OPERATING INSTRUCTIONS

for the

eSP™ SPIROMETRY TESTING SYSTEM

July 20, 2010

Version (Draft)

SYSTEM USER GUIDE

Part #

Customized for:

SPIROMICS Protocol

1.2R

1 GENERAL INFORMATION

1.1 IMPORTANT NOTICE

The intention of the System User Guide (SUG) is to provide basic operating instruction for eSP™ (electronic short path) software. This document does not serve as a protocol resource or to provide comprehensive test instructions outside of the published protocols.

Please refer to the study protocol published by the Sponsor for detailed instructions on study related procedures. This system is to be used by authorized study staff for this trial.

This User Guide and the accompanying pneumotach and syringe certification documents must be retained with the investigator's site file at the completion of this study.

Information in this SUG is specific to the SPIROMICS protocol. The software described in this document is furnished in conjunction with SPIROMICS and is only intended for use in this trial. Information is intended to assist nSpire Health customers in the use of our products; any other use of the information contained herein is prohibited.
nSpire Health reserves the right to change the content of this document at any time without prior notice. The software described in this document is furnished under a license agreement. The user is prohibited from copying, reverse engineering, disassembly, or decompilation of the software. No part of this document may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopying, recording, or storing in a retrieval system, or translated into any language in any form for any purpose without prior written permission of nSpire Health, Inc.

	This symbol indicates that the user must read and understand all instructions and warnings prior to use.
	This symbol indicates that this Class IIA equipment complies with the European Union Medical Device Directive 93/42/EEC.
	This symbol indicates a Class 2-power supply not requiring a grounded power outlet.
	This symbol indicates that this device provides a certain level of safety because the subject-applied part is floating.

Printed and Bound in the United States of America

1.2 CONTACT INFORMATION

Manufactured by
nSpire Health, Inc.
1830 Lefthand Circle
Longmont, CO 80501 USA

Authorized Representative
nSpire Health, Ltd.
Unit 10 Harforde Court
John Tate Road
Hertford, SG13 7NW U.K.

1.3 TECHNICAL SUPPORT

For subject testing and technical issues, please contact our 24-hour on-call staff using the numbers listed below and follow the prompts.

Important: If the voice mail system is reached, a message must be left with your name, protocol, principal investigator name, contact telephone number (including extension), and a brief description of your reason for calling. A phone call will be returned as soon as an agent is available.

1.3.1 SUMMARY OF PHONE AND FAX

Step 1: Dial your country's toll free access code.
Step 2: Wait for the prompt
Step 3: Dial 800 915 4737 for **Telephone** OR Dial 800 916 4737 for **Fax**

Country	Access Code
USA	No access code; dial 1-800-915-4737

1.3.2 ORDERING SUPPLIES

Throughout the course of this clinical trial, it may be necessary to order additional supplies from nSpire Health. To order items, contact nSpire Health Technical Support personnel or use the Sales Order Request Form provided. Be sure to allow enough time for delivery to your site.

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3 CONTENTS AND SET UP

3.1 GENERAL INFORMATION

When you receive your equipment, it is important to take the time to unpack and become familiar with all components. Review the packing slip to ensure that all items have been received. Compare the parts received to the packing list making sure you have received all components and supplies and that the serial numbers match the components sent. Sign and date the packing slip and fax back to nSpire Health.

NOTE: Save *all* boxes and packaging material for return of the equipment at the completion of the study.

3.1.1 CONTENTS

Equipment includes:

- ✓ Computer, power supply block, power cable
- ✓ Modem cable (RJ11)
- ✓ Ethernet Cable (RJ45)
- ✓ Printer, power supply block, power cable *(Standard sites only)*
- ✓ USB Printer or Printer
- ✓ KoKo Spirometer / Pneumotach
- ✓ PCMCIA adaptor OR DB9 Gender Changer
- ✓ KoKo Filters & Nose Clips
- ✓ 3 Liter Calibration Syringe
- ✓ Weather Station

NOTE: Your equipment may vary slightly.

The documents in the accompanying large white envelope include:

- ✓ System User Guide
- ✓ Investigator Statement
- ✓ Security Statement
- ✓ Technician Checklist
- ✓ Sales Order Request Form

NOTE: Please treat the last documents as masters and make copies for your files.

3.2 SYSTEM SET-UP

3.2.1 PLUGGING IN THE COMPUTER

3-1, Connecting the Power Supply to the Computer

1. Connect round end of the power supply cable to the back of the computer.
2. Plug the power supply block into an electrical outlet.

3.2.2 CONNECTING PRINTER

Remove the printer and its components from the shipping box. Make sure all packing materials and tape are removed.

Figure 3-2, Connecting the Printer

1. Add paper to the paper tray.
2. Connect the printer power supply cable to the back of the printer
3. Plug the power supply block into an electrical outlet.
4. Connect the printer USB cable to the back of the printer.
5. Connect the other end of the USB printer cable to an available USB port on the computer.
6. Insert ink cartridges into the printer.

3.3 SPIROMETRY CONNECTION

The spirometer will connect to the computer using the PCMCIA card.

3.3.1 PCMCIA CARD

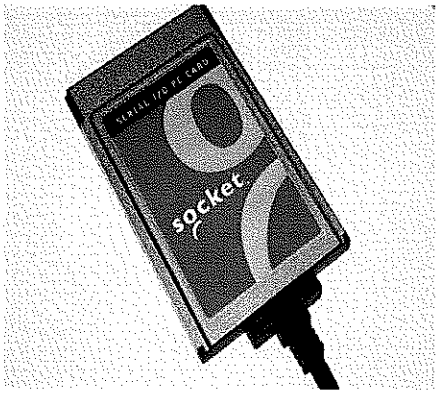


Figure 3-3, PCMCIA Card Adaptor

1. Attach the KoKo Mouthpiece filter to the KoKo Spirometer, see Error! Reference source not found.
2. Attach the KoKo Spirometer to the PCMCIA card adapter.
3. Insert PCMCIA card into the slot on the side of the computer.
4. The yellow button will extend out as card is inserted.

NOTE: To remove card from computer push yellow button in.

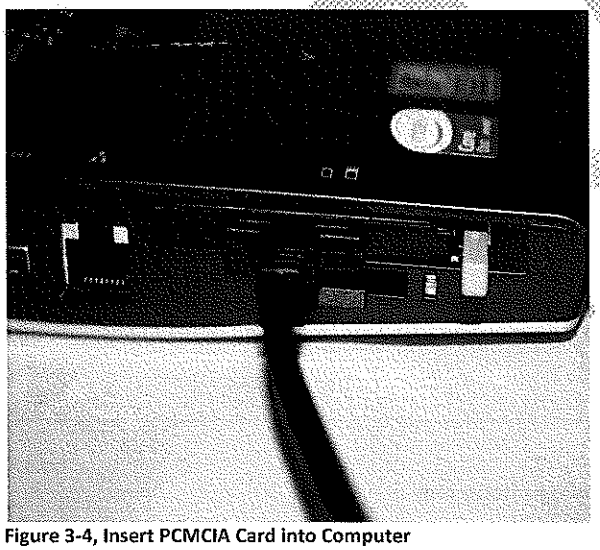


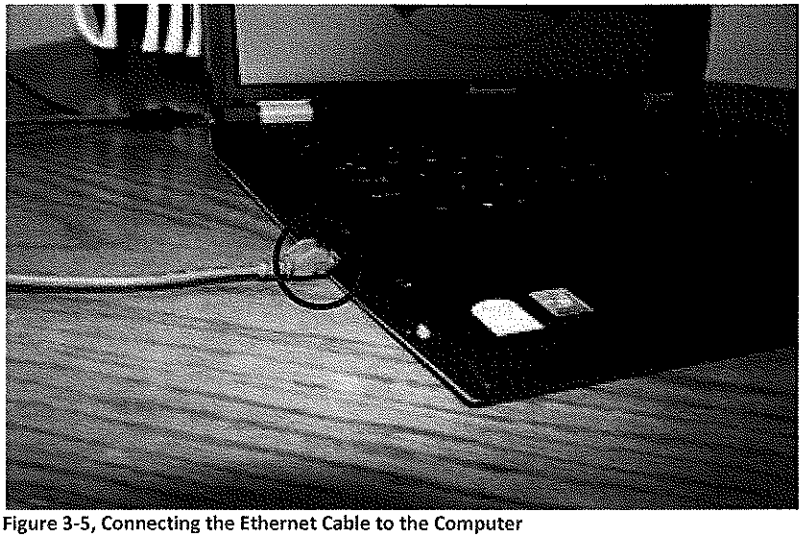
Figure 3-4, Insert PCMCIA Card into Computer

3.4 INTERNET CONNECTIONS

eSP synchronization will connect your computer to the nSpire Health central server. System updates and other important information will automatically download to your study computer.
Determine which type of internet connection you will be using.

3.4.1 ETHERNET CONNECTION

Using the **Ethernet** cable (RJ45) provided, insert one end into the LAN port and the other into the computer receptacle.



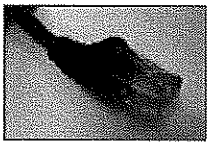


Figure 3-5, Connecting the Ethernet Cable to the Computer

If your network supports Dynamic Host Configuration Protocol (DHCP) (i.e. can acquire a network address automatically), and you have access to high speed Internet, the computer will transmit securely over this network. If you answer **YES** to the following questions, we suggest you try the LAN port for your first synchronization: (However, nSpire Health is not authorized to support or troubleshoot your network environment.)

- Do computers in your organization have high speed access to the Internet?
- Do they connect to a hub or a router?
- Is there someone in your facility that manages the access to the Internet, network equipment, or IP addressing that can answer these questions?

If you have answered **NO** to any of the above questions, use an analog phone connection.

****INFORMATION FOR YOUR NETWORK ADMINISTRATOR IN THE EVENT OF PROBLEMS WITH LAN CONNECTION EFFORTS****

IN ORDER TO FULFILL SECURITY COMPLIANCE REQUIREMENTS, OUR SYSTEM'S LAN CONFIGURATION IS STANDARD DHCP. IF YOU HAVE STATICALLY ASSIGNED IP ADDRESSES WITHIN YOUR LAN, YOU CANNOT TRANSMIT FROM OUR SYSTEM OVER LAN. NSPIRE HEALTH WILL NOT MODIFY OUR BASE WORKSTATION CONFIGURATION TO ACCOMMODATE THIS TYPE OF NETWORK.

Your site may need to open specific firewall ports. For a list of firewall ports that must remain open to support nSpire Health communications, see *Appendix 12.4* below.

3.4.2 ANALOG PHONE CONNECTION

1. Insert one end of the modem cable (RJ11) into an **analog** phone line
2. Insert the other into the modem receptacle on the back of the computer.

- The system will check to see if your modem is connected to an analog phone line.

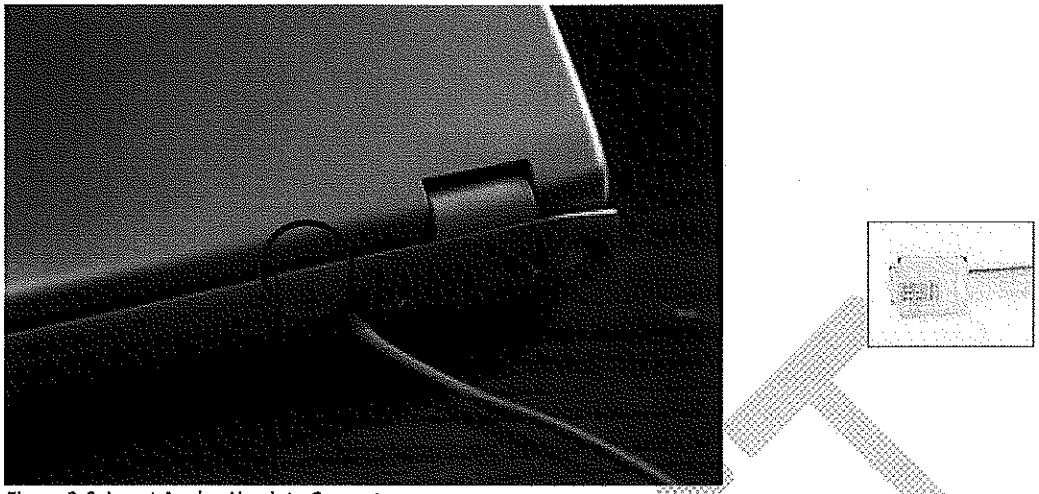


Figure 3-6, Insert Analog Line into Computer

NOTE: The telephone line MUST be an **analog** line. Connecting the system to a digital phone line could damage the eSP System.

