Standard Operating Procedure: Multiple Breath Nitrogen Washout
EXHALYZER® D, ECO MEDICS AG

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This SOP is intended as an operator’s guide to Nitrogen Multiple Breath Washout Testing using the ECO MEDICS AG EXHALYZER® D Pulmonary Function Testing Device with online testing software Spiroware 3.1.6 and should be used in combination with EXHALYZER® D manual (EXH-405-V2.0).
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Table of Contents

1 Introduction .................................................................................................................................................. 4
  1.1 General Information about Multiple Breath Inert Gas Washout ................................................................. 4
  1.2 MBW$_{N_2}$ Using EXHALYZER® D ............................................................................................................. 4

2 Daily System Start-up ..................................................................................................................................... 5
  2.1 Power on the EXHALYZER® D .................................................................................................................... 5
  2.2 Check Gas Sources ..................................................................................................................................... 5
  2.3 Start Spiroware 3.1.6 .................................................................................................................................... 6
  2.4 Flow and Gas Channel Calibration .............................................................................................................. 8
    2.4.1 Equipment Required for Calibration ........................................................................................................ 8
    2.4.2 Verify Software Settings ........................................................................................................................ 9
    2.4.3 Daily Calibration of EXHALYZER® D ....................................................................................................... 12
  2.5 End of Calibrations ...................................................................................................................................... 21
  2.6 Calibration Troubleshooting ....................................................................................................................... 22
    2.6.1 Flow Calibration Troubleshooting ........................................................................................................ 22
    2.6.2 Gas Calibration Troubleshooting .......................................................................................................... 22

3 Multiple Breath Washout Test ................................................................................................................... 24
  3.1 Create a Subject File .................................................................................................................................... 24
  3.2 Gather Additional Equipment Required for Testing ...................................................................................... 24
  3.3 Prepare Equipment for Testing .................................................................................................................... 25
  3.4 Description of Test Screen ........................................................................................................................ 26
  3.5 Beginning a Multiple Breath Washout Test .................................................................................................. 29
    3.5.1 Establishing a Stable Breathing Pattern ................................................................................................. 30
    3.5.2 Beginning Washout ................................................................................................................................ 35
3.5.3 End of Washout................................................................. 36

3.6 Post Test Quality Control and Generating a Report ................................................................. 38

3.6.1 Pre-Washout Phase Quality Control ................................................................. 40

3.6.2 Washout Phase Quality Control .............................................................................. 42

3.6.3 Appending Trials to Existing Subjects ........................................................................... 50

3.6.4 Preparing a Report ........................................................................................................ 50

3.7 Accessing/organizing data files .......................................................................................... 53

3.8 Database back up.............................................................................................................. 53

3.9 Reviewing studies............................................................................................................ 54

3.10 Cleaning of Equipment..................................................................................................... 57

4 Troubleshooting ...................................................................................................................... 58

4.1 Noisy Gas Signals.............................................................................................................. 58

4.2 Computer errors.............................................................................................................. 58

5 Lab Supervisor Responsibilities.............................................................................................. 59

5.1 Create User Accounts........................................................................................................ 59

5.2 Confirmation of Site Specific Dead Space Volumes ........................................................ 60

5.2.1 Automatic Start/Stop and Orientation of Flow.......................................................... 60

5.2.2 Site Specific Dead Space Volumes............................................................................... 61

5.3 Confirmation of BTPS Correction Parameters .................................................................. 64

5.4 Flow/Gas Signal Synchronization .................................................................................... 65

5.4.1 Set up equipment for Flow/Gas Signal Synchronization ............................................. 65

5.4.2 Perform Signal Synchronization .................................................................................. 65

5.4.3 Signal Synchronization Troubleshooting..................................................................... 69

6 References ............................................................................................................................... 72
# Introduction

## 1.1 General Information about Multiple Breath Inert Gas Washout

Multiple breath inert gas washout (MBW) testing measures the FRC and the efficiency with which gas mixes in the lungs. The non-uniformity of ventilation distribution across the lung is often referred to as ventilation inhomogeneity (2-4). MBW testing can be performed using both closed (re-breathing) and open circuit (bias flow) setups, and a variety of tracer gases, including resident gas such as Nitrogen (N₂) and non-resident gases such as Sulfur hexafluoride (SF₆) and Helium (He)(1). The accuracy of the MBW method depends on the accuracy of gas concentration and respiratory flow signals and the perfect synchronization of these signals.

In general MBW testing consists of two phases, a wash-in and a washout phase. During the wash-in phase of testing, subjects breathe a gas mixture containing a tracer gas until inhaled and exhaled gas concentrations are equal. During the washout phase, the tracer gas is allowed to disperse out of the lungs; respiratory flow and inert gas concentration are measured breath by breath over a period of time. By recording the integral of gas concentration with respect to respiratory flow and examining the drop in inert gas concentration over consecutive breaths of the washout phase, it is possible to calculate FRC and a number of parameters, which reflect ventilation inhomogeneity (VI) in the lung (1, 2).

## 1.2 MBW\textsubscript{N₂} Using EXHALYZER® D

The ECO MEDICS AG EXHALYZER® D is an open circuit system that uses resident N₂ as the inert tracer gas. The EXHALYZER® D uses an indirect technique to determine N₂ concentration. Carbon dioxide (CO₂) is measured using a mainstream infrared CO₂ analyzer and oxygen (O₂) is measured by side stream sampling (sample flow approximately 200 mL/min) to an internal laser O₂ analyzer (5). N₂ is then calculated by the following formula:

\[ 1 = F_{O_2} + F_{CO_2} + F_{N_2} + F_{Ar}^* \]

*F is the fractional concentration of gas; FAr (Argon) is treated as a fixed proportion of FN₂ during the washout (FAr = FN₂ x 0.0093/0.7881) (5).

This is in contrast to other direct gas analyzers used to perform MBW such as the respiratory mass spectrometer, which directly measure the concentration of the tracer gas of interest (2, 6).

As N₂ is a resident gas, equilibration of inert tracer gas has occurred at baseline by breathing room air. Thus during N₂-MBW with the ECO MEDICS AG system there is no wash-in phase with a foreign gas required before starting the first test, although subjects must be allowed to re-equilibrate with room air between subsequent testing trials. During washout resident N₂ is washed out of the lungs by 100% O₂. Current standards dictate that the washout phase should continue until the tracer gas has washed out to beyond 1/40\textsuperscript{th} of its starting end-tidal concentration (1).
Please Note: This SOP is applicable to N₂-MBW testing of school age children (age 6 years and older) and adults. The procedure for testing younger age groups on this device has not been standardized to date, but is the focus on a current ATS/ERS working group. The aim is to produce guidelines for testing younger age groups by the start of 2015.

2 Daily System Start-up

We recommend that initial set up of the EXHALYZER D system be performed by qualified personnel from ECO MEDICS AG or their distributors.

2.1 Power on the EXHALYZER® D

1. Switch on the EXHALYZER® D using the On/Off rocker switch at the back of the unit.

- Once the unit is turned on the O₂ LED on the front panel will light up and flicker.
- O₂ LED must be steady before using the equipment; this should happen after 3 minutes.
- The EXHALYZER D must be on for 5 minutes prior to calibration and testing to allow time for the temperature of the internal O₂ analyzer to stabilize.
  - The CO₂ LED will not illuminate until testing is initiated.

2.2 Check Gas Sources

- Gases may be supplied by either a high pressure wall outlet or gas tank with double stage regulator. As per manufacturer’s recommendations, gas sources must be pressurized to 44 - 87 psi (300 – 600 kPa).

MEDICAL AIR

1. Ensure Medical Air is connected to the unit.

- Medical air is connected to the back of the EXHALYZER D (see company manual) via a high pressure hose from either a medical air wall outlet or double stage gas tank regulator.
- Some systems will have an in-line on/off valve at the back of the unit which is OPEN when HORIZONTAL and CLOSED when VERTICAL. Newer units will have a medical air connection that is internally controlled and will open automatically when appropriate.
- Medical air must be flowing (in-line valve open in older units) to perform gas calibration and subject testing.
OXYGEN
1. Ensure O₂ is connected to the unit.

- 100% O₂ is connected to the back of the EXHALYZER D via a high pressure hose.
- Oxygen will only flow through the system when the valve is opened by the software during testing or if the “FRC TEST” button on the front panel of the unit is depressed.
- Once the O₂ high pressure hose is correctly attached to the wall, the O₂ supply is ready for calibration and testing.

