END Test ENQ050 Exercised strenuously last hour?

[Within the **last hour**] have you exercised strenuously?

Yes
 No

Begin Previous Next End
Ready Disconnected

ENQ060

Respiratory Health Exam '07 (END-SP)

SP: 385148 | MIGUEL MARCOS2 | Salt | Male | 14 years | Appt: 4102772 | Session: 410021 | Stand: 410

NCHS\NHANES_07\08\PH Suite 10\VRH 0\ENOS\PE\ehale\4hour0xds | END Test | ENQ060 | Had anything to eat or drink last hour?

[Within the **last hour**] have you had anything to eat or drink?

Yes
 No

Begin Previous Next End

Ready Disconnected

ENQ070

Respiratory Health Exam '07 (END-SP)

SP: 385148 | MIGUEL MARCOS2 | Salt | Male | 14 years | Appt: 4102772 | Session: 410021 | Stand: 410

NCHS\NHANES_07\08\PH Suite 10\VRH 0\ENOS\PE\ehale\4hour0xds | END Test | ENQ070 | Eaten nitro oxide rich vegetables?

Within the last **three** hours have you eaten beets, broccoli, cabbage, celery, lettuce, spinach or radishes?

Yes
 No

Begin Previous Next End

Ready Disconnected

ENQ080

Respiratory Health Exam '07 (END+SP)

SP: 305140 | MIGUEL MARCOS2 | Self | Male | 14 years | Appt: 4102772 | Session: 410021 | Stand: 410

NCHS\WHANES_07\08\RH Suite 10\7\RH 07\EN05\PE\ehale@rhous\Osde | END Test | ENQ080 | Eaten nitric oxide rich meats?

Within the last **three** hours have you eaten bacon, ham, hot dogs or smoked fish?

Yes
 No

Begin Previous Next End

Ready Disconnected

ENQ090

Respiratory Health Exam '07 (END+SP)

SP: 385148 | MIGUEL MARCOS2 | Self | Male | 14 years | Appt: 4103772 | Session: 410021 | Stand: 410

NCHS\WHANES_07\08\RH Suite 10\7\RH 07\EN05\PE\ehale@rhous\Osde | END Test | ENQ090 | Used oral or inhaled steroids?

Within the last **two days** have you used any oral or inhaled steroids? This list provides some examples.

Show HANDCARD

Yes
 No

Begin Previous Next End

Ready Disconnected

ENQ100

Respiratory Health Exam '07 (ENQ100)

SP: 365148 MIGUEL MARCOS2 Self Male 14 years Appt: 4103772 Session: 410021 Stand: 410

NCHS/MHMANES_07-09/RH Scale 107/RH 07-ENOSP-Ehaled/Ntrous/Orade ENO Test Had respiratory illness?

In the past 7 days, have you had a cough, cold, phlegm, runny nose or other respiratory illness? Do not count allergies or hay fever.

Yes

No

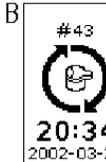
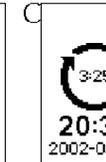
Begin Previous Next End

Ready Disconnected

Appendix C

Troubleshooting and Error Codes
from the *Aerocrine User Manual*

Troubleshooting

Warning	Action
	<p>Disconnect the power supply and mount a Sensor</p>
 <p style="margin-left: 20px;">Spinning circles symbol</p>	<p>The inhalation was too weak to initiate a measurement - Stop the procedure immediately when this warning appears. Wait for the "Ready for use" screen and repeat the inhalation with a stronger inhalation force.</p>
 <p style="margin-left: 20px;">Flashing card symbol</p>	<p>Test Card almost full – Change card. The card will continue to register information after it is full, but the oldest information will be overwritten.</p>
  <p style="margin-left: 20px;">Flashing number or date</p>	<p>Sensor almost expired – Order a new sensor (This will occur when 10% of the measurements are left or 2 weeks before expiry date and continue until the Sensor has expired)</p>
 <p style="margin-left: 20px;">Flashing warning sign and error code E9000 (shown during 3 sec. once a day after the instrument has been activated)</p>	<p>Instrument almost expired – Order a new instrument (This will occur 4 months before the instrument expires or when 50 measurements are remaining.) The instrument will not work after the indicated date, or after the indicated number of measurements.</p>
<p>A</p>  	<p>A Make sure that the ambient temperature is between +16 and +30°C. Wait for the Sensor to stabilize.</p>
<p>B</p> 	<p>B Remove any sources of disturbance (such as cordless or mobile telephones, or gas emitting appliances). Wait for the Sensor to stabilize.</p>
<p>C</p> 	<p>C Wait for the Sensor to stabilize. < 4 minutes.</p>

Error Codes

<p>Error messages and other information are shown as a code at the top of the unit display. The table below gives information on how to act upon an error code. If error persists, contact your local Aerocrine representative or Aerocrine Service Department.</p>		<div style="border: 1px solid black; padding: 2px; display: inline-block;"> E1005  </div>	
Error code	Action	Error code	Action
E1005	Press return icon and repeat measurement with the Test Card fully inserted or fully removed.	E6002– E6003	Sensor expiry date has passed (6002) or time and date settings are not correct. Check that time and date settings in unit are correct. If necessary, adjust settings and unplug and re-connect power supply to restart unit. If error still persists, replace sensor.
E2002	Exhalation too strong. Repeat measurement with less exhalation force.	E6010, E6012	Remove any sources of disturbance (such as cordless or mobile telephones, or gas emitting appliances). Unplug and re-connect power supply to restart unit. Repeat measurement.
E2003	Inhalation too weak. Repeat measurement and be sure to inhale to total lung capacity.	E6011	Sensor is faulty. Replace the sensor.
E2004	Repeat measurement and exhale into the unit directly after inhalation.	E6014– E6033	Sensor is faulty. Replace the sensor.
E2005	Exhalation too weak. Repeat measurement with greater exhalation force and exhale until signal for completed exhalation is heard.	E8001	Check that ambient temperature is within specification. If necessary, move unit to another location.
E2006– E2007	Repeat measurement and do not breathe through patient filter during analysis.	E8020– E8050	Unplug and re-connect power supply to restart unit.
E2101– E2120	Remove any sources of disturbance (such as cordless or mobile telephones, or gas emitting appliances). When unit is ready for measurement try to repeat measurement. If error persists, unplug and connect power supply to restart unit.	E8060– E8061	Check that the mains voltage is within specification. If necessary replace the power supply.
E2122	Unplug and connect power supply to restart unit.	E8100– E8213	Unplug and re-connect the power supply to restart unit.
E2123	Data is not stored on the Test Card. Change Test Card.	E9000*	Unit is close to expiry date or permitted number of measurements (4 months or 50 measurements left). Contact your local Aerocrine rep. or Aerocrine support.
E3901– E3926	IR communication error. Unplug and connect power supply to restart unit and printer.	E9001*	Unit is expired and must be replaced. Contact your local Aerocrine rep. or Aerocrine support. It is still possible to view or print measurements stored on a Test Card.
E5010– E5032	Check Test Card and that it is correctly inserted. Try with another card.		
E6001	All measurements on sensor have been used. Replace sensor.		
* warning code.			