NOTE: The AT&T Software will update the access numbers periodically. An icon in the system tray will appear when the updates are taking place. **Do not** cancel or bypass these updates. Follow the prompts allowing updates to run while you perform testing with the eSP System.

3.4.3 WIRELESS CONNECTION

- Laptop Computers need to show green on the wireless switch located on the front edge in order for the Wi-Fi to be enabled. The Switch displays not color then the Wi-Fi is disabled.

3.5 TURNING ON THE COMPUTER

1. Press the **power** button on the computer.

The following compliance message will appear:

> *In compliance with the United States FDA's 21CFR Part 11 regulations, this notice informs you of your responsibilities with regard to data entered into the KoKo Spirometry System.*
> *21 CFR Part 11.10 states: "Persons, who use closed systems to create, modify, maintain, or transmit electronic records shall employ procedures and controls designed to ensure the authenticity, integrity, and, when appropriate, the confidentiality of electronic records."*

2. After reading and agreeing to this statement, click **OK.**

You will be asked to use an identification code and password for all functions that create or modify subject data. It is important that you do not share this information. Should you suspect that someone else knows your identification code and password; have the site technician reset your account and create a new password.

NOTE: This computer is not for personal use.

3.6 WINDOWS LOG-ON

1. On the *Windows Login* screen type **"esp-user"** In the user name field.
2. In the *Password* field, type **"kokolink"** in all lowercase letters. This field is case sensitive.
3. Click **OK.**

Use this login information every time you log into Windows.

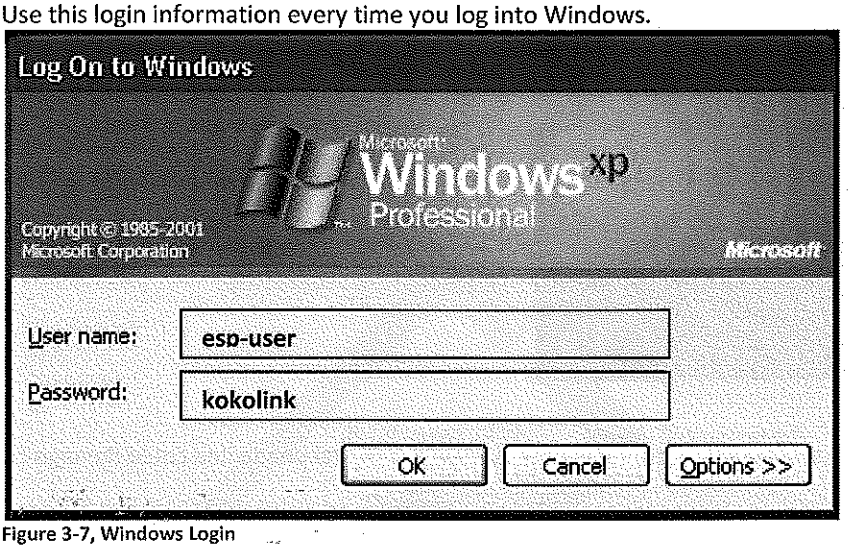


Figure 3-7, Windows Login

3.7 DATA TRANSFER (SYNCHRONIZATION)

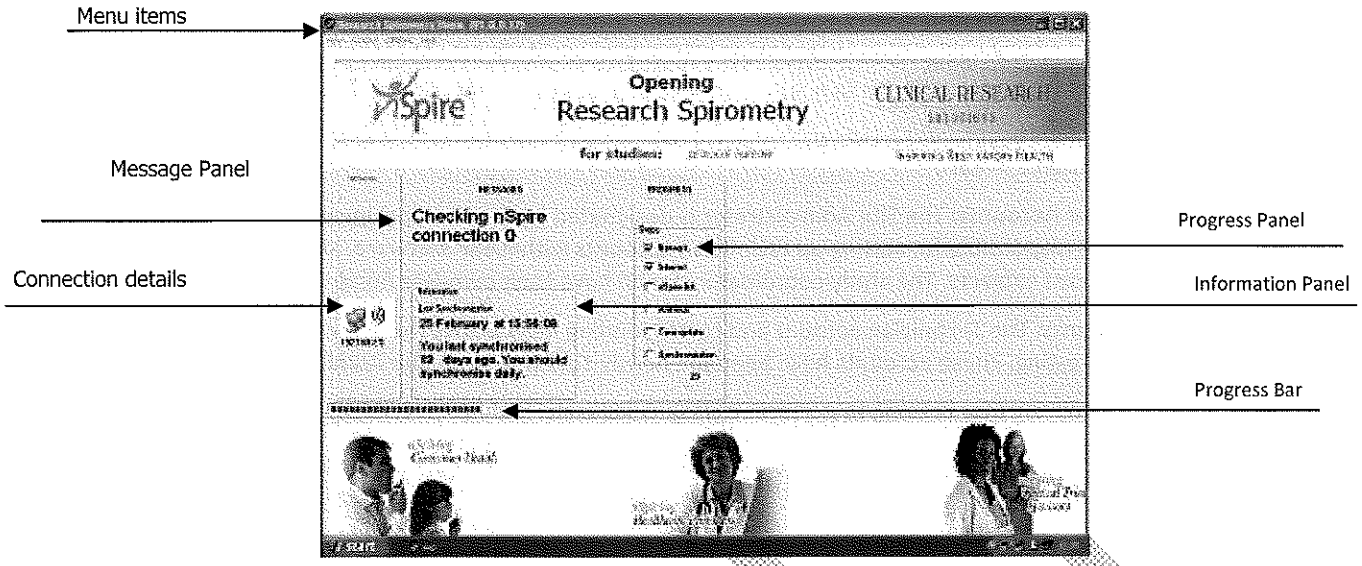
Synchronization will connect your computer to the nSpire Health central server and automatically download system updates and other important information to your study computer.

This crucial step will enable nSpire Health to:

- Confirm the system can synchronize with the central server
- Send eSP software updates and information
- Ensure the appropriate and current system setting
- Receive, assess and back up study data
- Send and receive eQueries

Data synchronization is automatically activated after logging into Windows *and* when closing down the eSP software. Throughout the study, synchronization MUST occur at the end of each testing day. Data is assessed by nSpire Health's Clinical Analysts and securely backed up.

NOTE: The system clock will be automatically updated to the correct date and time upon synchronization.



- **Menu Items** display submenus when selected.
- **Progress bar** scrolls, denoting activity.
- **Progress panel** reports the action being completed.
- **Message panel** describes the state of the action.
- **Information panel** shows the date of the last data transfer.
- **Connection details** show which network is being used to connect to nSpire Health, at least one mode should be displayed.


No connection to a network could be established.


A Modem Connection exists through an analog telephone line.


An Ethernet Network cable connection has been found.


A Wireless Network has been located and connected to.

When a network is found, the system will connect to the internet, establishing a secure connection and synchronizing your site's database with the nSpire Health server. During start up, the system will automatically update the antivirus software and correct the date and time. After successful synchronization the eSP application will open.

1. Disconnect from the internet.

After you've finished testing for the day, be sure to exit out of eSP and turn the computer off but do not close your laptop until the SYNC is finished and the Computer has powered off. If the laptop is closed during this process the SYNC will not complete and the computer will go into Hibernation mode.

If synchronization is unsuccessful you will be given the option to Test only and not connect

2. Select Option **Test Only.**

3.7.1 CONFIRMING REGIONAL SETTINGS

It is important that regional settings are correct, verification instructions are contained in *Appendix 13* below.

4 SETTING UP USER ACCOUNTS

4.1 TYPES OF ACCOUNTS

There are two types of accounts in eSP:

- **Site Administrator Accounts:** The Site Administrator is designated by the Principal Investigator (PI) as the only person at the site responsible for setting up technician accounts within eSP software. Site Administrator accounts cannot test subjects. The study coordinator should have their own Site Administrator account.
- **Technician Accounts:** The Technician account and corresponding login allows the individual Technicians to perform subject testing. These accounts have been previously set-up by your Site Administrator.
    - If the Site Administrator is going to perform testing a separate Technician account must be created.

4.2 SETTING UP SITE ADMINISTRATOR ACCOUNTS

4.2.1 LOG IN TO ESP

- The *eSP Login* screen will automatically open after synchronization.

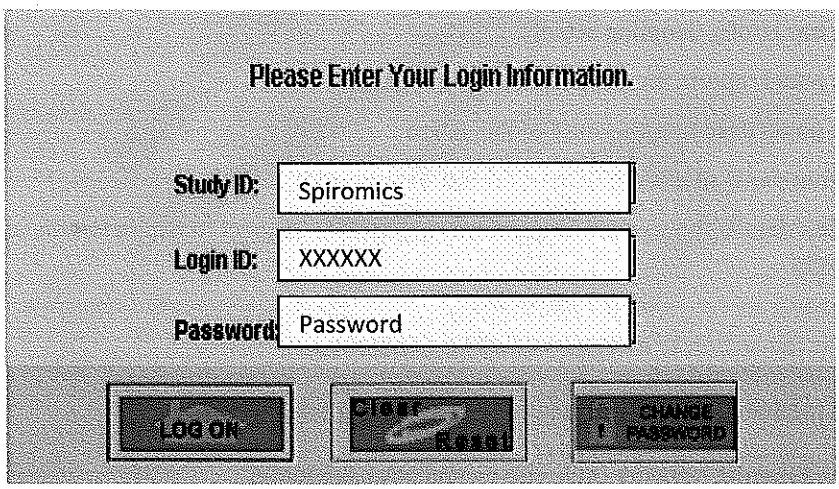


Figure 4-1, Study Log On Screen

4.2.1.1 CREATING A SITE ADMINISTRATOR ACCOUNT

1. Enter SPIROMICS in the *Study ID* field and press **Tab**.
2. Type the ***first 6 letters of the PI's last name*** in the **Login ID** field and press **Tab** to continue.

If the PI's last name contains less than 6 letters, use x's to fill in the remaining characters. (i.e. "Roy," becomes "Royxxx")

NOTE: If the PI wishes to designate someone else to function as the Site Administrator, the PI must first log on and create another Administrator account.

3. Type '**password**' in the *Password* field and click **LOG ON**.
4. eSP login fields are NOT case sensitive.

5. The system will prompt, *"Your Password is currently the Default Password. Please Change Your Password."* Click **OK**.

4.2.2 CHANGE PASSWORD

Upon logging onto the system for the first time, you MUST change your password.

- The system will proceed to the *Password Change* Screen.
- The *Study ID, Login ID* and *Current Password* will be populated based on your entries.

1. Enter your new **password** in the *New Password* field. (Passwords must be 5 to 15 characters in length.)
2. Enter your new **password** again in the *Confirm Password* field.
3. Click **SUBMIT**.
    - Read the ICPF Acceptance terms and, if acceptable, click **I Accept**.
4. Click **SUBMIT**.
5. Enter your *Login ID* and click **OK**.
    - Your password has now been changed.

NOTE: Do NOT share your new password with anyone.

You are now logged in as an Administrator and the system will display the *eSP Home* Screen.

4.3 SETTING UP TECHNICIAN ACCOUNTS

Technician and Site Administrator **Login ID** must be different from one another.

- An Administrator must be logged in to create Technician accounts.

1. Select **Contacts** from the *Admin* menu or click **CLIENTS** on the *eSP Home* screen.

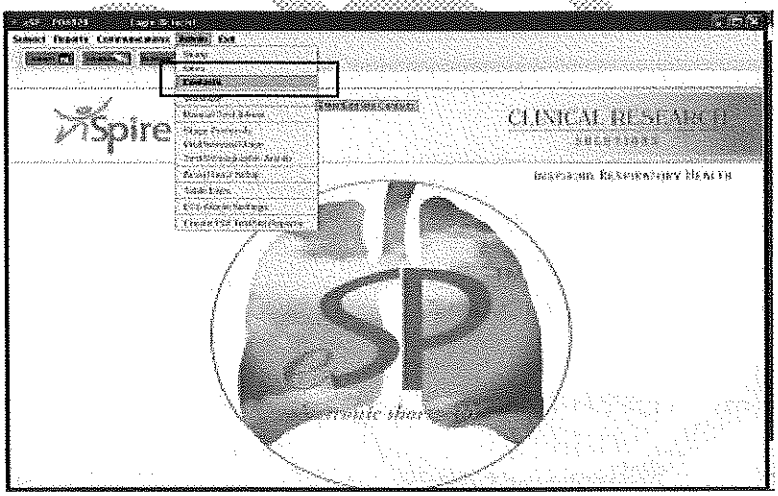


Figure 4-2, Admin Menu - Select Contacts

The title bar will display the Login ID of the Administrator who is currently logged in.