2.3 Start Spiroware 3.1.6
1. Power on the EXHALYZER® D computer and monitor.

2. The icon for Spiroware 3.1.6 software can be found on the desktop of the EXHALYZER® D computer.

3. When logging into Spiroware for the first time: enter the generic username “admin” and password “admin” in the appropriate fields of the login page.
4. Upon logging into Spiroware the ‘Select a Patient’ menu will appear. Navigate to the Administration menu by selecting the Administration button located at the bottom right of the screen.

- From the Administration menu the operator can access all menus required to complete flow and gas channel calibration.

***Of note: The error message Serial cable is not connected will appear when more than one person is logged into Spiroware (i.e. if the system has been idle and entered stand-by mode). To remedy the situation the system must be shut down and re-started. PLEASE REMEMBER TO LOG OUT OF YOUR ACCOUNT to avoid this!
2.4 Flow and Gas Channel Calibration

Section 2.4 guides calibration and system set up for testing school age children and adults.

2.4.1 Equipment Required for Calibration

To calibrate the EXHALYZER® D for N₂-MBW the following equipment is required:

1. 100% O₂ (wall outlet or tank).
2. Medical air (wall outlet or tank).
3. 1 Personal Computer with Spiroware software 3.1.6.
4. 1 Monitor (for measurement).
5. 1 Monitor (to show DVD, recommended for paediatric testing).
6. 1 EXHALYZER® D gas analyzer.
7. High precision thermometer, barometer and hygrometer.
8. Bypass flow supply with blue filter (attached to EXHALYZER® D).
10. Holding device for fixed bias flow block (arm).
11. Ultrasonic flow head (attached to EXHALYZER® D).
12. Dead space reducer (Set 2 DSR: 15 to 35 kg (blue), Set 3 DSR: >35 kg (green)).
13. SPIRETTE.
14. CO₂ airway adapter (consisting of cuvette and sensor).
15. Nafion tube (connects CO₂ airway adapter to EXHALYZER® D).
17. Cap for luer-lock sampling port on CO₂ airway adapter.
18. Calibration syringe (1000 mL).
2.4.2 Verify Software Settings

2.4.2.1 Confirm Equipment Dead Space Volumes

- Volumes measured during MBW (tidal volume and FRC) are corrected for the technical (or equipment) dead space volume. Technical dead space volume has been divided geometrically into pre and post gas sampling-point volumes (See Figures 3 and 4). (2)
1. To verify dead space volume settings navigate to the System Settings page found in the Administration menu. Pre and post gas sampling-point dead space volumes for each DSR set can be found under heading Insert Settings on the system settings page.

<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>Set 1</td>
<td>90</td>
<td>110</td>
<td>100</td>
<td>2</td>
<td>2</td>
<td>3.5</td>
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<td>✓</td>
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<td>Set 2</td>
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<td>900</td>
<td>1100</td>
<td>1000</td>
<td>25</td>
<td>33.3</td>
<td>22</td>
<td></td>
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<td>5000</td>
<td>3000</td>
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<td>25</td>
<td>25</td>
<td></td>
<td></td>
<td>✓</td>
<td>✓</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Figure 5. Default Dead Space Volumes

- Default pre and post gas sampling-point dead space volumes (based on the manufacturer supplied bacterial filters) are included in Spiroware software and should be adjusted by the Supervisor to reflect site specific values as outlined in Sections 5.2.1 and 5.2.2).

Environmental Settings

Gas concentrations are reported as dry. BTPS corrections will take water vapor pressure and relevant temperature into account when reporting respiratory flows, volumes and gas volumes.

1. Navigate to the Environmental Settings page from the main Administration menu. Internal instrument readings of temperature and pressure are displayed under the heading Environment Measurements.
2. Verify that the internal measurements are within acceptable limits. The temperature reading should be within +/- 0.5°C and the pressure within +/- 5 hPa of ambient conditions as measured by high precision reference thermometer and barometer.

- Each lab should have a high precision thermometer, barometer and hygrometer in the same room as test equipment to be used as reference for internal instrument readings.

- Ambient **Temperature**, **Pressure** and **Humidity** should be recorded on each day of testing in a calibration log.

*Note: ambient conditions at time of test are also stored as part of raw data files (A-files).*

3. If instrument readings are outside limits calibration of system temperature and pressure is required (see section 2.4.2.4.1 Calibration of Ambient Temperature and Pressure).
2.4.2.1.1 Calibration of Ambient Temperature and Pressure in Spiroware

1. Enter temperature (°C) in ambient temperature field; confirm by pressing “calibrate”, WAIT until system responds.

2. Enter pressure (HPa) in ambient pressure field; confirm by pressing “calibrate”, WAIT until system responds.

3. Select update measurement to display new values.

2.4.3 Daily Calibration of EXHALYZER® D

The operator should perform flow and channel (gas) calibrations on each day of testing and if changing DSR sets.

- **Synchronization** of gas signals to flow are to be performed by the supervisor, on a weekly basis or if signs of poor synchronization occur (See Section 5.4)

<table>
<thead>
<tr>
<th>DAILY CALIBRATION WITH SET 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>➢ The following is the appropriate sequence for operator’s calibration with DSR Set 3:</td>
</tr>
<tr>
<td>1. Flow calibration Set 3.</td>
</tr>
<tr>
<td>2. Channel/Gas calibration Set 3.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>DAILY CALIBRATION WITH SET 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IMPORTANT:</strong> Flow and Channel calibration must be performed with SET 3 PRIOR TO CALIBRATION WITH SET 2.</td>
</tr>
<tr>
<td>➢ The following is the appropriate sequence for operator’s calibration with DSR Set 2:</td>
</tr>
<tr>
<td>1. Flow calibration Set 3</td>
</tr>
<tr>
<td>2. Channel/Gas calibration Set 3</td>
</tr>
<tr>
<td>3. Flow calibration Set 2</td>
</tr>
</tbody>
</table>
Prepare Equipment for Flow Calibration; DSR Set 2 and 3

The following procedure applies to both DSR Set 2 and 3. However, the sequence of calibration will depend on the DSR Set to be used for testing (see section 2.4.3, Daily Calibration).

- DSR to be used for testing is dependent on the subject’s weight:
  Set 2 DSR: 15 to 35 kg (blue), Set 3 DSR :> 35 kg (green).

1. Insert appropriate set DSR into SPIRETTE (sheath) ensuring dot on DSR is aligned with arrow of SPIRETTE (Figure 7).

   - SPIRETTEs do not need to be changed with each test as they are upstream of filter, but should be changed every 2 weeks or if visibly soiled (see section 3.10).

2. Insert DSR + SPIRETTE into flowhead ensuring arrow of flowhead is aligned exactly with dot on DSR (Figure 7).

   - Correct alignment ensures proper function of ultrasonic flowhead, hence accurate flow measurement.

2.4.3.1 Flow Calibration

To be performed on each day of testing, between subjects and whenever DSR Set # is changed.

- Flow/volume calibration should ideally be performed as close to time of test as possible.
2.4.3.1.1 Flow Calibration Equipment Set Up

1. Select appropriate Set DSR.

2. Remove the flowhead (with SPIRETTE and DSR already inserted) from the bias flow block.

3. Ensure SPIRETTE and appropriate DSR are correctly inserted into flowhead (Figure 7).

   ➢ Correct alignment of SPIRETTE/DSR in flowhead is crucial for accurate measurement of flow.

   ➢ If the CO₂ cuvette has previously been connected to the warming sensor allow cuvette to cool to room temperature before proceeding with calibration.

4. Remove Nafion tubing and cap the luer lock sampling port with appropriate cap to prevent any leaks during flow calibration.

5. Connect 1000 mL Syringe with filter* attached to the patient side of the flowhead + CO₂ cuvette (Figure 8).

   ➢ The plunger of the calibration syringe should be pushed all the way in before start.

*Filter for calibration should be the same model filter to be used during testing.
2.4.3.1.2 Flow Calibration Procedure DSR Set 2 and 3

1. In the Administration menu select the appropriate DSR Set number from the drop down menu and select Flow Calibration (Figure 9).

![Fig 9](image-url)  
**Figure 9. Administration Menu; Flow Calibration**

2. Ensure there is zero flow through the flowhead. The plunger of the syringe must **not** be moved while baseline flow is being set.