2. The system will advance to the *Site Contact Administration* Screen.

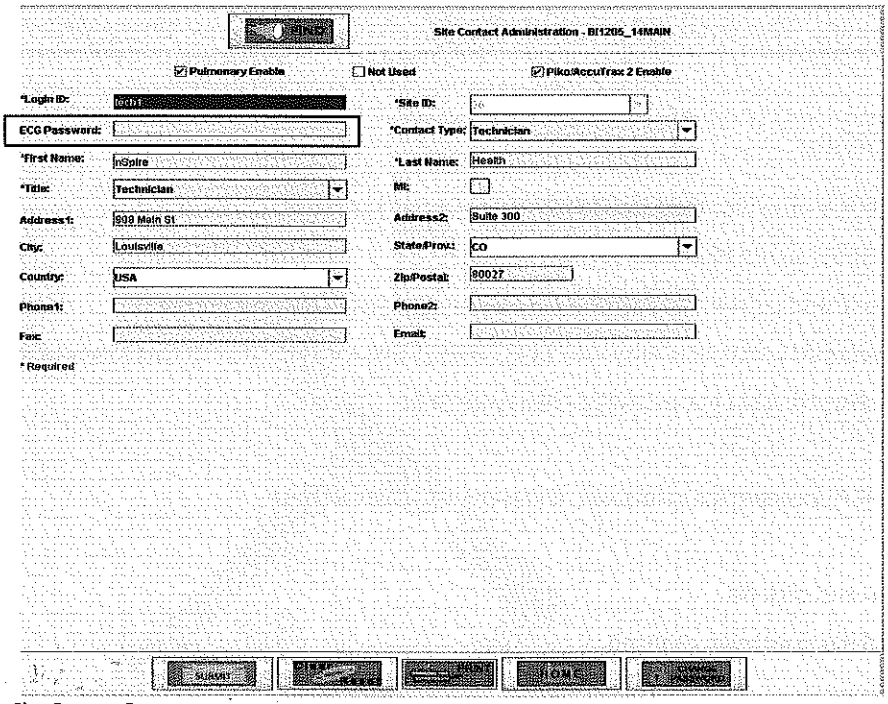


Figure 4-3, Site Contact Screen

3. Enter in a user ID for the Technician.
   - The *Site ID* field will be filled in automatically.
4. Select **Technician** at the **Contact Type** from the drop-down list.
   - The **Contact Type** selected will determine the level of access the user has to the system, if 'Technician' is not selected the account holder will not be able to perform tests.
5. Click **SUBMIT.**
   - A message box will appear stating the information has been successfully saved in the *eSP* System.
6. Click **OK.**

4.3.1.1 ENTER ADDITIONAL TECHNICIANS,

1. Click **Clear/Reset** to empty the content fields.
2. Repeat steps outlined in Step 3 above.

4.3.2 RECALLING AND EDITING EXISTING TECHNICIAN

1. Log on as an Administrator.
2. Select **Contacts** from the *Admin* menu *or* click **Clients** from the *eSP Home* Screen.

The system will advance to the *Site Contact Administration* Screen.

3. Enter the **Login ID** and click **FIND**.
   - The Technician information will appear.
   - The profile will display, edit information as necessary.
4. Click **SUBMIT** when complete.

4.3.3 LOGGING IN AS A NEW TECHNICIAN

1. Open the eSP application

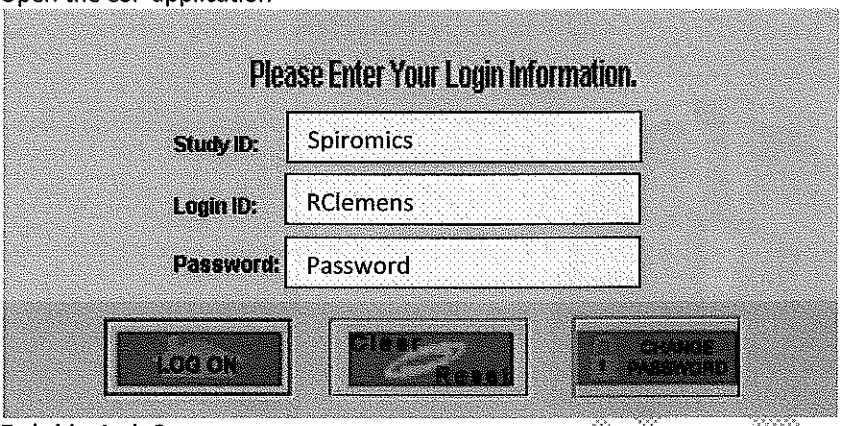


Figure 4-4, Technician Login Screen

2. Enter SPIROMICS in the *Study ID* field and press **Tab**
3. In the *Login ID* field type your **Login ID** and press **Tab**

NOTE: Your Login ID was setup by the Site Administrator.

4. Enter **password** in the *password* field, click **LOG IN**
   - The first time you login the system will prompt, "Your Password is currently the Default Password. Please change your Password."
5. Click **OK**.
   - The system will proceed to the *Password Change* Screen.
   - The *Study ID, Login ID* and *Current Password* will be populated based on your entries.
6. Enter your new **password** in the *New Password* field. (Passwords must be 5 to 15 characters in length.)
7. Enter your new **password** again in the *Confirm Password* field.
8. Click **SUBMIT**.
9. Read the ICPF Acceptance terms and, if acceptable, click **I Accept**.
10. Click **SUBMIT**.
11. Enter your *Login ID* and click **OK**.

Your password has now been changed. Do **NOT** share your new password with anyone.

You are now logged in and the system will display the *eSP Home* Screen.

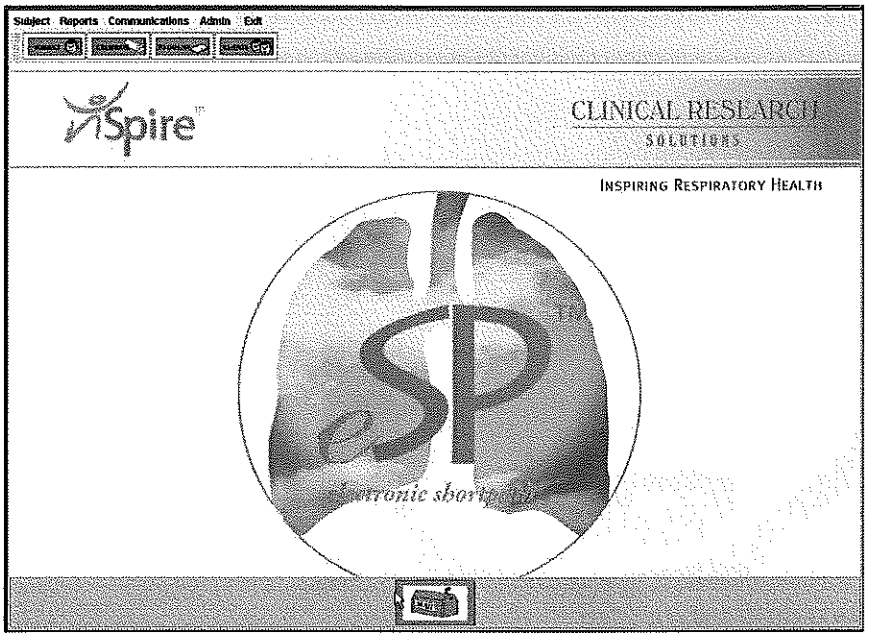


Figure 4-5, eSP Home Screen

4.4 TECHNICIAN CERTIFICATION AND ENABLEMENT

Certification and enabling are required for each Technician performing spirometry testing for the SPIROMICS clinical trial. At the end of this section, the following steps must be completed for Certification and Enablement within the eSP application.

1. Review the System Users Guide
2. Complete and fax the required Site Certification Forms (SCF) to nSpire Health.
   a. Calibrate the spirometer.
   b. Print the calibration report.
   c. Fax to nSpire Health.
3. Perform a practice FVC test, showing three (3) or more acceptable and two (2) or more repeatable efforts.
4. Synchronize the system.
5. Print and fax practice test results to nSpire Health.
6. Complete nSpire Health Training.
7. Allow enough time for nSpire Health's Clinical Analysts to review your submission.
8. When notified, synchronize the system again to download the 'enabled' status.

4.4.1 SITE CERTIFICATION FORMS (SCF)

As part of the Certification and Enablement process each Technician is required to complete and fax the following forms to nSpire Health:

- Investigator Statement – One per study site. Used to designate the Site Administrator
- Technician Certification Checklist – One per Technician
- Security Statement – One per Technician

These forms are part of the delivery of the system to each site.

5 CALIBRATION

5.1 HOW TO CALIBRATE THE SPIROMETER

In accordance with the study protocol, the testing system must be calibrated each testing day. Calibration can be performed at any time by following the steps below.

NOTE: Do not be alarmed by the daily "*Calibration Expired*" message. The system is only reminding you to calibrate at the start of each new testing day.

5.1.1 CONNECTING THE KOKO PNEUMOTACH

9. Connect the KoKo pneumotach to the computer.
10. Attach a KoKo filter to the KoKo pneumotach.
11. Connect the calibration syringe to the KoKo filter.

If an optional USB weather station is available, connect it at this time. Make sure not to place the weather station near a heat or cooling source, such as the computer or an air-conditioning duct.

Figure 5-1, KoKo Spirometer and Components

5.1.2 ENTER ENVIRONMENTAL CONDITIONS

12. Click **Calibrate** on the *eSP Home* Screen.
    - The system will advance to the *Calibration* Screen
    - If the weather station is connected it will automatically measure and enter values for the environmental variables.
    - If you change these values for any reason, you will be prompted to enter a reason for the change.
    - If a weather station is not available or not detected:
    - Warning Weather Monitor dialog will display.

Figure 5-2, Warning Weather Monitor Dialog

13. Click **Cancel** to manually enter the conditions.

- Temperature is in Celsius
- Barometric Pressure is in millimeters of mercury
- Humidity is a percent (if unknown use 50%)

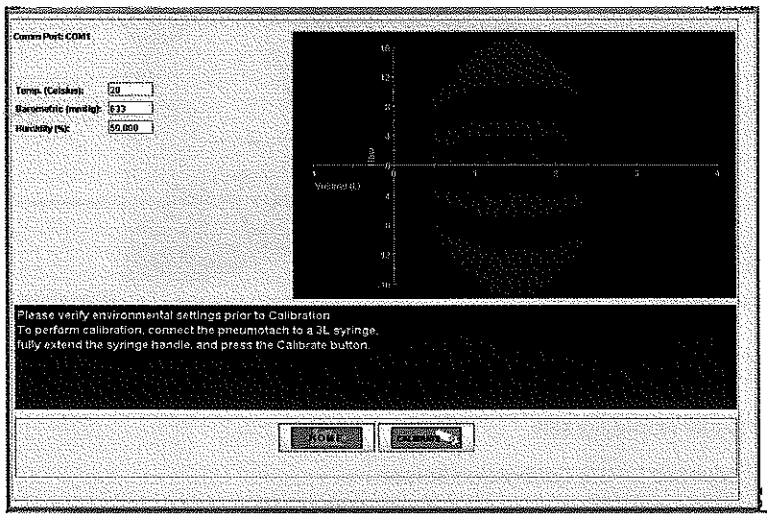
OR

- Connect the weather station, wait 10 seconds and click Retry.

Ensure that environmental variables are accurate to your ***testing room***. If they are not, click **Cancel** and manually enter the correct values.

NOTE: Room temperature is the most significant variable and must be properly monitored and entered. In the event that room temperature changes by more than ± 5º C, the system must be recalibrated.

14. Once all fields are filled in, fully extend the syringe handle.
15. Click **CALIBRATE.**
    - Wait for the pneumotach to zero, the message "*Zeroing Device*" will display in the red text area.
16. Perform calibration at Low, Mid, and High flow rates.
    - One stroke per flow rate



5.1.3 FLOW RATES

To achieve these flow rates vary the speed at which the syringe handle is pushed in and pulled out. The following is required for Certification:

- Low flow rate cycle (0-4L/sec)
- Medium flow rate (4-8L/sec
- High flow rate cycle (8-12L/sec).

Green shaded areas have been provided on the Calibration Screen to help guide your efforts.

17. Press the **<spacebar>** when complete.
    - The system automatically adjusts the calibration and displays the Calibration Report.
18. Select **Print** to print the *Calibration* Report.
    - A sample calibration report can be found in the *Reports* Section.
    - File the report

NOTE: The Calibration report with tracings can ***only*** be printed at this time. To verify calibration at any other time, select the **Calibration Log Report** from the *Report* Menu options.

19. Click **Close** to return to the *Calibration* Screen.
20. Press **HOME** to return to the *Home* Screen

TIP: TEMPERATURE AND BAROMTERIC PRESSURE VARIATION AFFECT TEST RESULTS.
All spirometers meeting ATS/ERS 2005 guidelines adjust the subject's spirometry values to normalize them for room temperature and barometric pressure conditions. Room temperature and barometric pressure are used to correct for the difference between the subject's exhaled/inhaled air volumes. The correction brings the measured volumes back to the condition of the air volume while in the subject's lungs (BTPS). A change of several degrees in room temperature can affect the accuracy of the spirometric results. A change in barometric pressure can also affect the BTPS correction of the spirometer.

Technicians are required to check current environmental conditions before performing SVC/IC or FVC tests. If environmental conditions have changed since the last calibration, recalibrating the spirometer with the new settings is recommended. eSP allows the Technician to enter the current envoronmental conditions at the time of the calibration. The testing room should have an accurate thermometer and barometer.

6 LINEARITY CHECK

A linearity check is an additional volume calibration check performed using a 3-liter syringe to deliver three constant flows at three flow rates: low, mid, and high, for a total of 9 strokes.

Linearity checks are performed per protocol guidelines. After successful calibration, a prompt will appear if a linearity check is required, advancing you to the linearity screen.

To manually open the linearity screen:

1. Click Linearity on the *eSP Home* Screen or select Linearity Check from the *Subject* Menu.

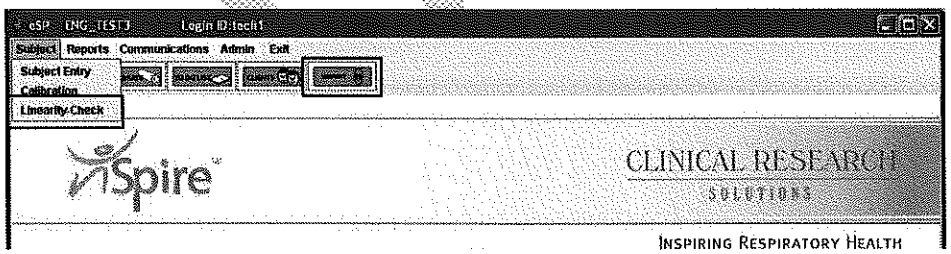


Figure 6-1, Opening the Linearity Screen

2. Follow the instructions in the colored box to perform three successful strokes at each target flow rate.
3. Click **Linearity**.

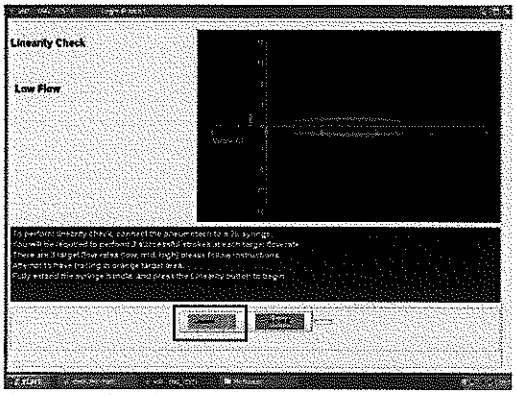


Figure 6-2, Linearity Screen

- If the system has not been calibrated a message will appear informing you to calibrate before performing a linearity check.

Figure 6-3, Calibration Required Dialog

- The system will display the message "**Zeroing Device**" in the colored text area.
- After zeroing, the system will prompt you to cycle the syringe at target flow rate until the linearity condition is met.
- Orange target lines are provided to help guide your efforts.
- Helpful hints to achieve target flow rates appear in color alongside the graph.

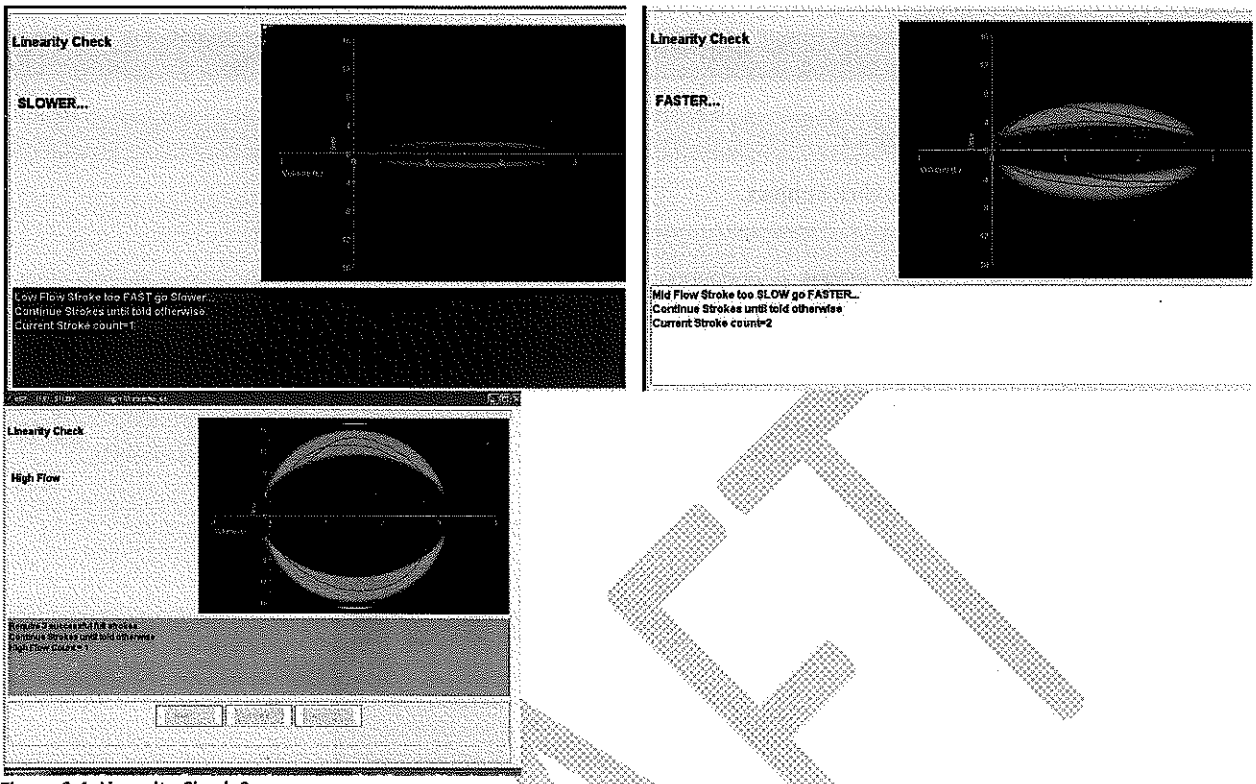
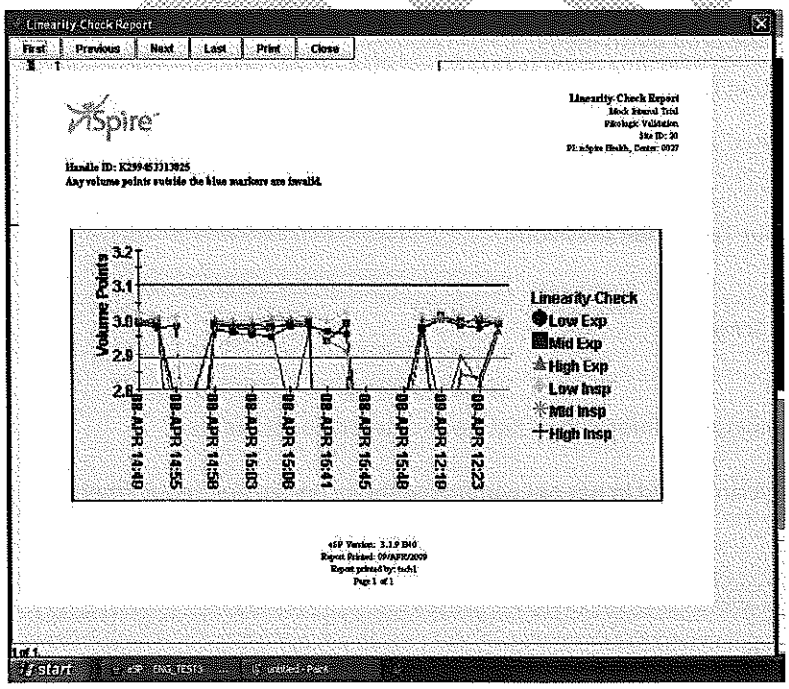


Figure 6-4, Linearity Check Screens

- Once 3 flows at the target rate have been achieved, the graph will switch to the next flow rate until all flow rates have been achieved.
- A confirmation message will appear once the check is complete.

4. Click **OK** to exit.

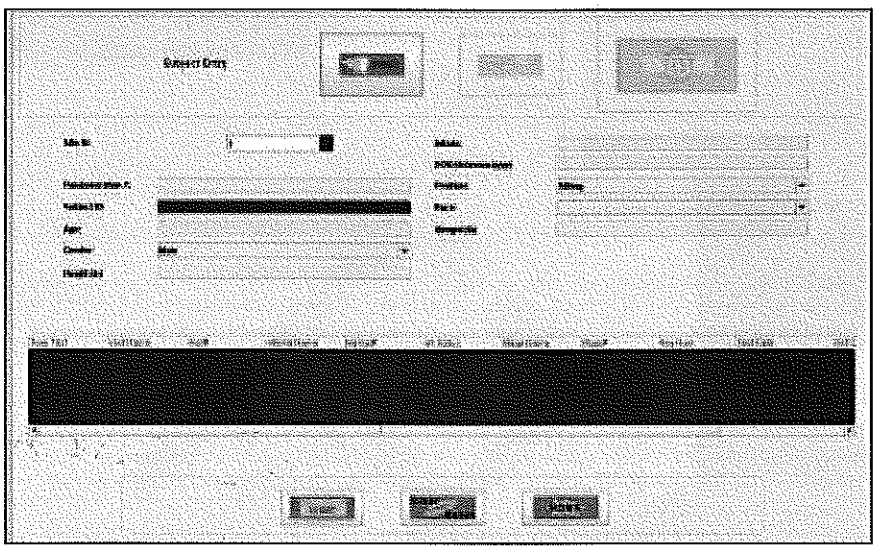
- The linearity report will display and can be printed.



7 SUBJECT ENTRY

7.1 CREATING A NEW SUBJECT

1. At the eSP *Home* Screen, click **Subject.**



2. Enter require subject demographic information:
   - 6-digit **Screening** number. Format = NNNNNN (range000001-999999).
   - **Age** (range 40-80).
   - **Gender** at Birth from the pull-down menu.
   - **Height** (range XX-XX) in centimeters.
   - **Date of Birth** as DD/MMM/YYYY (e.g., 22/JUN/1993).
   - Test **Position** via the options in the drop down menu.
     - This position must remain constant throughout the trial.
   - **Race** using the drop down menu.
3. Click **SUBMIT**.
4. For confirmation purposes, *enter* your Technician password.
5. Click **OK**.
6. Click **TEST** to advance to the testing screen.

NOTE: **TEST** will remain inactive until all demographic information has been entered and submitted.

NOTE: **TEST** will remain inactive if the Technician logged in has not completed their certification requirements and has not been enabled to test.

7.2 RECALLING A SUBJECT

1. At the eSP *Home* Screen, click **Subject**

2. If the screen is populated with data, click **CLEAR/RESET** to clear the entries.
3. Enter the **Subject ID**
4. Click **FIND**

The subject's demographics appear along with previously performed test sets. The **TEST** option will now be active. If the subject is not in the system, a window will appear stating that the subject does not exist. Recheck your ID number, if it does not work you will need to create a new subject.