3. Check that the correct DSR Set # is displayed and press Continue. *The software will then set the zero flow baseline.*

   - The flow/volume calibration requires 10 strokes using a certified calibration syringe.
   - 1000 mL syringe for Set 2 & 3

4. Perform 10 strokes with **peak flow of each in/out stroke** **WITHIN** the shaded green target area

   - Peak flow targets:
     - Set 2 = 500 mL/s
     - Set 3 = 1000 mL/s
   - Strokes should be relaxed and of equal flow rate, with peak flows guided by the green lines on the panels.
5. If peak flow is significantly higher or lower than the target flow, cancel and retry calibration.

![Flow calibration examples](image)

**Figure 10.** Examples of technically good flow calibrations; top graphs (red tracing in each panel) display volume tracing, bottom graphs (black tracing in each panel) display flow tracing.

- In the upper right corner of the flow calibration screen there is a running count of stroke number and real time display of flow. The syringe volume and set number of the DSR are also displayed here.

- The calibration software automatically stops after the number of required strokes has been detected (n=10).
6. Check the calibration report generated at the bottom of the screen to determine whether the calibration has been successful.

   An acceptable calibration should have (Figure 10):
   
   o Peak flows in the shaded target areas for all strokes.
   o Minimal volume drift (red tracing).
   o Volumes for each stroke are similar to expected, mean volume should be 1000 mL +/- 30 mL or 3% for both set 2 and set 3.
   o Inspiratory and expiratory deviation both less than +/- 2%.

7. A flow calibration will be deemed successful by the software if the inspiratory and expiratory deviation is within acceptable limits (less than +/- 2%).

   This will be indicated by a green check.

8. If the calibration is acceptable press save to store the new calibration parameters in the device software.

9. If flow calibration is unsuccessful press save to store new calibration parameters, check equipment set up and repeat flow calibration.

   ➢ *If flow calibration continues to be unsuccessful please refer to section 2.6.1 Flow Calibration Troubleshooting.
2.4.3.2 Gas Calibration (Channel Calibration); DSR Set 3

- Calibration to be performed daily.

**A FLOW CALIBRATION WITH DSR SET 3 IS REQUIRED PRIOR TO CHANNEL CALIBRATION**

2.4.3.2.1 Set Up Equipment for Channel Calibration

1. Ensure Set 3 DSR (with SPIRETTE) is inserted correctly into the flowhead.

2. Connect flowhead to bias flow block.

3. Attach CO₂ cuvette and connect Nafion tube to sampling port of CO₂ cuvette.

4. Ensure both gas sources (medical air and O₂) are connected and medical air valve is open (if applicable; see section 2.2).

5. Block the downstream (exit) port of the bias flow block. All flow will now be directed through the flowhead at approximately 1.0 L/s.

*Figure 11. Correct Equipment Set-up for Gas Calibration*
2.4.3.2.2 Perform Gas (Channel) calibration

- **How the system performs gas calibration.**
  - **Oxygen**
    - A two-point calibration is performed.
    - High = 100% O\textsubscript{2}  Low = 20.94% O\textsubscript{2} (medical air)
  - **Carbon Dioxide**
    - CO\textsubscript{2} is zeroed using 100% O\textsubscript{2}
    - The upper limit of the CO\textsubscript{2} analyzer is not checked, the assumption is that the signal is linear and does not drift.

1. Open the **Administration** menu and select **Channel Calibration**.

   ![Figure 12. Administration Menu; Channel Calibration](image)

2. Confirm DSR Set 3 for channel calibration.

   ![Figure 13. Channel Calibration; Set Selection](image)

- The system will also generate a reminder to ensure that the correct DSR is in place and that a flow calibration has been performed.
3. Ensure down stream port has been blocked (large red plug) and follow on-screen instructions (see below) and select confirm.

4. Wait for the system to register gas concentration and then begin two-point O₂ calibration by pressing start.

   - Medical air will begin to flow through the system and the low point calibration (20.94%) will commence.

   - After a few moments the system will automatically switch to 100% O₂, which should result in a stepwise change in the gas concentration from 20.94% to 100% O₂.

5. Check the flow reading (Figure 16) in top right corner of Channel Calibration screen to ensure there is at least 950 mL/s flowing through the system.
If there is less than 950 mL/s flowing through the system, first check that the downstream port of the bias flow block has been blocked.

If the bias flow is still not adequate see section 2.6.2, Gas Calibration Troubleshooting.

Gas calibration will stop automatically.

Once gas calibration is complete, press Save to retain the new calibration factors. The online testing software will now use these values.

Be sure to restore flow through the bias flow block by removing plug from the downstream port of bias flow block prior to testing.

2.5 End of Calibrations

Once all calibrations are complete (flow/volume and gas), select Back to exit Administration screen.
2.6 Calibration Troubleshooting

2.6.1 Flow Calibration Troubleshooting

- Common difficulties with flow calibration include:
  - Excessive volume drift.
  - Excessive inspiratory or expiratory percent deviation (more than 2%).
  - Mismatch of inspiratory and expiratory volumes (difference of more than 30 mL).

- When performing a flow calibration after changing DSR sets the gain and offset are often outside acceptable range. A message that the calibration is out of range may appear; following the steps outlined below should resolve this issue.

1. **Save** initial calibration to retain the new gain and offset and then repeat the calibration; new calibration should show improved values.

2. If still not achieving adequate flow/volume calibration consider the following:
   - Check DSR/flowhead/SPIRETTE alignment (Figure 7) to ensure openings in DSR are aligned with screens in SPIRETTE to allow ultrasonic flow measurement across the stream of air.
   - Consider changing SPIRETTE, which may be soiled or damaged due to repeated use or insertion.
   - Ensure calibration syringe is set at exactly appropriate volume.

2.6.2 Gas Calibration Troubleshooting

1. A “CO₂ transmission error” may occur at the end of channel calibration. This may be due to misalignment of DSR, SPIRETTE and flowhead or due to channel calibration being performed multiple times in a row. To resolve the matter, check assembly of flowhead (re-assemble, if necessary), close Spiroware and switch off Exhalyzer, re-start Exhalyzer and then re-start Spiroware. Attempt channel calibration again.

2. If the DSR Set has been changed or a flow calibration has not been performed the following message will appear (Figure 17). Perform a flow calibration with the appropriate set before continuing to channel calibration.

![Error Message: Flow Calibration Expired](Figure 17. Error Message: Flow Calibration Expired)
3. Varying pressure of gas sources (wall outlets, gas tanks) may lead to variation in delivered bias flow rates. In cases where the flow rate of either air or oxygen falls below 950 mL/s the software will give an error message indicating the bias flow rate is too low.
   - Ensure gas sources are connected properly.
   - If using gas tanks ensure pressure is adequate.
   - Ensure circuit is assembled correctly.
   - Repeat gas calibration.
   - If problem persists, then contact distributor or service agent.
3 Multiple Breath Washout Test

3.1 Create a Subject File

1. Navigate to the Select a Patient menu. This screen appears automatically once operator logs onto Spiroware software and can be accessed from the Administration menu by selecting the Back button.

![Figure 18. Select a Patient Menu](image)

2. Create a file for a new patient by selecting Register New Patient.

3. Enter subject demographics as appropriate.* Ensure height and weight entered are measured on day of testing*.

3.2 Gather Additional Equipment Required for Testing

In addition to equipment required for calibration, the following equipment is needed to execute testing:

2. Trimmed soft mouthpiece.
3. Nose clips.
3.3 Prepare Equipment for Testing

1. Ensure that correct DSR according to subject weight is inserted into flowhead (Recall: Set 2 DSR: 15 to 35 kg (blue), Set 3 DSR: >35 kg (green)).

   - If DSR is changed at this point a NEW CALIBRATION must be performed.

2. Assemble equipment as shown (Figure 19).

3. Ensure all daily calibrations have been performed.

4. Ensure that the CAPNOSTAT warmer/sensor and Nafion tubing have been re-attached after calibration and that the plug blocking the downstream port of the bias flow block has been removed.

5. Ensure medical air and 100% O₂ are connected and running.

*check that downstream port of bias flow block is unobstructed (Red plug is removed) *
6. Select an age appropriate DVD to be played during testing (optional).

- **A note about DVD selection:**
  - Popular videos for young children are often interactive and encourage clapping, singing or talking. These types of videos should be avoided as they discourage normal tidal breathing and encourage leaks!
  - The choice of DVD for older children and adults may also impact breathing patterns; avoid funny (laughing) or scary (breath hold/gasp) movies.