5. Click **Test** to advance to the *Visit Interval Stage* Selection screen.
    - You may be prompted to enter your Technician **password**.

- To view a previous test, **click on the row** containing the desired test.
- To recall a different subject, click **clear/reset** the repeat steps from above.

7.3 EDITING SUBJECT DEMOGRAPHICS

1. Recall a subject's demographics.
2. Change information directly on the *Subject Entry* screen.
    - For each change made, the system will prompt you to enter a reason for the change.

NOTE: Test results cannot be edited.

3. Click **SUBMIT**.
4. For confirmation purposes, enter your Technician **password**.
5. Click **OK**

8 ESP SPIROMETRY TESTING

8.1 PRACTICE SPIROMETRY TEST

Prior to subject testing, it is required to first perform acceptable practice spirometry tests using the eSP system. Each Technician must log on using their own *Login ID* to perform the following tasks.

1. Calibrate the spirometer and print the calibration report. (Refer to *Section 6* for instructions.)

NOTE: The system only allows entry of a temporary ID for the Practice Subject ID which must be in the format of "Test-*your Login ID*". (i.e., if your Login ID is "Tech1," you would enter "Test-Tech1".)

- Perform one (1) practice test of the FVC, as specified within the Technician Certification Checklist; each test consists of three (3) or more efforts for the FVC. (Refer to *Section 6* for testing instructions.)

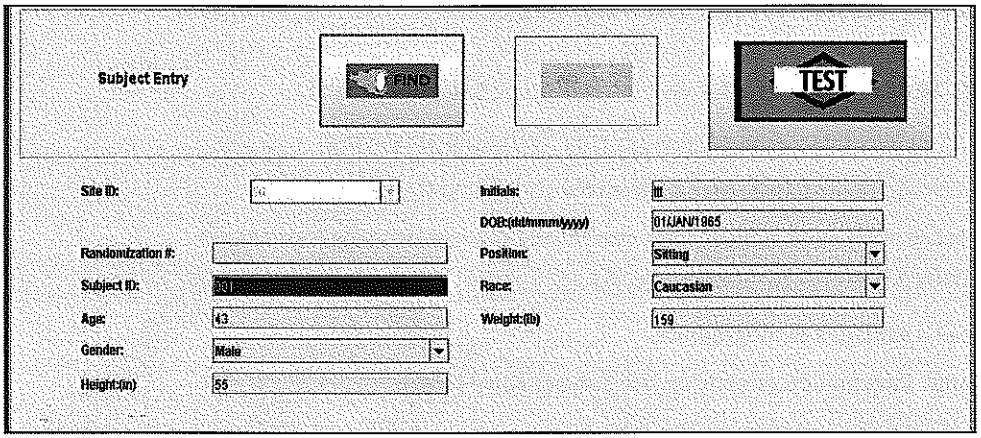
1. Once all practice tests are complete, synchronize to transmit efforts to nSpire Health.

- Once the SCFs have been received, and the calibration and practice spirometry tests have been approved, nSpire Health will enable the Technician.
    - Sites will be contacted if the calibration and/or practice spirometry do not meet acceptable criteria.

NOTE: A minimum of 48 business hours from time of transmission is required for enablement.

8.2 SPIROMETRY TESTING: FVC

1. Enter or Recall the Subject.
2. Click **Test.**



3. The system will prompt for confirmation, enter your **Technician Password.**
4. Click **OK.**
5. Confirm correct information at the *Visit/Interval/Stage* Screen .

- If it is *not correct, make* the appropriate changes from the drop down menu options.

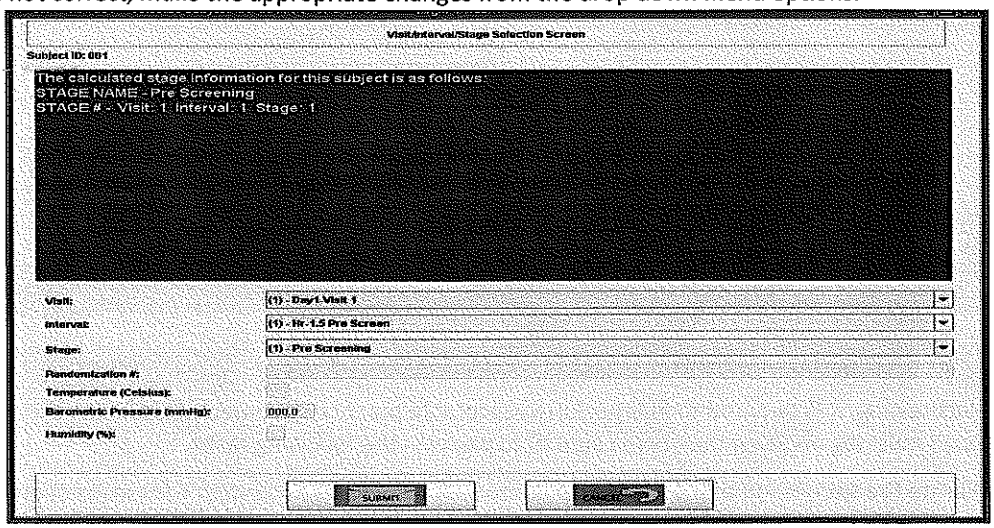


Figure 8-1, Visit/Interval/Stage Screen

NOTE: eSP calculates the next expected Visit, Interval and Stage for a selected subject. Once a test is complete, the system advances to the next expected Visit/Interval/Stage. When the system selected information is changed an exception box will appear, you must enter an explanation for the change.

6. Click **SUBMIT.**
7. The system will advance to the *Testing* Screen and prompt for confirmation of the Subject ID.
8. Enter the **Subject ID** and click **OK.**

9. Place a new filter on the KoKo Spirometer.
    - The arrows on the side of the spirometer indicate the direction of expiratory flow and point away from the subject.

NOTE: Use a new filter every time you test a subject.

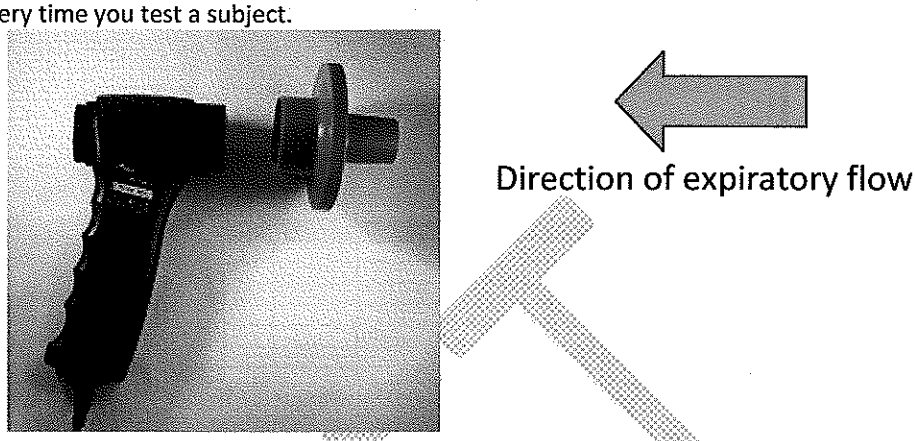


Figure 8-2, Attaching KoKo Filter

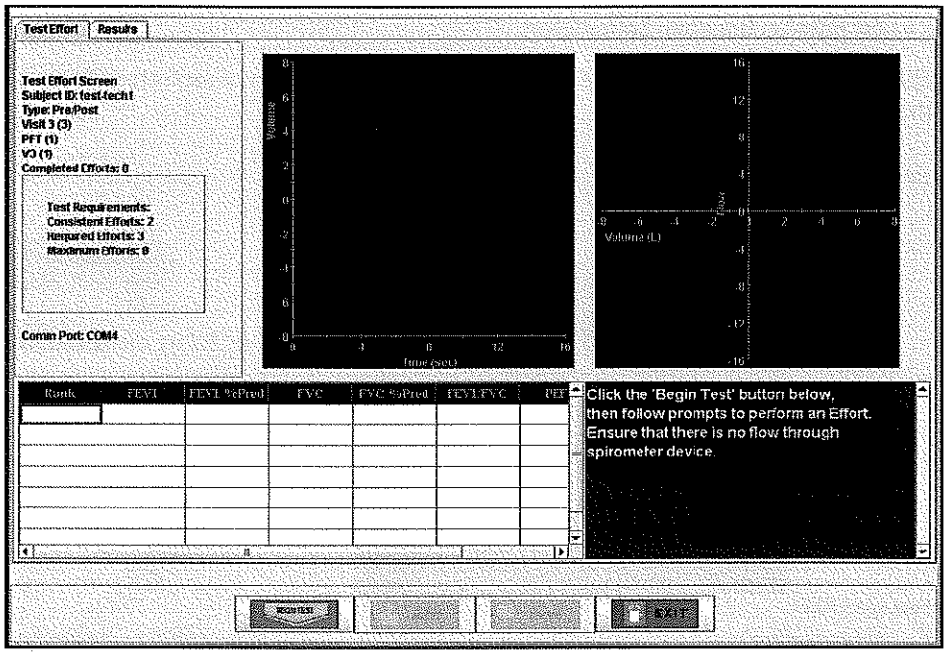
10. Click **BEGIN TEST** to perform each new effort.
    - Precise and forceful coaching by the technician is required to achieve maximal results
11. Wait for the KoKo Spirometer to zero before performing the maneuver.
12. Ensure that no flow moves through the pneumotach at this time. "*Begin Tidal Breathing Now*" will appear.
13. Place the mouthpiece/filter in the subject's mouth, ensuring a tight seal with no leaks.
14. Instruct the subject to breathe comfortably on the mouthpiece for 2-3 normal (tidal) breaths
15. Observe the subject's breathing. At the end of a normal exhalation, instruct the subject to take a maximal inspiration.
16. Press the **spacebar** during this maximal inspiration to start capture the effort.
    - The color of the tracing will change from yellow to red, to indicate that the system is in measurement mode.
17. Coach the subject to exhale as hard and as fast as they can without hesitation.
    - They should continue to exhale for at least 6 seconds.

Once the subject blasts the air out they must continue to blow until completely empty. A prompt will let you know that they've exhaled for more than six seconds and/or have reached a one second plateau. The information box will turn green when end-of-test criteria are met.

NOTE: The subject can continue exhaling, if necessary, even though the information box turns green.

18. To complete the maneuver ask the subject to inspire quickly and fully again.
19. Press the **Spacebar** upon completion of the effort.
20. The subject can remove the mouthpiece/filter.
21. The **ACCEPT** and **DISCARD** icons will become active.
22. Messages regarding test quality will be displayed in the red Information area.

NOTE: Test efforts should be graphically and numerically consistent.



8.2.1 VIEW MORE DETAILED TEST RESULTS

1. Click the **Results** tab.
2. Predicted values and test effort values will be displayed.

- The effort with the Highest FEV1 value will be indicated by a ☑ in the column labeled "**Best Test**"

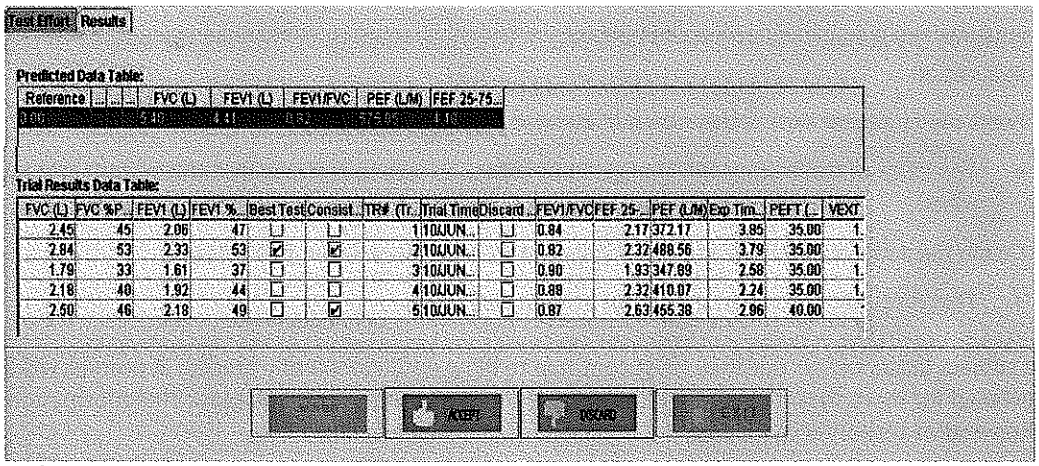


Figure 8-3, Accept / Discard Effort

3. After reviewing the information thoroughly, click **ACCEPT** or **DISCARD**.
4. Click **BEGIN TEST** to perform additional efforts.

NOTE: Testing should be performed until all test and acceptability requirements are met.

5. eSP software has an automatic discard feature, allowing the system to reject the test if predetermined protocol specific criteria are not met. If this occurs you will *not* be able to choose accept or discard and DIS will appear in the flag column on the *Results* tab screen.

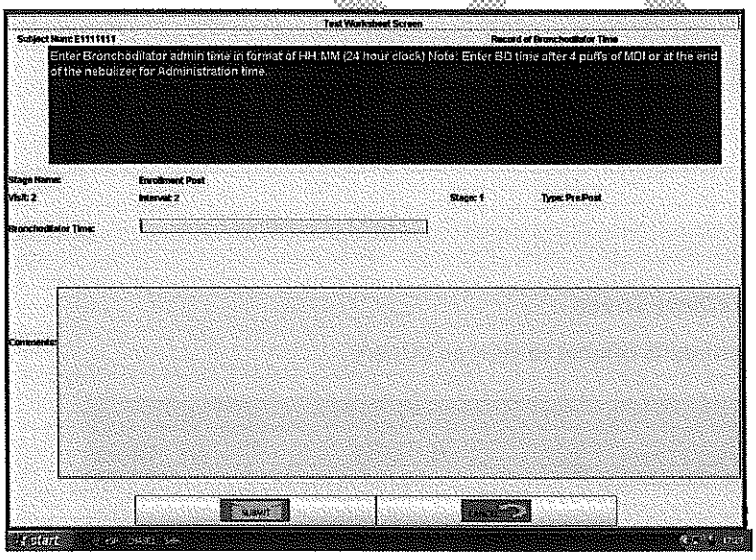
- You may see several quality flags during testing.

- Quality flags are described in Appendix 12.3.1

6. When testing is complete, click **EXIT**.
   - A comment box will appear displaying visit specific messages; review all messages thoroughly before advancing to the next screen.
7. Click **OK** to advance.
8. The system will prompt for confirmation of exiting.
9. Click **OK.**

8.3 WORKSHEET

At Visit 2 post test a worksheet will be presented for documenting the time of the bronchodilator. The time of Bronchodilator administration is a mandatory field. Please enter a value in HH:MM (24 hour clock).



After filling in the value click on Submit to perform the Visit 2 post test
At the testing screen a timer will appear showing elapsed time. The post test will not allow testing until 15 minutes after the entered bronchodilator time. When 15 minutes or more have elapsed click Begin Test to continue testing.

9 EQUERIES

eQueries allow communication between nSpire Health and study sites. An eQuery is an electronic data clarification form (DCF). Communication only occurs during routine data transfer or synchronization.
eQueries are bi-directional. Although they are typically generated by nSpire Health regarding data information, sites may also send eQueries to nSpire Health.
The most common eQuery topics are: new best selections, unacceptable testing, incomplete test sets, or protocol deviations.

9.1 ACCESSING AN EQUERY

Notification that an eQuery has been generated appears in the form of a mailbox on the eSP *Home* Screen.
There are two ways to access the eQuery:

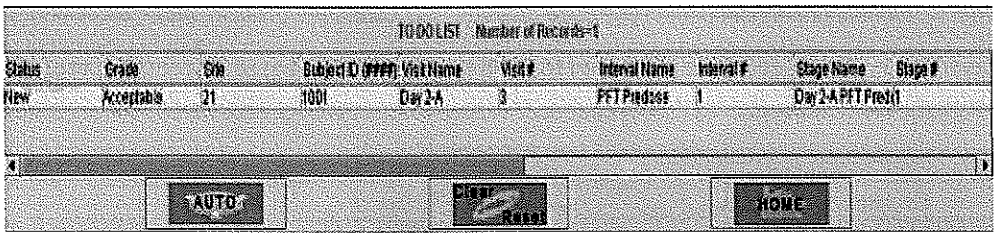
1. Click the **Mailbox** icon

   OR

2. Click the **To Do List** tab.

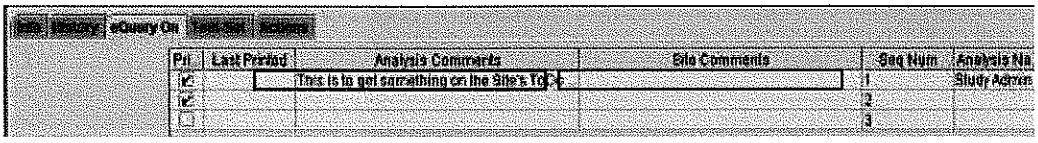
3. The system will advance to the subject records listed in the **To Do List**
4. Access an eQuery by clicking on the desired subject record listed below the header line

- The application will advance to the *QA* Screen for the selected record



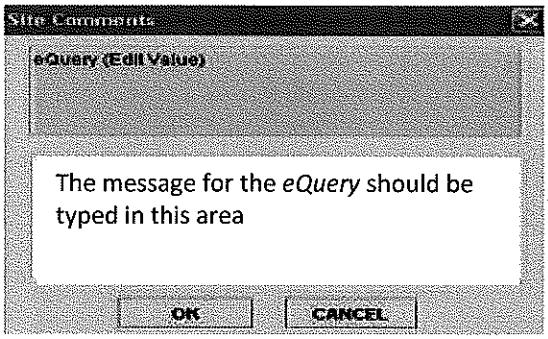
9.2 RESPONDING TO AN EQUERY

1. Click the **eQuery** tab to advance to the *eQuery* Screen
2. Click on the line within the **Analysis Comments** column to view an eQuery



3. Click **OK**
4. To respond, click on an entry within the **Site Comments** box, in the same row as the Analysis Comments.

5. In the resulting pop-up box, type your eQuery message



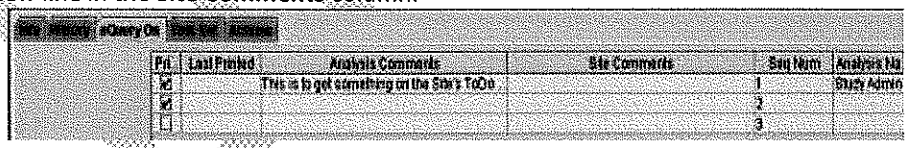
6. Click **OK** to continue
7. A pop-up box will appear
8. Type in your **password**
9. Click **OK**
10. Click **SUBMIT** to save your comment.
11. Failure to click **SUBMIT** will void your comment
12. Click **EXIT** to return to the **To Do List.**

eQueries are transmitted between nSpire Health and the study site during regular synchronization.

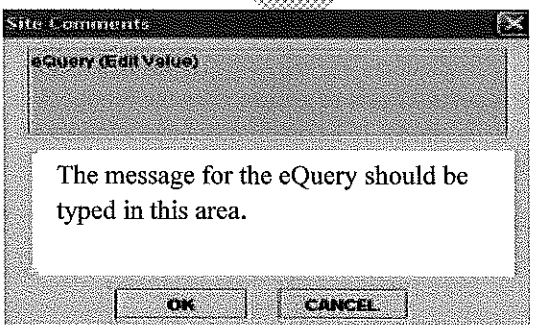
9.3 CREATING EQUERIES

Sites can create their own eQuery by following the instructions below:

1. Recall a subject (see section 7.2 for details)
2. Previously performed tests are be displayed in the lower portion of the *Subject Entry* Screen
3. Click on the row containing the desired test. The system will advance to the *QA* Screen
4. Click the **eQuery** tab
5. Click an new line in the **Site Comments** column.

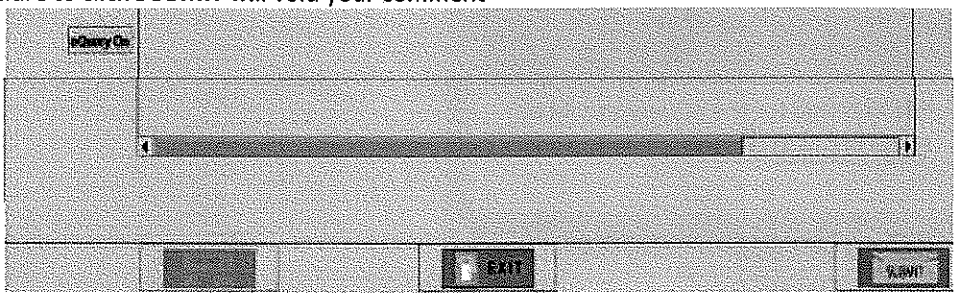


6. In the resulting pop-up box, type your eQuery message



7. Click **OK** when finished typing the eQuery message

8. Enter your **password** in the pop-up box
9. Click **SUBMIT** to save your comment
   - Failure to click **SUBMIT** will void your comment



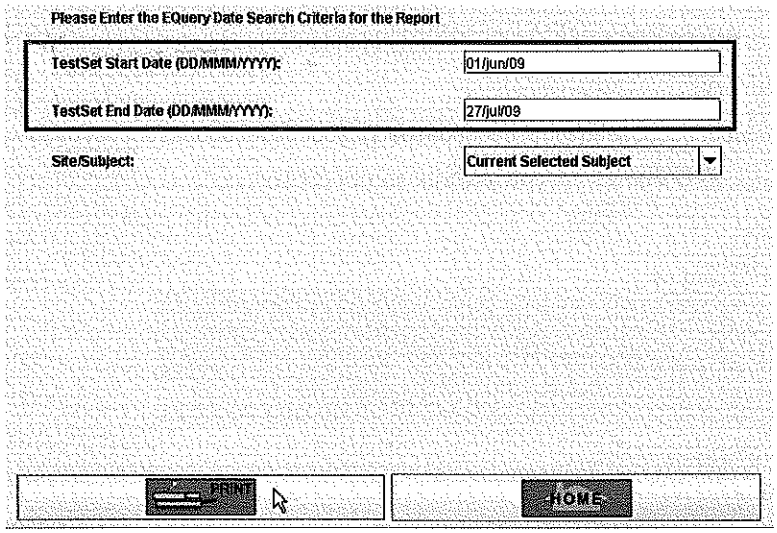
10. Click **EXIT** to return to the *Subject Entry* Screen

Your eQuery message will be transmitted at the next synchronization.

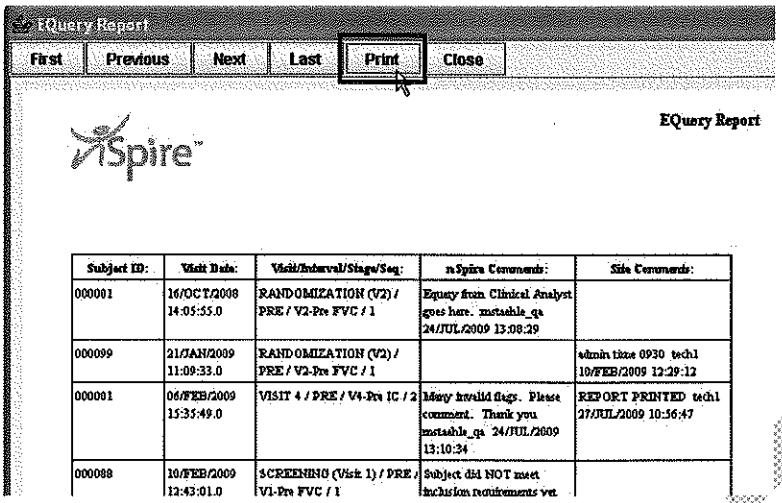
9.4 PRINTING EQUERY SUMMARY REPORT

To view a report:

1. Select **eQuery Summary Report** from the Report menu located on the *eSP Home* Screen.
2. Enter the desired date range for the report criteria you want to see.
3. Click **Print** to generate a preview.



NOTE: nSpire Health recommends that you review these reports weekly to ensure valuable feedback that could impact your study is not overlooked. Never assume an eQuery is closed. It is common to have a follow up eQuery. On the *report preview* screen you can print a copy of the report for your records.