### 3.4 Description of Test Screen

![Diagram of test screen with various signals and graphs]

- **Flow-volume loop**
- **Capnogram (CO₂)**
- **Expirogram (N₂)**
- **Airway dead space**
- **Measured end tidal [N₂]**
- **Limits for regression line of phase III slope**
- **CO₂ signal**
- **O₂ signal**
- **N₂ signal**
- **Graph scaling**
- **Switch between graphic types**
- **Flow and volume signals**

*Figure 20. Description of Test Screen*
Description of **Online Values** shown on right panel of test screen:

- Allowable limits for measured parameters can be found in system settings, indicator will turn red if limits are exceeded.

### Section I
- *Time* – timer begins when start button is pressed.
- *Flow (mL/s)* – measured in real time.
- Flow rate must remain below 1000 mL/s to ensure that there is no entrainment of room air during 100% O<sub>2</sub> breathing.
- *O<sub>2</sub>%* – measured in real time.
- *CO<sub>2</sub>%* – measured in real time.
- *N<sub>2</sub>%* – calculated in real time.

### Section II
- *Breath Number* - running count beginning when washout is started.
- *Turnover* - running count beginning when washout is started.
- *Cet N<sub>2</sub>%* - end tidal concentration of N<sub>2</sub>, displayed breath by breath.
- *Cet N<sub>2</sub> target (%)* – target end tidal concentration of N<sub>2</sub>, calculated as 1/40<sup>th</sup> of starting end-tidal concentration.
- *Vt Insp BTPS (mL)* – inspiratory tidal volume (Vt), BTPS corrected.
- *Vt Exp BTPS (mL)* – expiratory tidal volume, BTPS corrected.
- *RR (breaths/min)* – respiratory rate.
- *RQ* – respiratory quotient, displayed value is mean of last 3 breaths.
- *Cet CO<sub>2</sub>%* – end-tidal concentration of CO<sub>2</sub>, displayed breath by breath.
- *Mean N<sub>2</sub> insp (mL)* – volume of re-inspired N<sub>2</sub>; **if limits are exceeded leak is likely.**

### Section III
- *Stdv Cet CO<sub>2</sub>%* – standard deviation of end tidal carbon dioxide concentration.
- *Stdv RQ* – standard deviation of respiratory quotient.

### Section IV
- *FRC (L)* – functional residual capacity, running calculation that continues as washout proceeds.
- *Vol N<sub>2</sub> Reinsp (mL)* – volume of N<sub>2</sub> re-inspired, calculated as integral product of flow and gas signal. Proportional to dead space, an increase indicates leak.
- *LCI 2.5 (ext)* – lung clearance index at normalised Cet N<sub>2</sub> 2.5% extrapolated, running calculation which will stop (grey out) once the software detects Cet N<sub>2</sub> target has been met.
- *LCI 5* – lung clearance index at normalised concentration Cet N<sub>2</sub> 5.0%.
- *Sn<sub>III</sub>ms* – slope of alveolar phase (phase III) normalised by mean slope concentration.
- *Sn<sub>III</sub>ms * Vt* – normalised phase III slope multiplied by exhaled Vt to control for variable tidal volumes within tests and to facilitate comparison of small and large subjects.
Section V

- **Room Temp** – ambient temperature.
- **Pressure** – ambient pressure.
- **Flow Insp. Corr** – inspiratory flow BTPS correction factor.
- **Flow Exp. Corr** – expiratory flow BTPS correction factor.
- **CO₂ correction** – CO₂ correction factor for influence of O₂ concentration on CO₂ IR sensor.
- **Gas sensor correction** – gas sensor correction factor.
- **H₂O percentage** – relative ambient humidity, should be set to 0 in environmental settings because subject is inhaling dry gas (see Section 5.3).
3.5 Beginning a Multiple Breath Washout Test

1. Ensure subject is sitting upright in a comfortable, stationary, straight back chair.

   ➢ Some children may need to cross their legs on the seat, or use a footrest to help keep their legs still.

2. If using the supporting arm for the bias flow block; adjust it to ensure good posture (no leaning or hunching).

3. Advise the subject to breathe in a relaxed manner. They may swallow, however talking and laughing should be strongly discouraged.

   ➢ The mouthpiece and nose clips must stay in situ with no leak at all times during testing.

4. Once the patient is sitting comfortably, select New Test, then Multiple Breath Washout Test.

5. To begin data collection press Start.

6. The gas signals will appear and the software is now capturing data. Medical air is now flowing through the breathing circuit.

   ![Example of Test Screen](image)

   Figure 21. Example of Test Screen

7. Allow subject to settle into a relaxed breathing pattern.
3.5.1 Establishing a Stable Breathing Pattern

- The following guidelines are based on current standards (1), company recommendation and opinion of the authors.

- A stable resting breathing pattern prior to and during the washout portion of the test is essential for good quality testing. (1)

There are a number of feedback mechanisms built into the software to ensure that the subject is breathing at an appropriate end-expiratory lung volume (EELV), tidal volume, respiratory flow rate and to some degree respiratory rate.

1. TIDAL VOLUME (Vt)

- A green band on the flow volume loop gives the operator a visual indication of the subject’s Vt.

- The target range is based on weight and can be adjusted in the system settings menu; default is 10-15 mL/kg.

- Some subjects will have tidal volumes outside this estimated range. The volume targets are based on weight so a subject who is significantly over or underweight may not breathe precisely within defined target range.

- Breathing outside the target range is acceptable provided the breathing pattern is steady, relaxed and representative of the subject’s usual breathing pattern (useful to assess usual breathing pattern prior (to connecting) to beginning test as a reference).

- Attempts to direct tidal volume may result in irregular breathing in younger children; a better approach is to ensure they are relaxed and appropriately distracted by a DVD.

- In addition, when older children and adults are breathing at an appropriate tidal volume, a clear phase III slope, representing 50 to 75% of Vt, will be seen on N₂ expirogram.
2. FLOW RATE

- Tidal flow, volume and end-expiratory lung volume should all be relatively constant throughout the washout (1). The real time flow rate is shown on the right panel of the online testing screen.

- The EXHALYZER® D supplies approximately 1000 – 1100 mL/s fresh gas flow through the bias flow block.
  
  - Fresh gas flow rate can be checked by blocking the downstream port of the bias flow block, as if performing a gas calibration, and then beginning a mock test in Spiroware.
  
  - With the bias flow now directed through the flow head the value for flow shown on the test screen in Spiroware reflects the bias flow rate.

- An error message indicating that flow is too high will appear if the subject’s inspiratory flow rate exceeds 950 mL/s.

- It is important to ensure that the subject’s peak inspiratory flow does not exceed bias flow due to the risk of entrainment of room air.

- If this occurs subjects should be coached or distracted during subsequent testing.

3. PATIENT INCENTIVE

- A patient incentive screen is available for use with adults and older children. Younger children may actively try to manipulate the incentive and may breathe at a more natural rate and depth when distracted by an appropriate video and encouraged to breathe calmly.

To access feedback screen, select Show Feedback Screen in lower right corner of testing screen. This will also hide the feedback screen if it has already appeared.

Feedback screen can also be controlled in System Settings.

- The patient feedback screen should be in easy view of the subject.
The subject should be encouraged to breathe in such a way that the smiley face moves into the grey target box (this corresponds to the target tidal volume set in the device settings menu).

- When the smiley face is in the correct range it will change from red to green, frown to smile, and an audible cue (optional in settings menu) will indicate that the target tidal volume is being reached.
- Once target volume is reached the subject should be instructed to passively exhale.
- Flow rate is also displayed and can be monitored to ensure that the subject’s inspiratory flows do not exceed system bias flow rate.

4. RESPIRATORY QUOTIENT (RQ)

- Respiratory quotient and standard deviation are displayed on the right panel of the test screen.

- RQ is assumed to equate to respiratory exchange ratio at rest and is calculated as volume of CO₂ expired /volume of O₂ consumed. A patient sitting quietly breathing in room air (~21% O₂) should have a normal (0.8 – 1.0) stable (stdev <0.03) RQ.

- The premise for using RQ as an indicator of normal/physiologic breathing pattern is that it is difficult to have a normal RQ (stdev <0.03) while hyper-/hypoventilating or in the presence of a leak.
3.5.1.1 Pre-washout Phase – When to Open Valve

During testing the pre-washout phase should be critically appraised for the following:

- Subject is sitting upright (neither sitting forward with back bent nor supporting arms such that shoulders are raised).
- End-expiratory lung volume (EELV) is stable for a minimum of 5 breaths.
- Flow pattern is stable (and peak flow less than 1000 mL/s), subject appears comfortable. No evidence of distorted breathing pattern. RQ suggests normal tidal breathing.
- End-tidal O₂, N₂ and CO₂ concentrations are appropriate
  - CetO₂ is < 17%
  - N₂ is stable at approximately 78%
  - CetCO₂ is stable and between 4-6%

1. Assess stability of EELV (end-expiratory lung volume)
   - Tidal volumes (Vt) should be within target (green band) of flow volume loop.
   - Volume tracing is stable with no abrupt change in baseline(1).