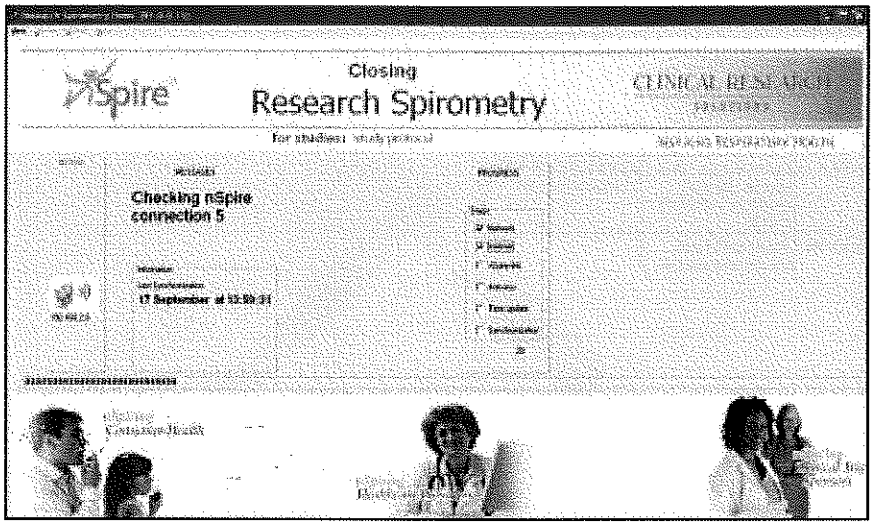


4. Select **Print.**

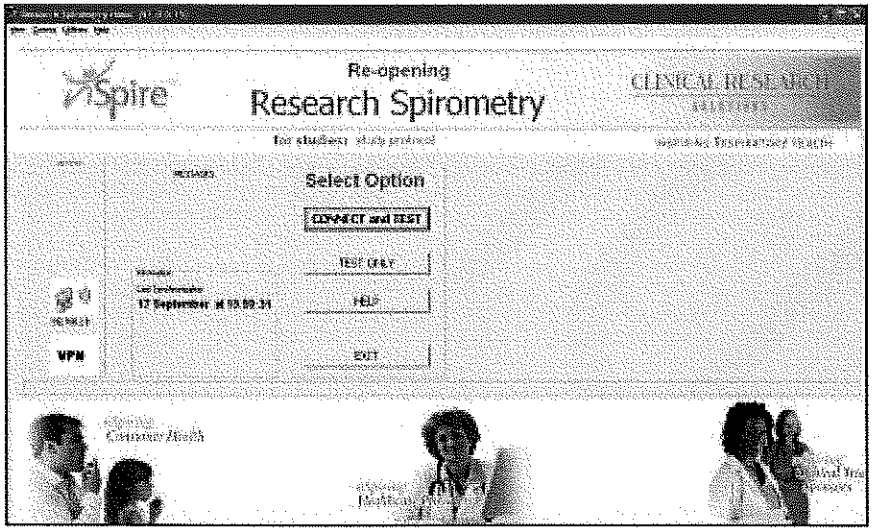
10 EXITING THE ESP SYSTEM

1. Click **Exit** in the menu bar to "log off" but not closing the eSP application.
2. Click the close window **(X)** box in the upper right corner of the window to close out of the eSP application.

- eSP will close and the following screen will display.



3. Upon successful synchronization the screen will show *Research Spirometry 'Re-Opening'*.
4. At this point the test session is usually finished and 'EXIT' would be used to close the computer, but other options are presented via **'Select Option'**.



5. Choose **CONNECT and TEST**, if another session is required.
6. **HELP** shows user instruction for the study or the program.
7. **TEST ONLY** is used when no network is available.

- Synchronization should always be done within hours of testing.

11.1 CALIBRATION REPORT

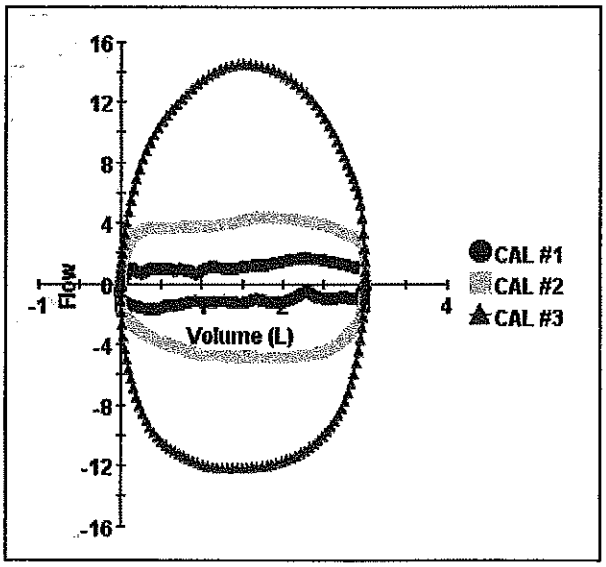
Calibration Report

nSpire Site ID: 22
PI: No Primary Investigator

Calibration Performed: 04/DEC/2009 16:12:49
Calibration Successful on Device #K299A38313025

Measured Value	Expected	Measured	% Expected	Measured	% Expected	Measured	% Expected
FVC	3.000	2.997	99.89	2.999	99.97	3.006	100.19
PEF (L/S)		1.674		4.367		14.495	

Temperature (Celsius): 22 Barometric Pressure (mmHg): 630 Humidity (%): 50
Calibration Performed by: tech1



Authorized Signature:_____ Date:_____

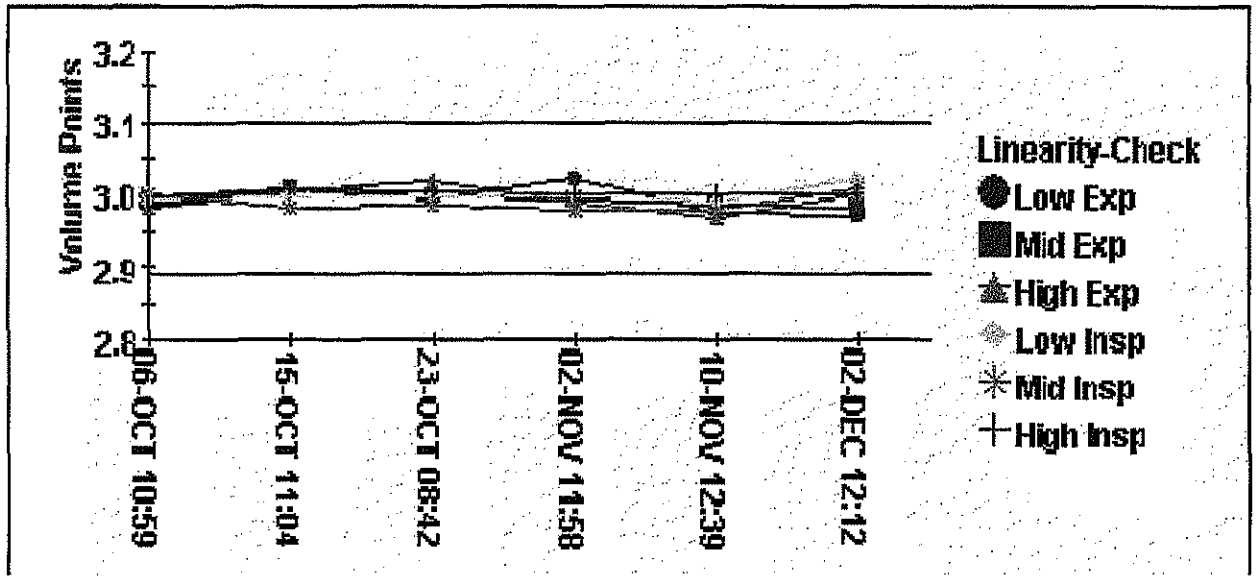
eSP Version: 3.1.9 B95 SPXXX
Report Printed: 04/DEC/2009 16:12:49
Report printed by: tech1
Page 1 of 1

nSpire

Linearity-Check Report

nSpire Site ID: 22
PI: No Primary Investigator

Handle ID: K299A38313025
Any volume points outside the blue markers are invalid.



eSP Version:
Report Printed: 04/DEC/2009 16:09:47
Report printed by: tech1

11.3 SPIROMETRY REPORT

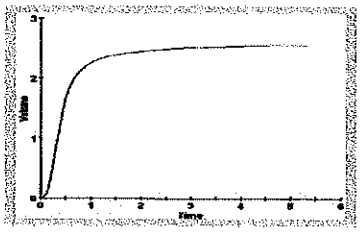
Spirometry Report

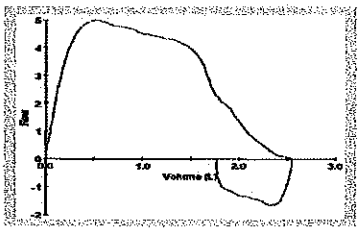
nSpire Site ID: 23
PI: No Primary Investigator

Screening ID: S-00005 | Initials: | Race: Non-Black
Gender: F | Age: 46 | Date of Birth: 12/OCT/1963
Position: Sitting | Height: 160.0 | Weight: 66.0
Visit: Visit 1 Screening (1) | Interval: Pre FVC (2) | Stage: V1 Pre FVC (1)
Randomization #: 1001 | Enrollment Code: | Tech: tech1
Predicteds: nHANESIII_P05575
First Test: 09/DEC/2009 08:46:55 | Best Test: 09/DEC/2009 08:46:55 | Last Test: 09/DEC/2009 08:46:55
Report Comments:
Repeatability Check NOT Reached.(FVC & FEV1)

Function	Pred	B-Meas	%Prd	Meas	Meas	Meas	Meas	Meas	Meas	Meas	Meas	Comp
FVC (L)	3.489	2.554	73.20%									2.554
FEV1(L)	2.8	2.309	82.46%									2.309
FEV1/FVC (%)	0.81	0.90	111.11 %									0.90
PEF(L/M)	402	299	74.38%									299
FEF25-75% (L/S)	2.855	3.597	125.99 %									3.597
VEXT L		0.100										
VEXT (%)		3.91										
FLAGS		BST										
EXP TIME		5.340										

Attempts for this Stage: 1. Ranking order: 1 Graphs in Rank Order





Authorized Signature:_____ Date:_____

eSP Version: 3.1.9 B108
Report Printed: 16/DEC/2009 14:48:09
Report printed by: tech1
Page 1 of 1

[Please note: Percentage figures are rounded to the nearest whole number for convenience. This can lead to confusion where for example in reversiblity a subject does not meet inclusion at 11.6% but is reported to be 12%]

12 APPENDIX

12.1 KOKO SPIROMETER SPECIFICATIONS

The KoKo Spirometer is manufactured by nSpire Health, Inc. as a pulmonary function testing device.

Pneumotach:	Brass Fleisch-type
Dimensions:	18 x 10 x 6 cm
Weight:	0.3 kg
Data Sampling Rate:	128/sec
Volume Scaling:	10 mm/L, user variable
Volume Range:	0-19.9 L
Flow Scaling:	5 mm/L/sec, user variable
Flow Range:	±16 L/sec
Accuracy:	±2%
Power source:	Serial port; battery; or AC power pack; 110, 220, 240 VAC, depending on model
Computer Requirements:	DOS 6.22 or higher Pentium or higher, minimum 100MHZ, minimum 32MB RAM, minimum 60MB available space on hard drive, available Com port
Operating Environment:	20°-35°C
Safety:	EN 60601-1 Class I (grounded typed for both specified power supply and personal computer) Type BF subject applied part. Ordinary equipment (not protected against harmful ingress of moisture). Not suitable for use with flammable anesthetics. Suitable for continuous operation.
EMC:	EN 60601-2 IEC 801-2 / EN 61000-4-2: 3 kV CD, 8 kV AD IEC 801-3 / EN 61000-4-3: 3 V/m IEC 801-4 / EN 61000-4-4: .5 kV I/O, 1 kV AC mains IEC 801-5 / EN 61000-4-5: 1 kV DM, 2 kV CM

12.1.1 CONFORMANCE TO STANDARDS

Industry Recommendations:	ATS 1999, NIOSH, SSD, OSHA, ECCS
Quality System Regulations:	FDA QSR, ISO 9002, EN 46002
Product Testing Regulations:	IEC 601 series, 601-1-1, 601-1-2
European Union Standard:	MDD 93/42/EEC

12.2 ESSENTIAL PRESCRIBING INFORMATION

12.2.1 INTENDED USE AND INDICATIONS

The nSpire Health KoKo Spirometer is indicated for use in pulmonary function diagnostic testing and monitoring of allergies, asthma, and respiratory diseases.