![Flow Volume Loop](Image)

Figure 26. Test Screen; stable EELV (illustrated by blue hatched line inserted into this screen shot).
2. Assess flow pattern
   ✓ Flow pattern should be regular (1).
   ✓ Peak flow should not exceed 1000 mL/s.

3. Respiratory quotient (RQ) should be normal (0.8-1.0) and stable (stdev <0.03)

4. Assess gas concentrations
   ✓ O₂, CO₂ and N₂ concentrations are visible in upper right of test screen.
   ✓ The values noted here should be used as baseline reference for subsequent trials. This confirms adequate time between trials.

OXYGEN CONCENTRATION
   ✓ End-tidal O₂ concentration should be less than 17% (and should return to baseline concentration in subsequent trials)

   ✓ At the beginning of washout, end-tidal O₂ concentration is typically 15-16%. An error message should appear if O₂ concentration is not below 17%.

NITROGEN CONCENTRATION
   ✓ N₂ concentration should be relatively stable at approximately 78% throughout the breath cycle while breathing medical air.

CARBON DIOXIDE CONCENTRATION
   ✓ End-tidal CO₂ concentration should be approximately 5% (between 4-6%) and remain stable (stdev <0.25).
3.5.2 Beginning Washout

Once a stable resting breathing pattern has been established washout may begin by selecting Start Washout. 

- Auto start and stop options are available but are not recommended.

Figure 29. Test Screen; Start Washout

1. Gas concentrations (CO₂, N₂, and O₂), volume and flow should be monitored closely throughout the test to watch for leaks or changes in breathing pattern.

- Any of the following should prompt investigation of leak (1) (see section 3.6, Quality Control)
  - Sudden spike in N₂ concentration during inspiration (consistent with post gas sampling-point inspiratory air leak).
  
  - Premature rise in N₂ signal early in the N₂ expirogram where concentration of N₂ should be zero in the initial absolute dead space portion. This is consistent with pre gas sampling-point inspiratory air leak (i.e. between lips and mouthpiece).

  **Comparing the N₂ expirogram to the capnogram right above will confirm an adequate absolute dead space!**

  - Decrease in N₂ airway dead space volume.
  
  - Sudden step change of the volume tracing.
  
  - Step-up of N₂ concentration plotted against turnover.
  
  - Sharp dip in O₂ concentration tracing.
2. Any aberration in concentration or breathing pattern should be noted.

3. Cet $N_2$ % expresses the end tidal $N_2$ concentration of each breath (and thus changes breath by breath). This value should be used to follow the steady decline of end tidal $N_2$ concentration and used to determine when washout is complete.

### 3.5.3 End of Washout

1. The operator can manually stop the washout maneuver by pressing the **stop** button. **Auto Stop is not recommended.**

   - **End of washout** is defined as the first of three consecutive breaths where Cet $N_2$ falls below the Cet $N_2$ Target.

   - Current convention is that end of washout has been reached when 3 consecutive tidal breaths are below target concentration, even if CetN$_2$ were to subsequently go above target concentration (1).

   - Cet $N_2$ Target will become grey when the software determines the end of test criteria has been met.

   - To ensure end of washout is achieved subjects should be allowed to breathe 5 breaths below the target before the trial is terminated.

2. Upon completion of a trial the Analysis screen will automatically appear. Quality Control should be performed promptly upon completion of testing (see section 3.6 Quality Control).
3.5.3.1 Performing Subsequent Trials

1. Allow subject to re-equilibrate with room air between trials.
   
   - Re-equilibration is estimated to take 1 to 1 ½ times the length of the previous washout maneuver (time subject was exposed to 100% O₂) (1).
   
   - As a quality control mechanism the system software will lock the ‘next trial’ button for one and a half times the length of time as the previous washout. The next trial cannot begin until the timer runs out.

2. Check re-equilibration before starting a new maneuver; O₂ and N₂ concentrations should be back to baseline values before starting the next trial.

3. If gas concentrations have not returned to baseline ask subject to take a number of slow deep breaths or to take a short walk between trials.

4. Ensure lab is well ventilated; an increase in ambient O₂ will affect measurement.

5. To resume testing, select Next Trial located in the lower right of the Results Screen.

3.5.3.2 Session Completion

- Ideal test situations have 3 MBW trials with (1):

  ✓ Stable resting breathing pattern (EELV, flow, volume and rate) throughout test (pre-washout phase and during washout).

  ✓ No obvious leaks.

  ✓ No cough.

  ✓ No evidence of significant trapped gas release with larger breaths.

  ✓ Measured CetN₂% washed out to at least 3 consecutive tidal breaths below CetN₂% Target (1/40th of start N₂ concentration).

- Test session should continue (within reason) until 3 technically sound trials are obtained.
3.6 Post Test Quality Control and Generating a Report

1. The following results page will be populated with each trial as it is completed. The results page can be accessed by selecting **Switch to Analysis** at the bottom right of the test screen once the test has ended.

2. It is highly recommended that quality control for technical acceptability occur promptly post-testing.

   - In the rare circumstance when this is not possible the results may be saved in draft form by selecting **Save as Draft**, to be reviewed at a later date.
3. The mandatory wait time between trials is an ideal time to perform quality control on the previous trial. The operator may toggle between the Analysis page and the Sampling page by selecting the Return to Sampling button.

4. Return to Sampling will bring the operator back to the test screen where he or she may scroll back through each breath of the washout to examine the gas, flow and volume signals for technical acceptability.

5. An intake form or record of test events filled out at time of test provides valuable reference information about testing. This document becomes even more important if quality control is not undertaken immediately post-test.
3.6.1 Pre-Washout Phase Quality Control

- Pre-phase breaths are important for calculation of FRC and are used by the software to set the target CetN₂; therefore it is very important that these breaths be representative of normal tidal breathing (1).

1. The middle panel of the results page allows the user to examine the pre-washout breaths. Highlighting a breath in the Pre-phase panel turns the corresponding breath red in the flow volume loop and green in the expirogram.

2. A drop down list of possible parameters can be accessed by selecting the chevron in the yellow Pre-phase breaths panel. The operator may then place a check next to desired parameters.

Figure 32. Results Page; Pre-washout Phase Breaths
3. Examine each trial for the following (1):
   ✓ Each trial should have at least 5 breaths of pre-washout phase breathing.
   ✓ Look for regular tidal breathing with stable end-expiratory lung volumes (EELV).
   ✓ Normal and stable RQ (within 0.8 – 1.0, stdev < 0.03) and CetCO2 (within 4-6%, stdev<0.25).
   ✓ Flow/volume loops should be superimposed breath to breath and volume time tracing stable.

![Figure 33. Stable EELV (indicated by inserted hatched red line).](image)
3.6.2 Washout Phase Quality Control

- The following guidelines are based on current standards (1), company recommendation and opinion of the authors.
- Ideal trials will be free of leak, have stable tidal breathing pattern and satisfy end of washout criteria.

Figure 34. Results Page - Washout

1. The lower panel of the Results page allows the user to examine various parameters measured breath by breath during the washout phase of testing. Highlighting a breath in the washout panel displays that breath in the \( N_2 \) concentration by exhaled volume graph in the lower left panel.

2. A drop down list of possible parameters can be accessed by selecting the chevron in the yellow Washout breaths panel. The operator may then place a check beside desired parameters.

3. **Return to Sampling** will bring the operator back to the test screen where he or she may scroll back through each breath of the washout to examine the gas, flow and volume signals for technical acceptability.
The following criteria should be assessed:

**Stable Breathing Pattern**

1. Breathing pattern in washout phase can be assessed in the same manner as pre-phase (see section 3.6.1).

2. Older children and adults will likely have stable EELV, tidal volumes, regular flow and breathing rate. *However, perfectly stable tidal breathing throughout wash-out is unlikely to be achieved in young school age children.*

3. Pauses in breathing will be seen in most subjects as they swallow saliva; these are often accompanied by slight upward/downward deflections of the flow curve.

4. Such instances are acceptable, but preferably not in the first few breaths of washout, and not to an extreme (Figures 35-40).

**End of Washout**

1. Current convention dictates the subject must have at least 3 consecutive breaths with CetN₂ below 1/40th of initial concentration (1). Should the subject’s CetN₂ subsequently go above the target the first of 3 consecutive breaths below target should still be considered the last valid breath of washout.

2. CetN₂ may be falsely low with very small breaths and falsely high with deep breaths; therefore it is prudent to check the tidal volumes of the 3 breaths below target to ensure the endpoint is accurate. (1)

**Leaks**

1. Each trial should be examined for the presence of leaks (Figures 35-40) as evidenced by:

   - Unexplained, sustained rise in N₂ concentration partway through wash-out.
   - Sudden spikes/dips in N₂ or O₂ concentrations.
   - Loss of CO₂ signal.
   - Absence of dead space gas on N₂ expirogram, in contrast to findings in capnogram (CO₂ expirogram).
   - Post gas sampling-point leak will be seen as a rapid spike in N₂ during inspiration (reflecting inhalation of room air as opposed to 100% O₂).
   - Major leaks will appear as large, abrupt stepwise changes in the volume tracing (partial or complete loss of the volume/flow signal).
Minimum Number of Trials

1. The consensus for minimum **number of trials** to be completed is 3 (1).
2. It is recommended to report the mean of technically acceptable trials and intra-session coefficient of variation (CoV) for same day of testing.

Figure 35. Example of technically sound washout maneuver. Stable pre-washout phase; stable breathing throughout test; clear washout of N₂; CetCO₂ stable.
Figure 36. Example of very unstable tidal breathing and large, exaggerated breath hold/swallow early in wash-out.
Figure 37. Single leak at end of maneuver. Leak is shown in close-up on the right; swallow with pause is also seen.
Figure 38. Poor quality trial. Subject uncomfortable; noisy signals secondary to pooling of saliva and excessive swallowing.
Figure 39. Leak between lips and mouthpiece. Note the loss and extreme/a abrupt drift of flow tracing (top graph), lack of decline in [N\textsubscript{2}] for last 4 breaths and instability of peak CO\textsubscript{2} (bottom graph).
Figure 40. Example of washout with loosely connected Nafion tubing & flow head not well seated in bias flow block. Note instability of gas signals, appearance of washout at start of maneuver but with lack of subsequent, continued drop in \([N_2]\).

Magnified view of the same trial:

- Flow head not seated properly in bias flow block results in irregular flow and volume signal.
- Irregular \(N_2\) signal, which is a direct result of loose connection between Nafion tubing and \(O_2\) analyzer.
- \(CO_2\) signal unaffected as it is measured by mainstream infrared gas analyzer.
3.6.3 Appending Trials to Existing Subjects

- Further trials may be appended to a test session which has been saved as a draft within 24 hours of saving provided patient demographics have not changed.

1. Select the appropriate patient from the patient list. Draft files will be displayed below the patient’s demographics and are denoted by a yellow D next to the event name in the history list (Figure 41).

2. Highlight and select desired draft file, this will bring the operator to the Analysis page of the test session where testing maybe continued by selecting Next Trial.

![Figure 41 Locating Draft File](image)

3.6.4 Preparing a Report

- Firm criteria for quality control have not yet been finalized; we recommend any questionable results be saved and labeled as such.

- A ranking scheme may be employed where all, some or none of the QC standards have been met (Figure 42).

1. The following aspects of the study should be considered when attempting to determine technical acceptability (results screen and intake sheet)(1).
   a. End-expiratory concentration of O₂ has returned to baseline, initial N₂ % is as expected during pre-washout phase.
   b. Breathing pattern is stable, if not comment on degree of variability.
   c. Any abnormal breathing pattern noted on intake sheet (laugh, cough etc.) should be examined for leak.
   d. Last 3 breaths before start of washout are representative (no sigh, panting etc.) of tidal breathing.
   e. Comment on volume signal drift.
   f. Comment on gas signal alignment.
## Standard Operating Procedure: Multiple Breath Nitrogen Washout

### Reject
1. EELV during pre-washout phase is very unstable; evidence of sigh or very small breaths in 5 breaths prior to beginning of washout.
2. Start N₂/O₂ concentration has not returned to baseline.
3. Vt is much higher than mL/kg target with evidence of hyperventilation.
4. Vt is much smaller than mL/kg target with evidence of hypoventilation.
5. Confirmed leak.
6. Study does not satisfy end of washout criteria.

### Questionable
1. EELV during pre-washout phase is somewhat unstable but 5 breaths prior to washout appear to be within tidal volume target.
2. N₂/O₂ concentration has returned close to, but not back to, baseline.
3. Query leak; not confirmed.
4. Vt is somewhat higher or lower than target Vt, no evidence of hyper/hypoventilation.
5. Sigh, +/- trapped gas release.
7. Irregular flow profile without evidence of leak (breath hold, coughing, talking, moving, laughing etc).
9. Subject moved to ‘non-optimal’ position while testing.
10. Excessive volume drift.

### Accept
1. No leak.
2. EELV is stable during pre-washout phase and Vt within target.
3. Pre-washout [N₂] and [O₂] are normal and have returned to baseline in all subsequent trials.
4. Vt is within target range throughout washout.
5. [CO₂] is normal (4-6%) and stable throughout washout.
6. Flow profile is clean and homogeneous throughout washout (no PF >1000 mL/s).
7. Trial clearly satisfies end of test criteria.

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**Figure 42. Proposed Ranking Scheme**
2. Trials deemed technically acceptable should be included in calculation of the summary. Values generated on the report are the mean of all included trials.

3. Trials can be excluded from the summary by placing a check next to the trial number in the middle panel of the results page (Figure 43).

![Figure 43. Post Test Results Page](image)

4. Once the operator has chosen the files to be used in the report the test session can be concluded by selecting Conclude Test.

5. Once the test session has been concluded the operator may **Print** the report.
3.7 Accessing/organizing data files

- Each MBW trial generates four files:
  - An **A-file** – the raw data not synchronized and without BTPS correction.
  - A **B-file** – raw data synchronized and with BTPS correction factors applied (set that day).
  - A **C-file** – same as B-file but have the option of changing the sampling frequency.
  - **Breath and trial tables** – results pages.

1. Files are automatically labeled by the software with subject ID number as entered into patient record, date and time of testing and DSR set number.

2. Each type of file is automatically saved to a pre-determined folder on the C: Drive of Spiroware computer.

These folders are specified during initial device setup and installation. *We recommend installation and initial set-up be done with a representative from ECO MEDICS AG.*

3. The number of files can quickly become overwhelming; **files should be organized by study, subject and test occasion.**

4. As A-files are typically used for off-line analysis, and are used for re-running of studies, we also suggest renaming A-files to make them easier to access and track. *Typically, we rename A files as:*
   - A.SubjectID.Visit number_ Trial number_ DSR Set number_ Interface_Date.
   - Files are then placed into the appropriate Subject/Visit folder.

5. All raw data study files should be backed up onto either a central server, external hard drive, or both.

3.8 Database back up

1. The database can be found on the C:Drive of the EXHALYZER® D system by the following pathway:

   C:Drive->Program Files->EcoMedics->Spiroware 3.1 Server->DB

   ![Figure. 44 Pathway to database](image)

2. The database should be backed up to a separate hard drive or network at regular intervals to prevent any loss of data.
3.9 Reviewing studies

- Studies can easily be reviewed (for quality control, to obtain missed data, etc.).

1. Navigate to the patient database screen and highlight the subject whose files will be re-run.
   
   **Be sure you have selected the correct subject!**

2. Click **Reload N\textsubscript{2}-MBW Test** button in upper right hand corner of patient registration screen.

   ![Figure 45. Patient Registration Screen; Re-load N2-MBW Test](image)

3. An “Open” screen will appear – choose the appropriate A-file to reload.
   - The computer may not recognize re-named A-files. If no files are visible in the appropriate folder, select “All files” from the drop down menu in the ‘Files of type’ field.

   ![Figure 46. Sample Subject Files](image)
4. Select appropriate A-File. More than one file can be selected at a time. If multiple trials are selected, files will run in sequence automatically.

5. If the raw data file (A-file) has been re-named the software will not automatically recognize the test type and will ask the operator to confirm. Select N₂ Multiple Breath Washout Test from the drop down menu and press Ok to continue.

![Figure 47. File Re-run; Test Type Options]

6. A message will appear asking the operator to confirm the replay settings.

![Figure 48. Confirmation of Replay Settings]

- Ambient conditions and BTPS correction parameters, DSR Set # and system settings (including delay times) from day of test are embedded in the A-file.

7. The operator may choose to re-run the file with these embedded parameters by selecting ‘Use settings from A-file’

8. Alternatively, if for instance the operator was not satisfied with signal alignment on day of test, environmental settings, delay values, dead space volumes etc. can be manually entered into system settings menu by a Supervisor.

Selecting ‘use current settings’ will then apply settings currently saved in system settings to the raw data file being re-run. The results generated by the re-play will reflect any changes from original settings accordingly.
9. Select **Confirm** to continue.

10. Confirm correct DSR Set number (will apply corresponding dead space volumes listed in **System Settings**).

11. The results generated by re-running files should be identical to the results from day of test *provided day of test conditions were used during re-run*. If the operator selects ‘use current settings’ which differ from conditions on day of test the results will change accordingly.

12. Once the trial(s) has run to completion the operator may then navigate to the analysis page where results are displayed in exactly the same manner as original data collection. If desired a new report can be generated using these newly generated data.

13. Re-running an A-file will result in the **generation of new breath and trial tables** in the pre-determined “dump” folder on the C: Drive. It is important that these files be dealt with promptly to avoid confusion. These are duplicates, and have not replaced the original test run.

***Important**: if the patient record selected/highlighted (chosen on the Patient registration screen) is not the same subject whose A-file is being re-run, the files generated will be labeled with the ID of the selected patient record (a potential source of confusion!).
3.10 Cleaning of Equipment

- In addition to the following recommendations each center should comply with institution specific infection control policies.

1. **Filters** are disposable and should be changed with each subject and within a testing session if notably soiled or damp.

2. **Mouthpieces and masks** are typically reusable, if cleaned with an appropriate enzymatic cleaning solution between each patient.
   
   Operators should always follow manufacturer’s instructions to determine if pieces are reusable, and, if so, how to optimally clean.

3. **Dead space reducers** should be cleaned every 2 weeks using enzymatic cleaning solution.

4. **SPIRETTEs** are disposable but need only be replaced periodically as they are downstream of the filter. SPIRETTEs should be replaced every 2 weeks.
   
   If spirette or DSR become visibly soiled or are known to be handled with dirty hands both should be promptly replaced with clean equipment.

5. **CO₂ cuvette** can be removed from the device and cleaned in enzymatic cleaning solution. This should occur every 2 weeks, or if problems develop with gas signal/tracing.

   Capnostat must be COMPLETELY DRY before re-attaching Nafion tubing sample line. Ideally, capnostat is dried overnight and then vigorously dried with application of pressurized medical air via a flow meter.

6. **CO₂ sensor/warmer** should be wiped thoroughly with appropriate disinfectant between each subject. Optic sensors on inside of warmer should be wiped carefully with sterile alcohol swabs if necessary.

7. **Flow head** should be wiped down with appropriate disinfectant between each subject.

8. The EXHALYZER® D unit, wires, desk surfaces, chairs, etc. should be wiped down with hospital approved disinfectant between each patient, particularly when dealing with patients with respiratory disease and potential pathogens.

*Please refer to EXHALYZER® D Operators Manual for further information regarding cleaning of equipment.*
4 Troubleshooting

4.1 Noisy Gas Signals
1. Noisy CO$_2$ signal may occasionally be due to fingerprints or debris on the optical sensors and/or windows of the CAPNOSTAT:
   ✓ Attempt to clean with sterile alcohol swabs or glass cleaner.
   ✓ For further cleaning, CAPNOSTAT may be placed in appropriate enzymatic cleaning solution to remove oils/debris from handling.
2. Consider leaks in/loose connection of Nafion tubing, age of tubing, etc:
   ✓ As per manufacturer Nafion tubing should be changed every 6 months or earlier if turning yellow.
3. Misaligned signals will appear noisy:
   ✓ Re-do flow gas synchronization.

4.2 Computer errors
1. Occasionally, the software may stall during the initiation of an MBW test, with the “In Progress” screen never disappearing.
   ✓ If this occurs, force the software to close.
   ✓ Switch off the EXHALYZER® D.
   ✓ Turn the EXHALYZER® D back on after approximately 30 seconds and then reboot software.
2. Computer Error screens may appear during an MBW Maneuver.
   ✓ Often, these can be ignored until test completion; the maneuver will finish without incident.
   ✓ Operator may have to click OK several times for error screen to disappear, then immediately click Stop.
   ✓ If results are not generated the A-file can be re-run.

*Please refer to the EXHALYZER® D Operators Manual for further information related to software error messages. If software errors persist please contact ECO MEDICS AG.
5 Lab Supervisor Responsibilities

5.1 Create User Accounts

- The person responsible for making software changes and updates should be designated supervisor.

1. To create a supervisor account select the Administration button then User Management. The following screen will appear:

![User Management Screen](image)

Figure 49. User Management screen

2. Select Register New User. Another screen will appear where User name, Password and Access rights can then be selected and saved.

3. One (or more) user(s) must have a supervisor account; supervisors are granted permission to make changes to system settings and are required to create other user accounts.

![User Details Screen](image)

Figure 50. User Details

4. The system supervisor should then “add users”. Users may be granted the following levels of access:
   a. Operator – may perform test and flow and gas channel calibration only.
   b. Patient Administrator – may add/edit subjects.
   c. System Administrator – may add/edit/delete patients, access system settings, perform calibration.
   d. Supervisor- has access to all aspects of the Spiroware program.

- Logging into the system using user specific accounts allows tracking of calibration and any changes to system settings.

- Once user accounts have been set up the generic admin/admin account should only be used by company personnel for remote technical support.

***Of note:** The error message Serial cable is not connected will appear when more than one person is logged into Spiroware (i.e. if the system has been idle and entered stand-by mode). To remedy the situation the system must be shut down and re-started. PLEASE REMEMBER TO LOG OUT OF YOUR ACCOUNT to avoid this!
5.2 **Confirmation of Site Specific Dead Space Volumes**

5.2.1 **Automatic Start/Stop and Orientation of Flow**

1. Confirm inspiratory flow is set to positive, leaving this option un-checked reverses the orientation of the flow and volume tracing on the test screen.

2. Ensure Automatic start and stop of test are disabled (un-checked).

![Figure 51 System Settings; Flow Positive, Auto Start/Stop Settings](image)
5.2.2 Site Specific Dead Space Volumes

5.2.2.1 Pre Gas Sampling-point Dead Space Volume

Pre gas sampling-point dead space volume is measured from patient to gas sampling port.

- Pre gas sampling-point dead space volume will be influenced by the size of filter and type of interface (mouthpiece) used during testing.
- The recommended filter for testing school age children and adults is the Air Safety Eco Slimline, cat No 4222/01, manufactured by Air Safety Ltd, Morecambe, UK. This is the filter used during the collection of normative data for this equipment.
- Hard plastic mouthpieces should be avoided and soft mouthpieces should be trimmed as much as possible to avoid adding any unnecessary dead space volume to the breathing circuit. Ensure all soft mouthpieces used are trimmed in the same manner.
- Results corrected for both pre and post gas sampling-point dead space volume are calculated to the airway opening (1).
The size and shape of mouthpieces will vary between sites. Although every effort should be made to minimize excess dead space by trimming the mouthpiece, pre gas sampling-point dead space will likely vary somewhat between centers and will differ from default Spiroware values.

Therefore, it is recommended that individual sites measure the pre gas sampling-point dead space volume of their equipment set up. This can easily be done using water displacement, and care should be taken to account for overlap between mouthpiece, filter and CAPNOSTAT.

The following centers have measured pre gas sampling-point dead space:

<table>
<thead>
<tr>
<th>Site</th>
<th>Pre-Gas-Sampling Point Dead Space including filter and mouthpiece</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skövde</td>
<td>35.0 mL</td>
</tr>
<tr>
<td>Bern</td>
<td>30.0 mL</td>
</tr>
<tr>
<td>Toronto</td>
<td>33.3 mL</td>
</tr>
<tr>
<td>Sydney</td>
<td>26.4 mL</td>
</tr>
<tr>
<td>Copenhagen</td>
<td>36.0 mL</td>
</tr>
<tr>
<td>Default SPW</td>
<td>24.0 mL</td>
</tr>
</tbody>
</table>

*Table 1: Measured pre gas sampling-point dead space at different sites. Between site Differences are due to the use of site specific interface and filter.*

The Skövde setting was used during collection of normative N₂ MBW data in 510 subjects using the Exhalyzer D with Air Safety Eco Slimline anti-microbial filter (cat No 4222/01, Air Safety Ltd, Morecambe, UK) and trimmed mouthpiece.

1. The Administrator or the Supervisor should enter measured values into the pre gas sampling-point dead space (Pre-Cap. Dead space) fields for Set 2 and Set 3.

*Figure 53. Pre gas sampling-point dead space fields in system settings*
5.2.2.2 Post Gas Sampling-point Dead Space Volume

- **Post gas sampling-point dead space volume** is measured from the sampling port of the CO₂ cuvette to the attachment port of the bias flow block. (2)

![Post gas sampling-point dead space](image)

- **Figure 54. Post Gas Sampling-point Dead Space**

- Post gas sampling-point dead space volume reflects the volume of the breathing circuit between the fresh gas supply (bias flow block) and the gas sampling-point. (2)

- This volume will change according to which dead space reducer (DSR) is used during testing.

- The volume of each set DSR has been determined by the manufacturer. These dead space volumes are the default values found in the **System Settings** menu in the Spiroware software.

1. Ensure that 9.5mL has been entered in the post gas sampling-point dead space (Post-Cap. Dead Space) field for Set 2 and that 22ml has been entered for Set 3.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Set 1</td>
<td>80</td>
<td>110</td>
<td>100</td>
<td>2</td>
<td>3.5</td>
<td>3.5</td>
</tr>
<tr>
<td>Set 2</td>
<td>450</td>
<td>590</td>
<td>100</td>
<td>15</td>
<td>9.5</td>
<td>9.5</td>
</tr>
<tr>
<td>Set 3</td>
<td>800</td>
<td>1100</td>
<td>1000</td>
<td>25</td>
<td>9.5</td>
<td>22</td>
</tr>
</tbody>
</table>

**Figure 55. Post gas sampling-point dead space fields in System Settings Menu**
5.3 Confirmation of BTPS Correction Parameters

1. **Visually CONFIRM** the following default Manual BTPS Correction Parameters before navigating away from the Environmental Settings screen.

   Manual BTPS Correction Parameters:

   - **BTPS correction active:**
     - Target Humidity for online values (%): 0
     - Temperature at Flowhead (°C): 30
     - Relative Humidity at Flowhead (%): 60
     - Body Temperature (°C): 37
     - Body Humidity (%): 100
     - **Humidity at Bypass (%):** 0  

2. If humidity at bypass is not set to 0, adjust accordingly.

3. **ENSURE** the following boxes **ARE TICKED**:
   - □ CO₂ Correction Active.
   - □ Inspiratory Flow Correction Active.
   - □ Expiratory Flow Correction Active.

4. **ENSURE** the following box is **NOT TICKED**:
   -手动ATPS to BTPS correction factor (Insp. only).

5. Press **Save** to update any changes.
5.4 Flow/Gas Signal Synchronization

To be performed weekly by Supervisor.

Please Note: Flow and channel calibrations must be performed prior to Signal Synchronization.

- The lag time between flow and gas signals may vary between Exhalyzer D units and may differ depending on which DSR is used. This is mainly due to differences in sample flow rate between systems but also results from subtle variances in Nafion tubing length and characteristics of the gas analyzers. Therefore the default delay values in Spiroware will not result in optimal signal alignment.

- The supervisor should perform a number of signal alignment maneuvers to determine the “characteristic” delay of their machine.

- Results within +/- 10 ms of previous or characteristic delay times are acceptable. Results outside this limit should prompt investigation into technique and equipment (see section 5.4.3, Signal Synchronization Troubleshooting).

5.4.1 Set up equipment for Flow/Gas Signal Synchronization

1. Ensure analyzer has been on for at least 5 minutes to ensure temperature stabilization of internal oxygen analyzer.

2. Ensure flowhead, appropriate DSR+ SPIRETTE, CO₂ cuvette, and CAPNOSTAT sensor are in place with Nafion tubing connected and bias flow on (if applicable) (Figure8).

   - Flow/Channel Signal Synchronization should be performed using the DSR Set to be used for testing.

3. The supervisor will require filter, mouthpiece and nose clips to perform calibration.

5.4.2 Perform Signal Synchronization

- To ensure accurate calculation of results, gas and flow signals must be aligned in time.

- The algorithm used to synchronize gas and flow signals is dependent upon a step change in gas signals produced when post gas sampling-point dead space volume is re-inspired.
1. Navigate to the **Administration** menu and select **System Settings**.

2. Confirm that the correct post gas sampling-point (Post-Cap.) dead space volume is listed in the Insert Settings for the appropriate DSR Set to be used for synchronization and testing (Figure 56).

3. Confirm number of washout breaths for synchronization is set to a minimum of 10 (Figure 56).

4. From the **Administration** menu, select **Flow/Channel Signal Synchronization**.

![Figure 56. Post gas sampling-point dead space values, values entered here will be applied to raw data.](image1)

![Figure 57. Administration Menu; Flow/Channel Signal Synchronization](image2)
5. Wearing nose clips, place mouth on mouthpiece and begin tidal breathing through the system; press Start (Figure 58).

6. As soon as breathing pattern is stable, select Open Valve (Figure 58).

- Inhalation must be sharp enough to depict a clear zero crossing but not forceful enough to exceed bias flow and entrain room air. Exhalation must not be too slow or hesitant.

![Figure 58. Flow/Channel Signal Synchronization; Set 3, 10 breaths](image)

7. The supervisor should aim to achieve peak flows in the target range indicated by green bands along the flow tracing of the synchronization screen. The target range will vary with DSR Set # (Set 2 peak flow = 500 mL/s; Set 3 peak flow = 1000 mL/s).

- The system will then collect the **pre-determined number** of washout breaths and will stop automatically.

- The resulting Flow/ O₂ and Flow/CO₂ signal offsets (delay times) represent how much the CO₂ and O₂ signals will be shifted in time during recording in order to align with flow. Values are displayed at the bottom of the screen.
8. Confirm that the values for $O_2$ are between 0.500 and 0.800s and that the values for $CO_2$ are between 0.040 and 0.070s

- $O_2$ and $CO_2$ delay times are influenced by sample flow rate and to some extent properties of the respective gas analyzers and, in the case of $O_2$, the state and length of the Nafion sampling tube (see Exhalyzer D operator’s manual for further information on sampling rate and gas analyzers).

- As such, providing the equipment set up is correct, the post gas sampling-point dead space volume is entered properly in system settings and the breaths used for calibration clearly cross zero flow the delay times should remain within +/- 10 ms.

9. Atypical delay times (see above) should prompt investigation (see section 5.4.3, Signal Synchronization Troubleshooting).

10. Record delay times and ambient conditions, these values may be required to review data at a later date.
5.4.3 Signal Synchronization Troubleshooting

- Poor gas/flow synchronization can result in abrupt spikes or dips at start or end of N₂ signal.

*How to recognize signal delay problem:*

1. As mentioned, the EXHALYZER® D employs an indirect technique to determine N₂ concentration. [CO₂] and [O₂] signals are subtracted to define [N₂]. If signal alignment is off, abrupt spikes or divots in N₂ concentration during a breath can be seen (Figures 59 and 60).

2. These errors can affect FRC calculation and measured CetN₂ which in turn can affect determination of end of washout and LCI, and also other indices calculated.

![Spikes in N₂ signal caused by O₂/flow and/or CO₂/flow misalignment.](image)

*Figure 59. Example of Signal Misalignment*
Ensure Nafion tubing is not kinked and is securely attached to both the CAPNOSTAT and the back of the EXHALYZER® D.

**Note:** changing the Nafion tubing will result in different synchronization characteristics.

- Ensure metal tip of sample line, which extends into the CAPNOSTAT, is free of obstruction.

- Ensure that flow/channel synchronization has been performed with the correct DSR Set # (ie. the set to be used for testing).

- Ensure that the correct post gas sampling-point dead space has been entered into the dead space fields in system settings.

- Ensure that peak flow of breaths used for synchronization is within target range (green band) and that the flow signal clearly crosses zero with no hesitation (Figure 61).

![Figure 60. Example of Signal Misalignment](image)

![Figure 61. Hesitation resulting in imperfect zero crossing](image)
Ensure the CO₂ cuvette is clean and working appropriately and that the sensors on the inside of CO₂ warmer are clean.

Ensure the 3000 hour lifespan of the internal O₂ analyzer has not been exceeded.
   i. Check usage in Administration screen, Device Status.
   ii. Under Oxigraph, see Operating time (Figure 62).

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Figure 62. Device Status Screen
6 References