The spirometry software is contained on a computer supplied by nSpire Health. The spirometer connects via its signal input/output port to the serial port of the computer.

During testing, the KoKo pneumotach must be connected to a single subject use, viral/bacterial KoKo Filter and operated by trained medical personnel. The operator must maintain a subject area of 1.5m horizontally and 2.5m

vertically and at no time bridge the subject and the computer/printer specified power supply system. The subject holds the pneumotach, but it does not in any way interact with or influence the subject when used as specified.

12.2.2 WARNINGS AND PRECAUTIONS

NOTE: Federal Law restricts this device to sale by or use on the order of a physician.
The computer and specified power supply used with the KoKo Spirometer must be located outside of the subject environment.

Always use the power pack that accompanied your system. Using a different power pack can cause permanent damage to your system. Plug the power supply and all associated computer equipment into grounded outlets.
Always use the KoKo Filter with the KoKo Spirometer. Failure to use the filter could affect accuracy due to expectorated matter in the pneumotach.

The KoKo Filter is designed for single subject use only. Do not attempt to clean or sterilize.
Do not attempt to wash or submerge the KoKo Spirometer in water or cleaning fluid, as there are electronic components inside the handle that will be permanently damaged.

Do not use anti-static or electrically conductive hoses or tubing with this device.

This device complies with the minimum electromagnetic compatibility requirements of the MDD. However, electromagnetic interference may still be encountered. If the device is behaving erratically due to electromagnetic interference, contact Technical Support.

If the power supply included with this device is Class 1 (grounding type), please ensure that it is plugged into a properly grounded receptacle.

Do not attempt to wash or submerge the PiKoLogic in water, there are electronic components inside the device that will be permanently damaged.

12.2.3 QA FLAGS / ABBREVIATIONS

BST - Best Effort

CON - Effort Consistent With Best

AE- Abrupt End

CG - Cough

6 SEC - Expiration Time < 6 seconds

DIS - Discarded

PEFT – Peak Expiratory Flow Time $\geq$ 150 ms

BE – Back Extrapolation (VEXT) $\geq$ 5% or 150ml, whichever is larger

RB –Rebreathing.

12.3 FIREWALL PORTS

IP ADDRESSES AND PORT REQUIREMENTS REQUIRED FOR ESP COMMUNICATIONS			
216.183.118.190	VPN Concentrator		
216.183.118.184	Internet Ping Test		If you are behind a hardware firewall that supports IPSEC pass thru, please enable this option. If your router does not support IPSEC Pass thru you need to open UDP Port 500, protocols 50 and 51 outbound for the Cisco VPN Client to work.
129.6.15.28	Time Server	Gaithersburg, MD	The NIST servers listen for a NTP request on port 123
129.6.15.29	Time Server	Gaithersburg, MD	The NIST servers listen for a NTP request on port 123
132.163.4.101	Time Server	Boulder, CO	The NIST servers listen for a NTP request on port 123
132.163.4.102	Time Server	Boulder, CO	The NIST servers listen for a NTP request on port 123
132.163.4.103	Time Server	Boulder, CO	The NIST servers listen for a NTP request on port 123
128.138.140.44	Time Server	Boulder, CO	The NIST servers listen for a NTP request on port 123
192.43.244.18	Time Server	Boulder, CO	The NIST servers listen for a NTP request on port 123
131.107.1.10	Time Server	Redmond, WA	The NIST servers listen for a NTP request on port 123
66.243.43.21	Time Server	San Jose, CA	The NIST servers listen for a NTP request on port 123
216.200.93.8	Time Server	(Abovenet) VA	The NIST servers listen for a NTP request on port 123
208.184.49.9	Time Server	San Jose, CA	The NIST servers listen for a NTP request on port 123
207.126.98.204	Time Server	Sunnyvale, CA	The NIST servers listen for a NTP request on port 123
205.188.185.33	Time Server	(AOL) VA	The NIST servers listen for a NTP request on port 123
64.156.240.50	liveupdate.symanteclive update.com		RTVScan makes a request to Winsock for port 2967/UDP for IP and port 33345 for IPX - Live Update requires access to ports 80 (HTTP), 21 (FTP) and 443 (HTTPS).
204.10.30.16	liveupdate.symanteclive update.com		RTVScan makes a request to Winsock for port 2967/UDP for IP and port 33345 for IPX - Live Update requires access to ports 80 (HTTP), 21 (FTP) and 443 (HTTPS).
204.10.30.15	liveupdate.symanteclive update.com		RTVScan makes a request to Winsock for port 2967/UDP for IP and port 33345 for IPX - Live Update requires access to ports 80 (HTTP), 21 (FTP) and 443 (HTTPS).
204.10.30.5	liveupdate.symanteclive update.com		RTVScan makes a request to Winsock for port 2967/UDP for IP and port 33345 for IPX - Live Update requires access to ports 80 (HTTP), 21 (FTP) and 443 (HTTPS).
209.133.111.3	update.symantec.com		RTVScan makes a request to Winsock for port 2967/UDP for IP and port 33345 for IPX - Live Update requires access to ports 80 (HTTP), 21 (FTP) and 443 (HTTPS).

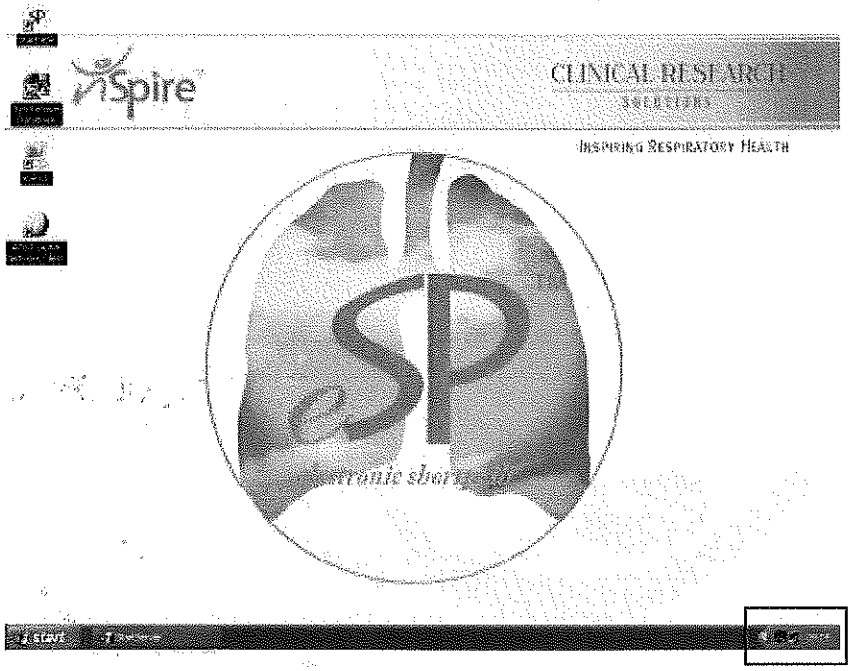
64.124.186.85	update.symantec.com		RTVScan makes a request to Winsock for port 2967/UDP for IP and port 33345 for IPX - Live Update requires access to ports 80 (HTTP), 21 (FTP) and 443 (HTTPS).
216.200.68.150	update.symantec.com		RTVScan makes a request to Winsock for port 2967/UDP for IP and port 33345 for IPX - Live Update requires access to ports 80 (HTTP), 21 (FTP) and 443 (HTTPS).
208.254.75.146	update.symantec.com		RTVScan makes a request to Winsock for port 2967/UDP for IP and port 33345 for IPX - Live Update requires access to ports 80 (HTTP), 21 (FTP) and 443 (HTTPS).
	MobiLink		
	Manage Anywhere		
	Sybase		

13 REGIONAL SETTINGS

Upon installation at nSpire Health, the *eSP* Testing System is set as closely as possible to your regional date and time settings. It is important that these settings are verified and adjusted, if necessary.

NOTE: Your clock will automatically update to the correct date and time during synchronization. Once you have confirmed your regional settings, you should never have to adjust the time.

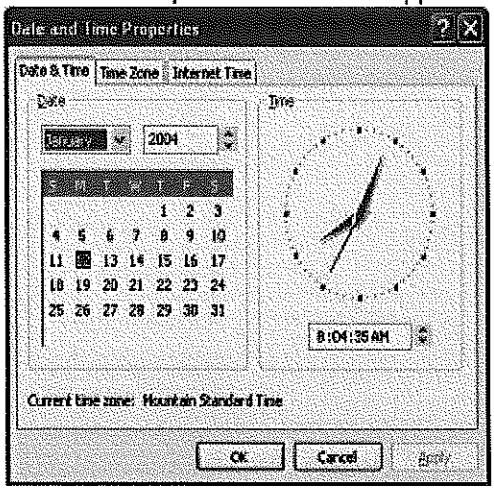
To confirm your regional settings, please follow the steps listed below.



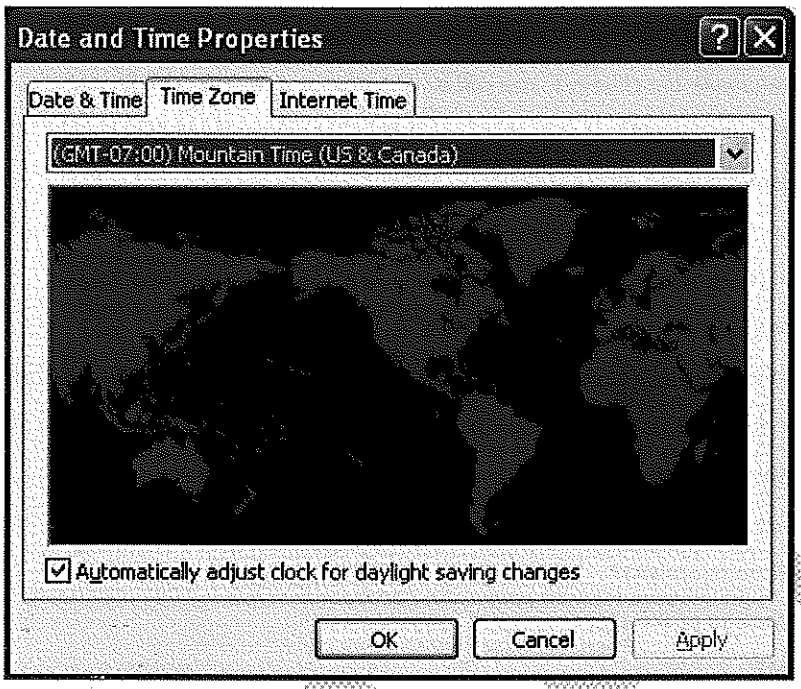
1. On the Windows Desktop, the bar across the bottom of the screen is called the Taskbar.

- The *System Clock* is displayed in the lower right corner on the Taskbar.

2. Double-click the *System Clock*.
3. The **Date and Time Properties** window will appear. Click the **Time Zone** tab.



4. The currently selected Time Zone will appear highlighted at the top of the screen. If the displayed Time Zone is correct for your area, click **OK**. If the Time Zone is incorrect, click the drop-down arrow.



5. A list of Time Zones will appear. Using the cursor or the scroll bar. Go through the list and select the correct Time Zone for your area.

Some areas follow the "Daylight Saving Time" system. If your location does, be sure that the checkbox labeled "*Automatically adjust clock for daylight saving changes*" is checked. If your location does not use daylight saving time, be sure that this checkbox is not checked.

6. Click **OK** when complete

14 FAQ

Q: How are demographic changes made?

A: On the subject entry screen make the changes. You will be required to note a reason for the change.

Q: What if the site administrator leaves?

A: Ask them to create an account for the new administrator before they leave, or

A: Contact nSpire technical support to reset the PI Admin account (First six letters of PI's last name.)

Q: What if a new technician is hired?

A: Follow the certification process

Q: After Synchronization, must the system stay connected to the analog phone line or internet during testing?

A: No, the system should be disconnected during testing

Q: Must calibration be performed every day?

A: No, just on days you will be testing

Q: Can the computer be left on overnight?

A: No. Please shutdown at the end of the day

Q: How are passwords reset?

A: Your site administrator can reset your password. nSpire Health's Technical Support can also reset the password

15 NOTES: