Standard Operating Procedure:

Multiple Breath Nitrogen Washout

Exhalyzer D ® (Eco Medics AG, Duernten, Switzerland)

SIGNAL RE-ALIGNMENT

CF Clinical Research Team

The Hospital for Sick Children

Toronto

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SickKids®

Contents

1. What is Signal Alignment?

Signal alignment or synchronization refers to the temporal alignment of the flow, oxygen and carbon dioxide trace. 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.

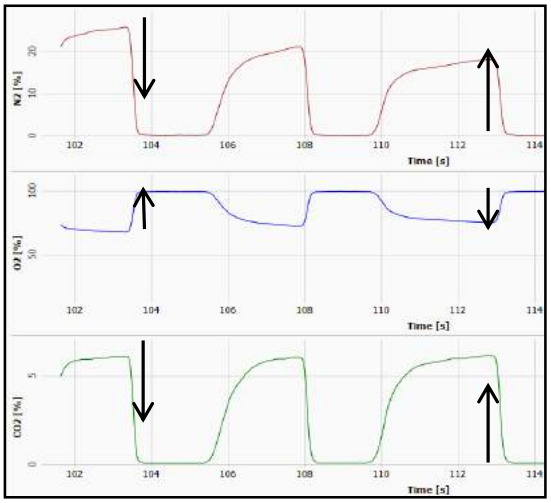
Recall that:

$[N_2]$ is calculated from $[O_2]$ and $[CO_2]$

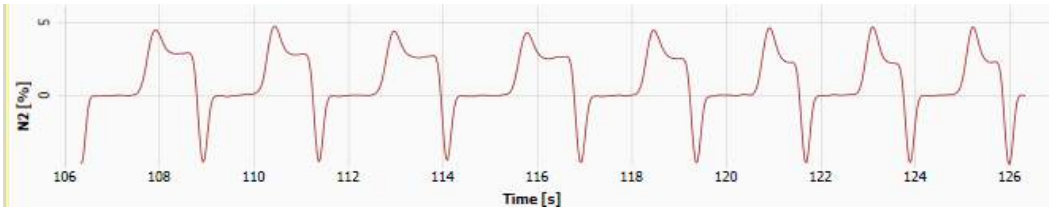
$[N_2] = 100-[0_2]–[CO_2]$

During the breathing cycle $[O_2]$ and $[CO_2]$ travel in opposite directions.

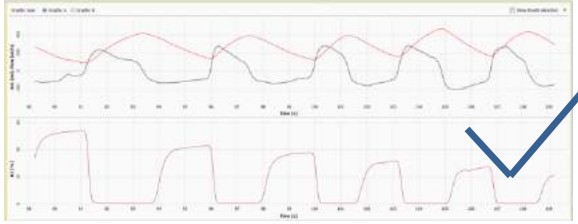
Inspiration: $[O_2]$ increases↑ and $[CO_2]$ decreases↓
Exhalation: $[O_2]$ decreases↓ and $[CO_2]$ increases ↑



Therefore, if $[O_2]$ and $[CO_2]$ are out of phase with one another characteristic spikes and dips will appear in the $[N_2]$ signal. These deflections can alter FRC calculation and measured $CetN_2$, which in turn affects determination of end of washout and LCI measurements.

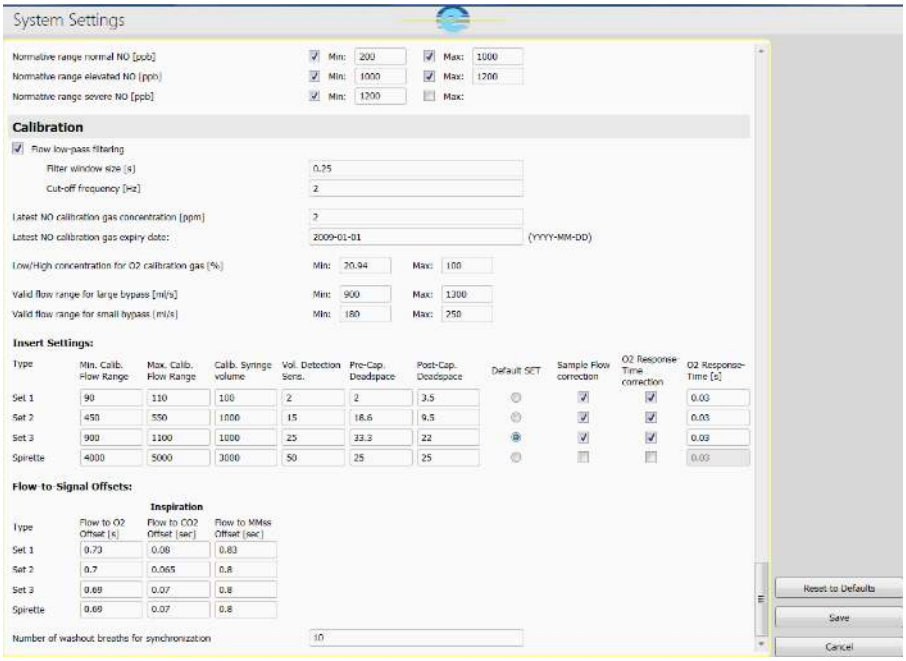


Gas and flow signals must be accurately aligned with one another in time in order to ensure precise estimation and accurate calculation of gas concentration and volume.



Prior to beginning all testing, a trained operator should have performed a number of signal alignment maneuvers to determine the "characteristic" delay of the machine, which is then saved in the system's settings. These values are found in the **Flow-to-Signal Offsets** section at the bottom of **System Settings**.

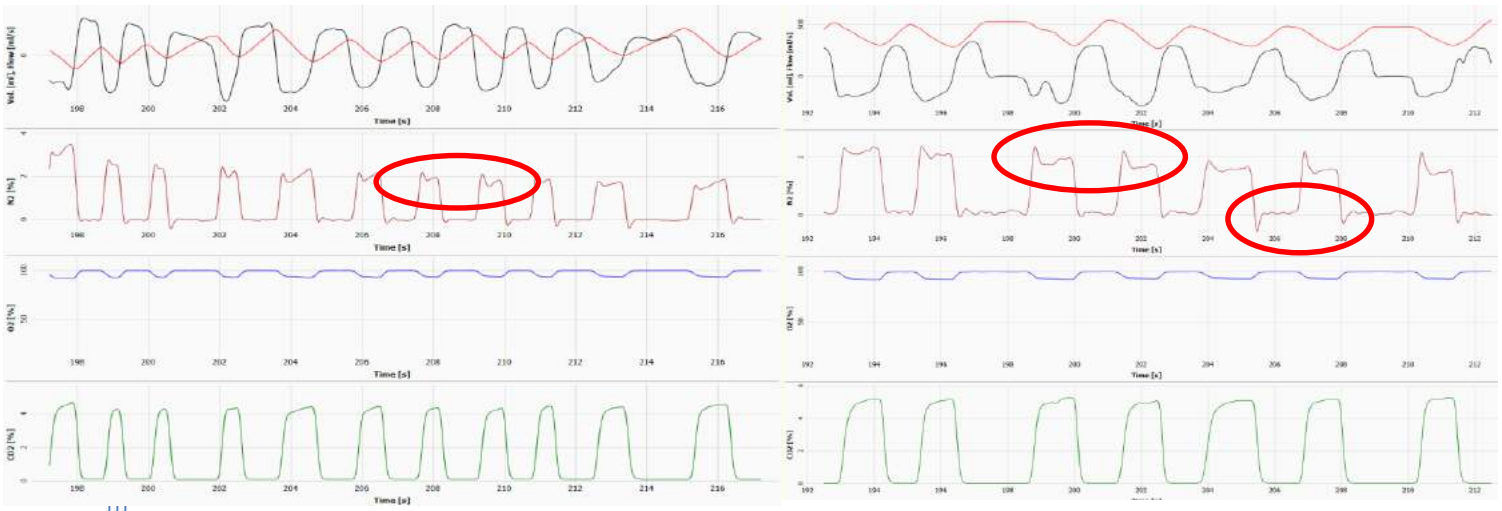
Signal alignment should then be repeated (values recorded but not saved!) every week to verify that results are within +/-10 ms of previous characteristic delay times. **See section 5.4 of the Multiple Breath Nitrogen Washout SOP.**



The resulting **Flow to O_2 Offset** and **Flow to CO_2 Offset** values (synchronization values/delay times) represent how much the CO_2 and O_2 signals will be shifted in time during recording in order to align with flow.

Examples of poor signal alignment:

Poor signal alignment can be identified by repetitive deflections in the N_2 concentration trace.



The N_2 signal should return to zero between breaths, and provided gas calibration has been performed, should not be a negative value (dip below zero).

2. Why is it necessary to correct signal misalignment?

Signals can occasionally become misaligned during testing. This may occur for a variety of reasons, someone may have unintentionally saved a poor synch calibration to the system settings, or possibly the subject being tested has a breathing pattern that is outside the range of values generated by operator synchronization.

Signals must be aligned in order to generate accurate MBW outcomes, therefore signal realignment must be performed before analysis can occur.

3. Determining correct *Flow to O_2 Offset* and *Flow to CO_2 Offset* values (synchronization values/ delay times).

Determining correct delay times depends on why the original delay values were incorrect:

1. Synchronization Values Known (Section 4)
    - Incorrect synchronization times were accidentally saved to system settings and need to be set back to usual settings. Values can be found in recorded in calibration log.

- Nafion tube was changed and synchronization calibration needs to be performed to determine new characteristic values.

2. Synchronization Values Unknown (Section 5)
    - Trials were collected using the usual synchronization settings but the signals were still misaligned.
    - Generate new values by **performing a *Flow/Channel Signal Synchronization*** with existing data.

4. Synchronization Values Known

In order to properly correct signal alignment, system settings must be returned to day of test conditions and correct flow to O_2 Offset and flow to CO_2 offset values (synchronization values/ delay times) must be determined. The following values will be required:

1. **Environmental settings**: ambient temperature (°C) and pressure (hPa) **from the time of test**
    - Environmental values should have been recorded in a log at the time of test.
    - If values were not recorded or known, they can also be found in the subject's **A-files** (see Section 4.1).

2. **Dead space volumes:** corresponding to the equipment used at **time of test.**
    - ****Study specific;** dead space settings used should be based on the study the subject is enrolled in.
    - If values were not recorded or known, they can also be found in the subject's **A-files** (see Section 4.1).

3. **Flow to O_2 and Flow to CO_2 Offset values (synchronization values/ delay times):**
    - Correct synchronization values can be:
        1. Found as recorded in calibration log
        2. Determined by performing synchronization calibration with new Nafion tubing.

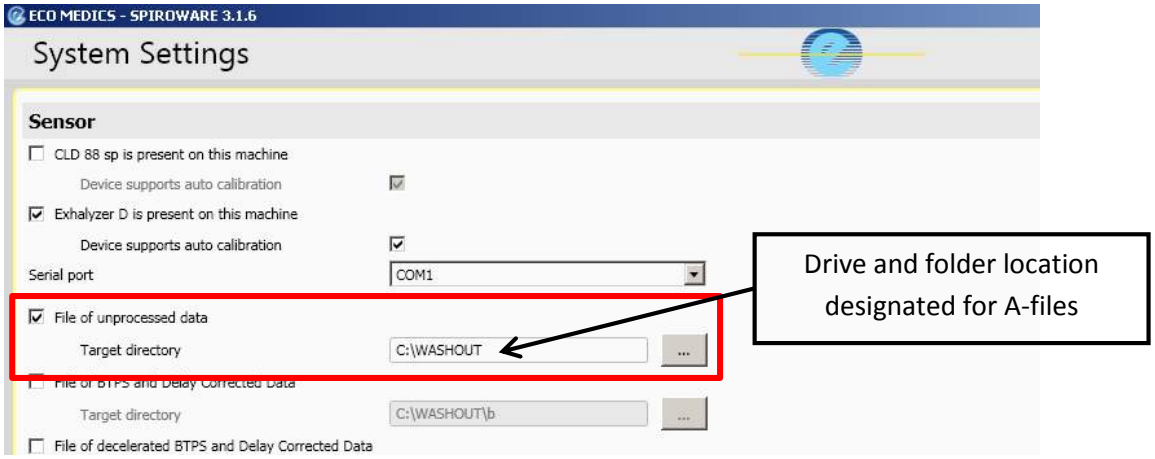
4.1 Where to find Environmental settings and dead space volume measurements if not recorded.

Environmental conditions and other system settings from time of test are recorded within the raw data or A-file. An A-file is a text document generated for each patient recording (per trial) and contains the raw flow, O_2 and CO_2 offset (synchronization) values.

The location of A-files is specified in the System Settings.

4.1.1 WHERE ARE A-FILES STORED?

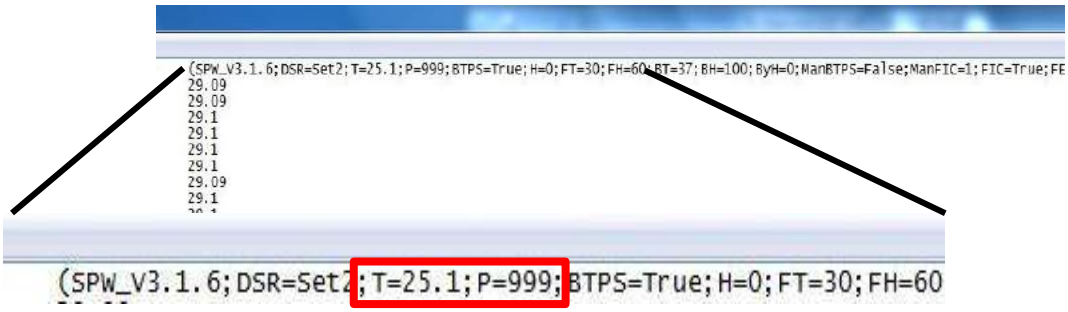
1. Open Spiroware and navigate to the **Administration** menu
2. Open **System Settings**, under **Sensor** heading locate **File of unprocessed data**



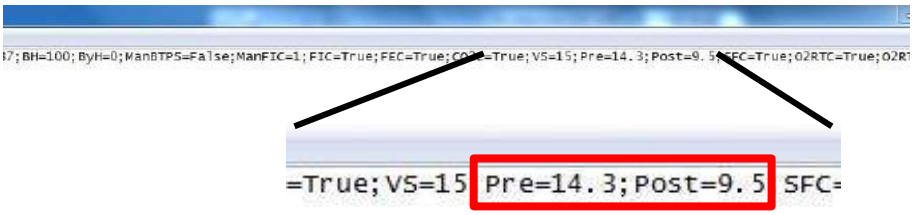
3. Open the folder that contains raw data and select any A-file from the subject and test occasion you need to correct for signal misalignment. All A-files from the same test will have the same settings.

4.1.2 WHAT INFORMATION DOES THE A-FILE CONTAIN?

1. **Environmental Settings:** Temperature and Pressure can be found in the header of the A-file.



2. **Pre and post capillary dead space volumes** corresponding to the DSR used during testing can also be found in the A-file.



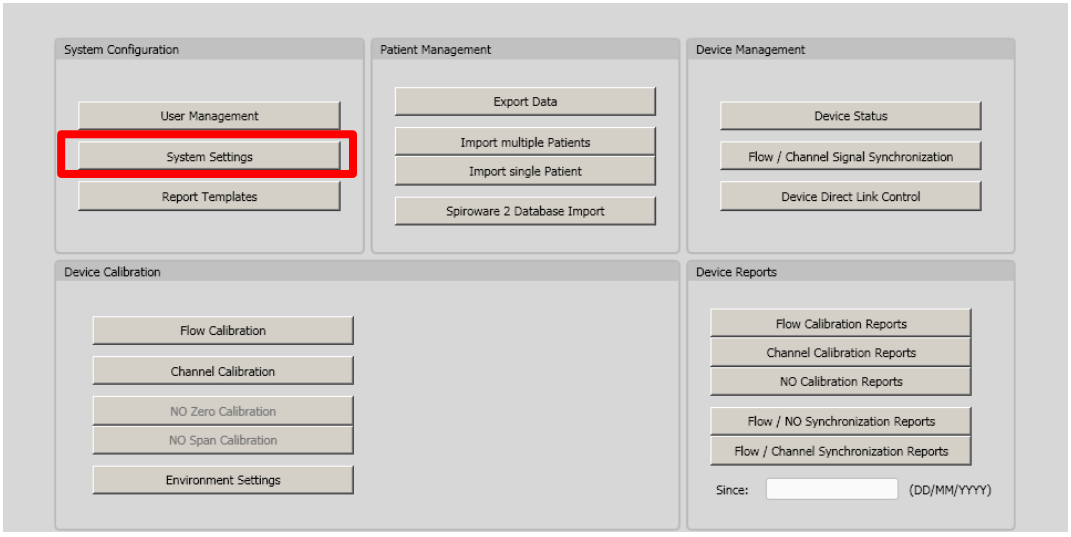
4.2 Restore System Settings to day of test conditions and Correct Synchronization Values.

All system settings influence calculation of results; ONLY delay times should be corrected and all environmental and other system settings should be restored to day of test values.

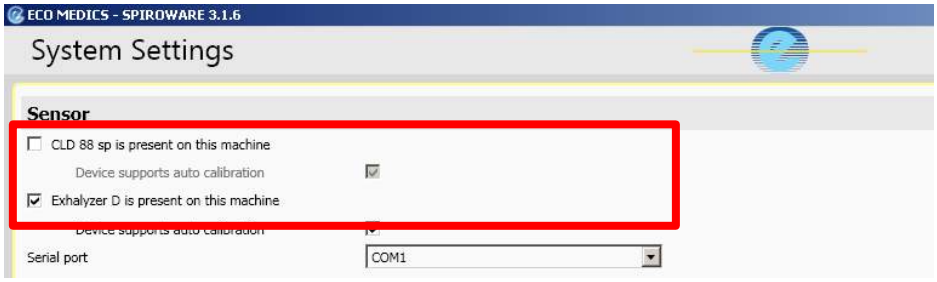
4.2.1 Set General System Settings

1. If Exhalyzer D® system is **not actively running** (i.e. turned off) Spiroware must be set to simulator mode.
    - Right click on Ecomedics symbol in the header of the Administration page
    - Select **Simulation**
    - Select **Enable Patient Simulator**
    - Deselect **Simulate in real-time**

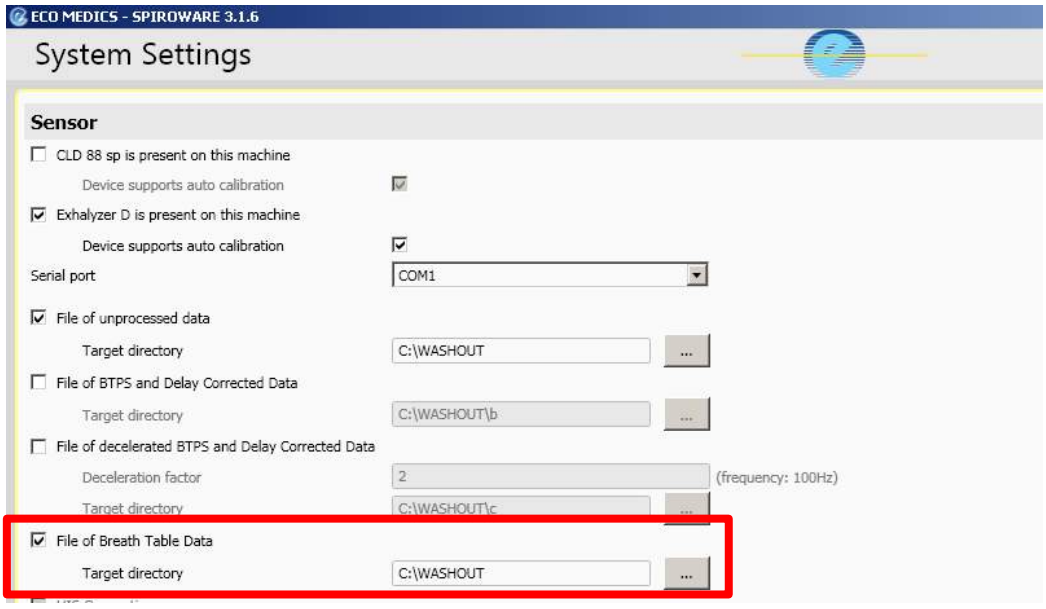
2. From the **Administration** menu, open **System Settings**



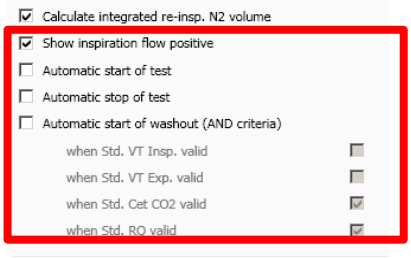
3. Under **Sensor** heading Ensure CLD 88 (exhaled nitric oxide (NO) analyzer) is disabled if not present on device. Ensure Exhalyzer D® is enabled (Check in the box). **Note- NO analyzer is specialized hardware that is NOT standard equipment.



4. Raw data files (unprocessed data) should ALWAYS be selected but **new A-files will not be created** by re-running files. If desired, B, C or Breath Table data re-calculated with new settings can be saved to a folder on your local hard drive *provided the following settings are correct:*
   - Ensure that the **data type** is selected
   - Ensure that the data is mapped to an **existing** folder on the C:\ Drive

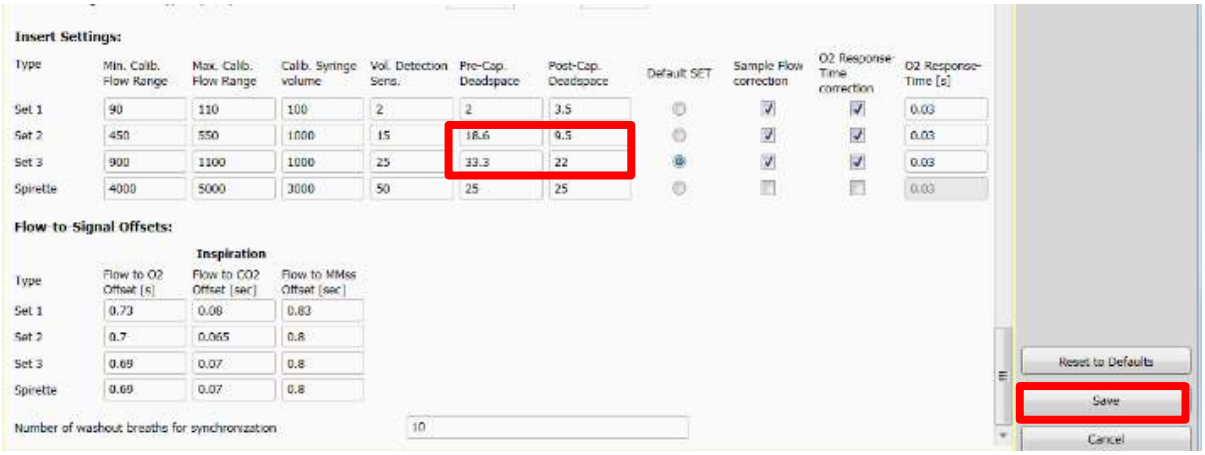


5. Ensure orientation of the flow signal is correct and automatic start and stop are disabled.
   - Scroll down in System Settings confirm **Show inspiration flow positive is selected** and confirm **Automatic start** and **Automatic stop** of the test are **NOT selected.**



4.2.2 Enter Day of Test Dead Space Values

- Scroll to the ***Calibration*** header in System Settings
- Enter the **Pre-Cap Deadspace and Post-Cap Deadspace** values that correspond to equipment used at time of test for appropriate DSR Set # (Set 2 or Set 3, depending on which set was used for the test).
- Different studies have specific values
- Press **SAVE** before returning to the main menu



4.2.3 Enter Correct *Flow to O_2 Offset* and *Flow to CO_2 Offset* values (synchronization values/ delay times).

- Under the **Calibration** header in **System Settings**, Scroll to **Flow –to-signal Offsets** enter the correct values in the **Flow to O2** and **Flow to CO2** Offset fields for corresponding DSR.

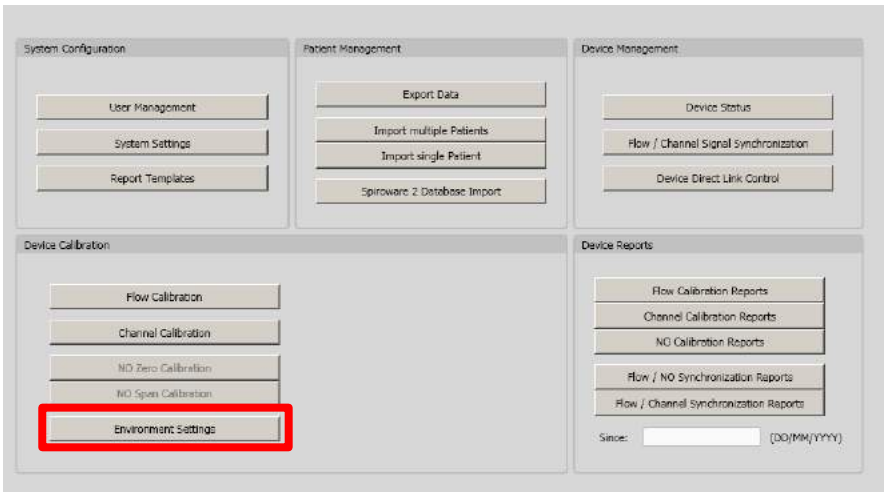
- Press **Save.**

Flow-to-Signal Offsets:

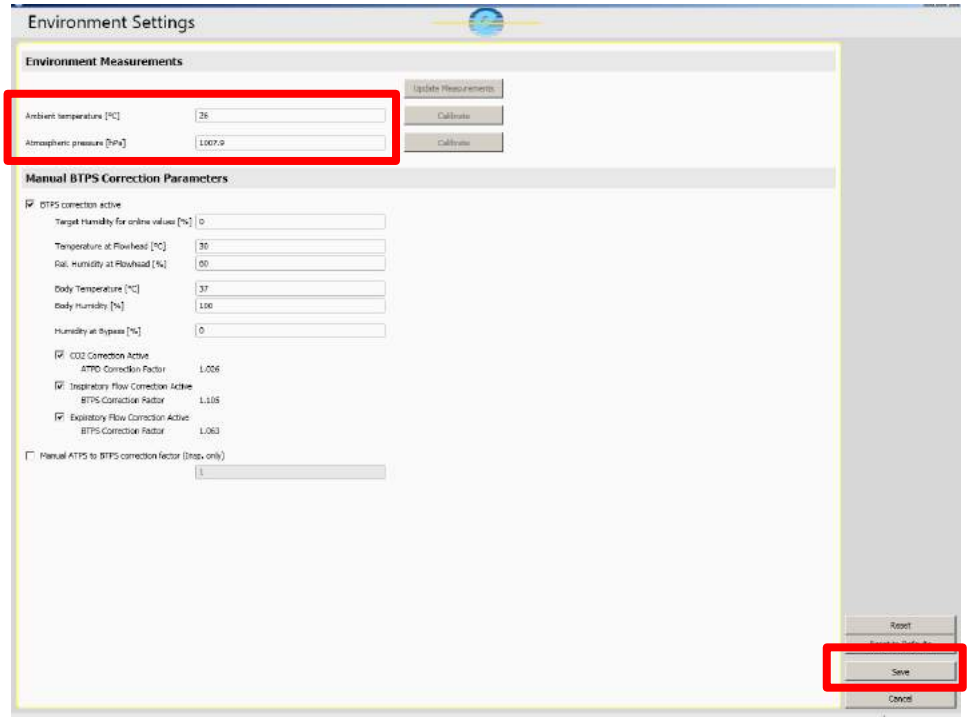
	Inspiration		
Type	Flow to O2 Offset [s]	Flow to CO2 Offset [sec]	Flow to MMss Offset [sec]
Set 1	0.73	0.08	0.83
Set 2	0.68	0.065	0.68
Set 3	0.553	0.0715	0.553
Spirette	0.69	0.07	0.8

4.2.4 Enter Day of Test Environmental Conditions

1. From the **Administration** menu, select **Environment settings**



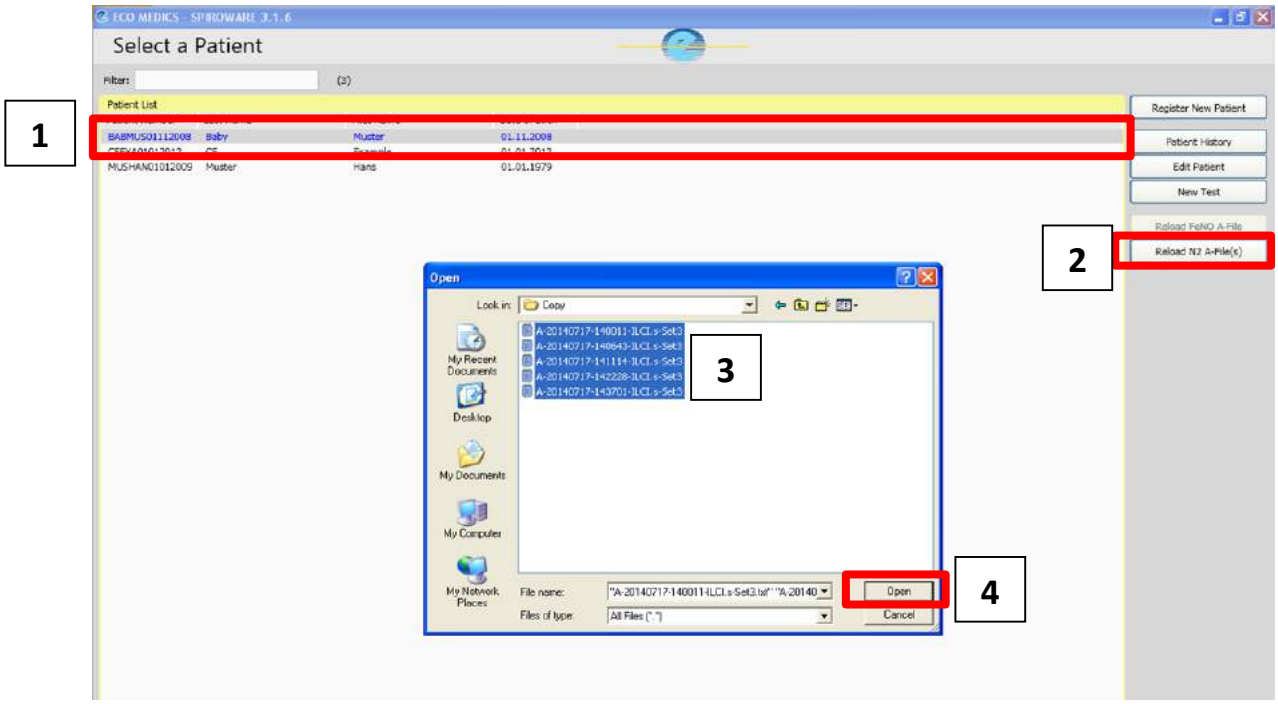
2. Enter the ambient Temperature and Pressure from the time of test, press **SAVE** before returning to the main menu.
    - Note – **do not** need to press Calibrate or Update Measurements



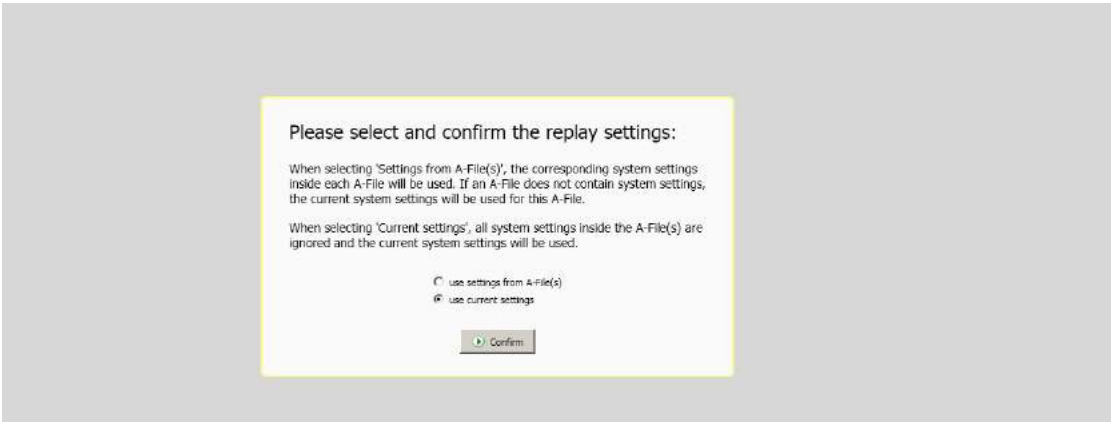
4.3 How to re-run A-files to correct signal misalignment.

Now that all of the system and environmental settings have been restored to day of test and the new delay values have been saved to system settings the operator may proceed with re-running files to correct signal misalignment.

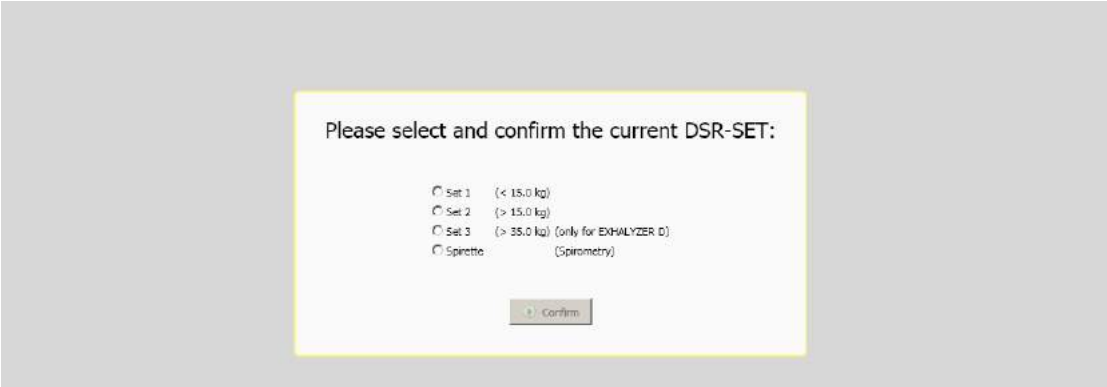
1. On the Select a Patient page, **highlight** the subject whose raw data files will be re-run
2. Press **Reload N_2 A-file(s)**
3. Find the files for be re-run **(can select all at once)**
4. Press **Open**.



3. Select **Use current settings** and press **Confirm.**



4. Select the **DSR set** to be used and press **Confirm**. Use the same set as the time of test.



- The rerun will then begin and the A-files will automatically re-play in sequence, once the re-run is complete the software will stop automatically.

- **Once the re-un is complete, navigate to the Analysis Page (exactly the same as during a live test) and be sure to SAVE AS DRAFT before leaving the test occasion or the results will not be saved.**

- In addition to the draft file saved at the time of test, a second draft file, with the date of the re-run, will now be visible in the subject file. **DO NOT DELETE THE ORIGINAL DRAFT FILE!**

5. Prior to submitting the corrected file for analysis check that the signals have now been aligned by opening the draft file, and scrolling through each trial inspecting for evidence of signal misalignment.

- If alignment is still not corrected proceed to Section 5

5. Synchronization Values Unknown

In order to properly correct signal alignment, system settings must be returned to day of test conditions and correct flow to O_2 Offset and flow to CO_2 offset values (synchronization values/ delay times) must be determined. The following values will be required:

1. **Environmental settings**: ambient temperature (°C) and pressure (hPa) **from the time of test**
    - Environmental values should have been recorded in a log at the time of test.
    - If values were not recorded or known, they can also be found in the subject's **A-files** (see Section 5.1).

2. **Dead space volumes:** corresponding to the equipment used at **time of test.**
    - ****Study specific;** dead space settings used should be based on the study the subject is enrolled in.
    - If values were not recorded or known, they can also be found in the subject's **A-files** (see Section 5.1).

3. **Flow to O_2 and Flow to CO_2 Offset values (synchronization values/ delay times):**
    - Synchronization values must be generated using existing raw data files.

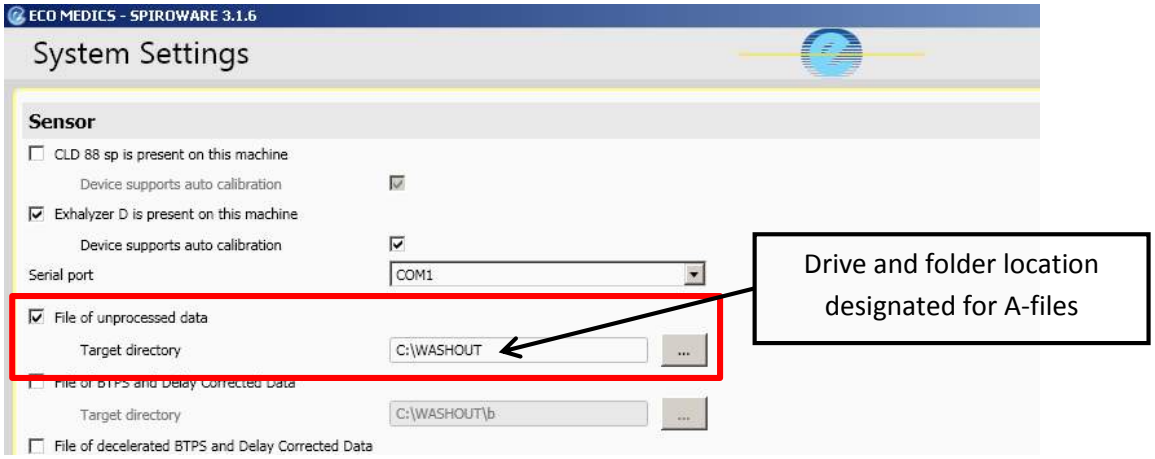
5.1 Where to find Environmental settings and dead space volume measurements if not recorded.

Environmental conditions and other system settings from time of test are recorded within the raw data or A-file. An A-file is a text document generated for each patient recording (per trial) and contains the raw flow, O_2 and CO_2 offset (synchronization) values.

The location of A-files is specified in the System Settings.

5.1.1 WHERE ARE A-FILES STORED?

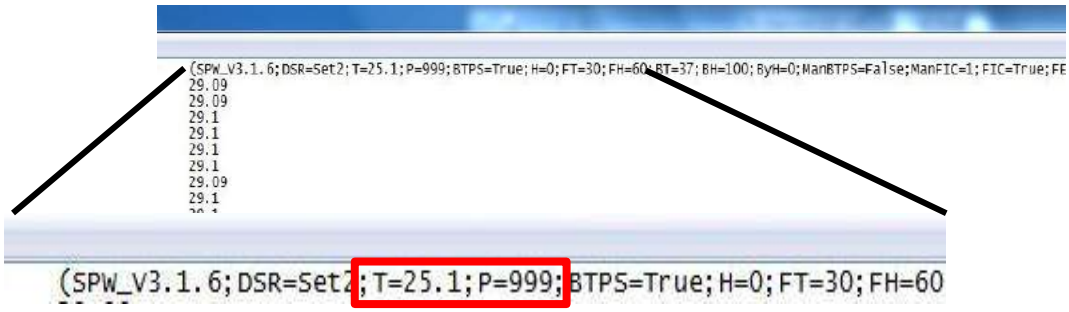
1. Open Spiroware and navigate to the **Administration** menu
2. Open **System Settings**, under **Sensor** heading locate **File of unprocessed data**



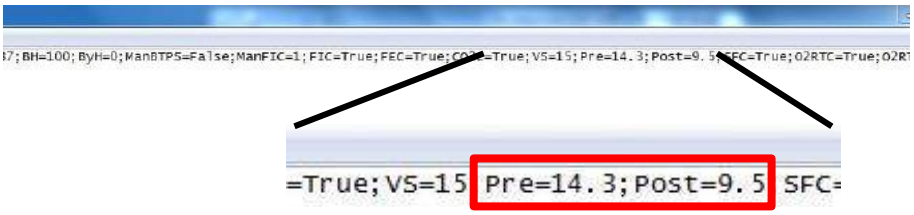
3. Open the folder that contains raw data and select any A-file from the subject and test occasion you need to correct for signal misalignment. All A-files from the same test will have the same settings.

5.1.2 WHAT INFORMATION DOES THE A-FILE CONTAIN?

1. **Environmental Settings:** Temperature and Pressure can be found in the header of the A-file.



2. **Pre and post capillary dead space volumes** corresponding to the DSR used during testing can also be found in the A-file.



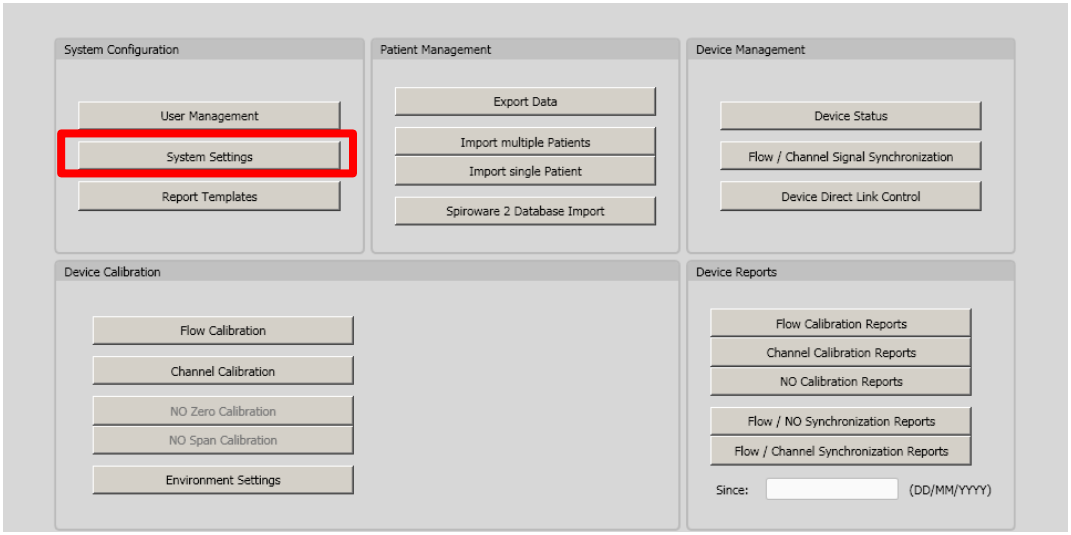
5.2 How to generate new Synchronization Values

When generating new synchronization values, current system settings will influence signal synchronization algorithm, therefore all environmental and other system settings should be restored to day of test values prior to using existing data to generate alternative delay times.

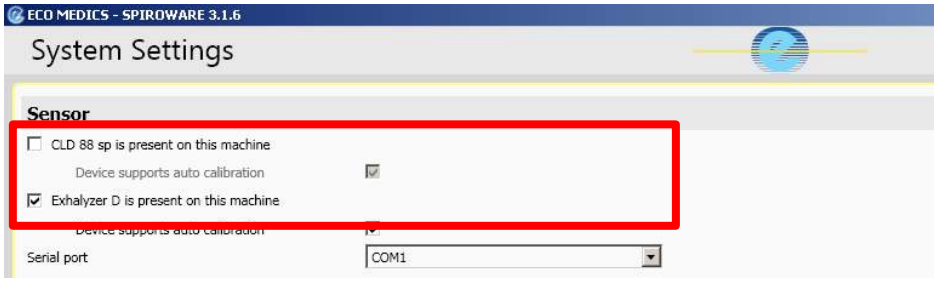
5.2.1 Set general system settings to perform Flow/Channel Signal Synchronization

1. If Exhalyzer D® system is **not actively running** (i.e. turned off) Spiroware must be set to simulator mode.
    - Right click on Ecomedics symbol in the header of the Administration page
    - Select **Simulation**
    - Select **Enable Patient Simulator**
    - Deselect **Simulate in real-time**

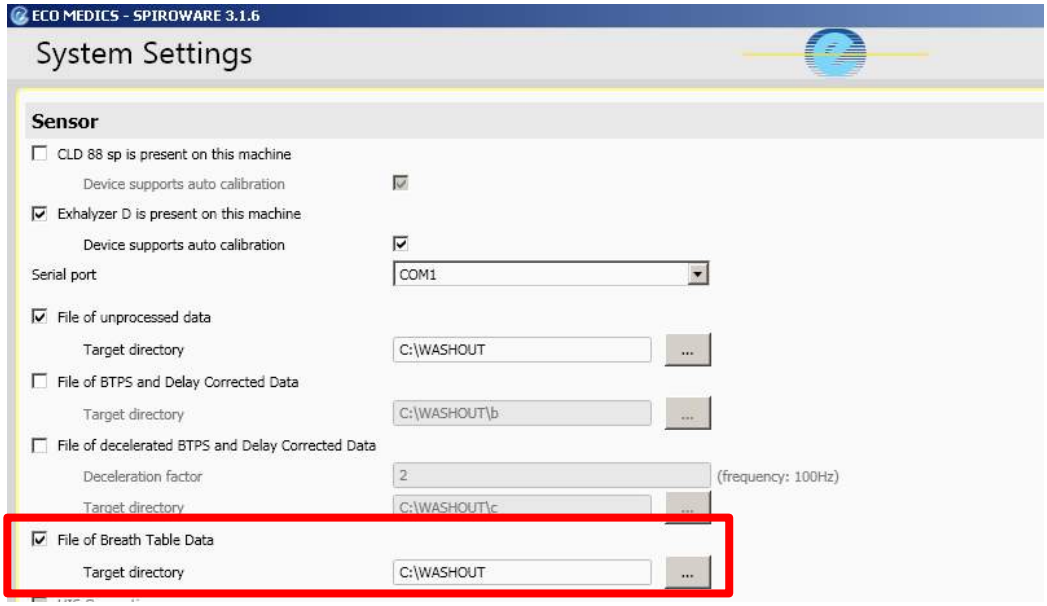
2. From the **Administration** menu, open **System Settings**



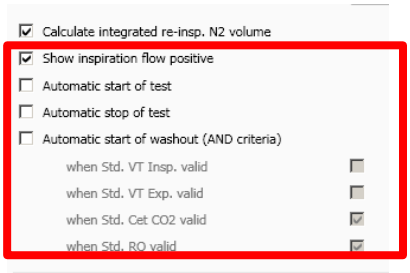
3. Under **Sensor** heading Ensure CLD 88 (exhaled nitric oxide (NO) analyzer) is disabled if not present on device. Ensure Exhalyzer D® is enabled (Check in the box). **Note- NO analyzer is specialized hardware that is NOT standard equipment.



4. Raw data files (unprocessed data) should ALWAYS be selected but **new A-files will not be created** by re-running files. If desired, B, C or Breath Table data re-calculated with new settings can be saved to a folder on your local hard drive *provided the following settings are correct:*
   - Ensure that the **data type** is selected
   - Ensure that the data is mapped to an **existing** folder on the C:\ Drive

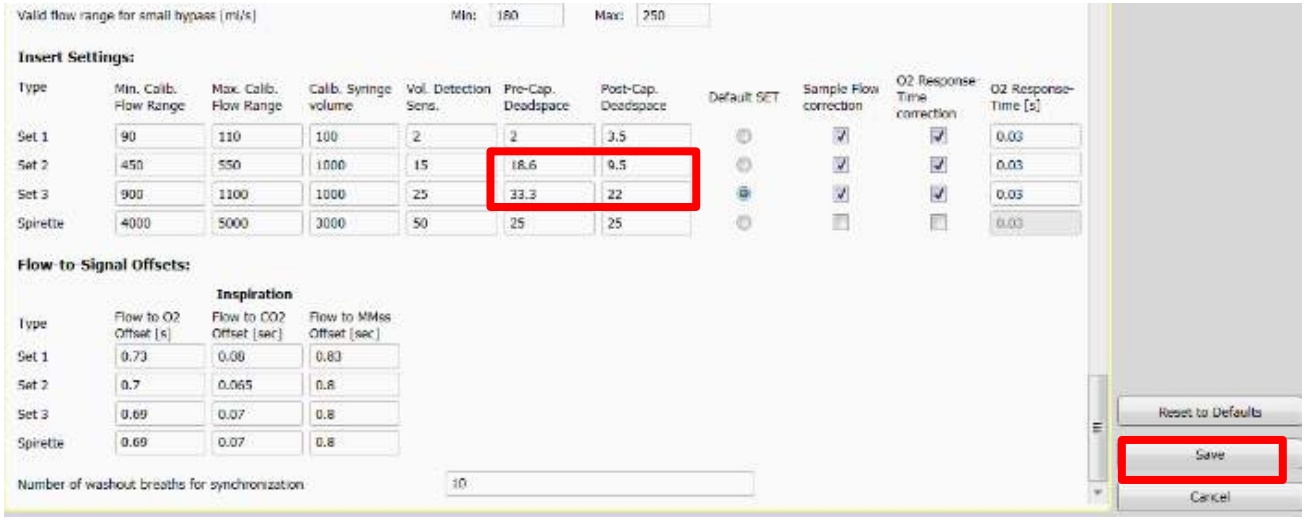


5. Ensure orientation of the flow signal is correct and automatic start and stop are disabled.
   - Scroll down in System Settings confirm **Show inspiration flow positive is selected** and confirm **Automatic start** and **Automatic stop** of the test are **NOT selected.**



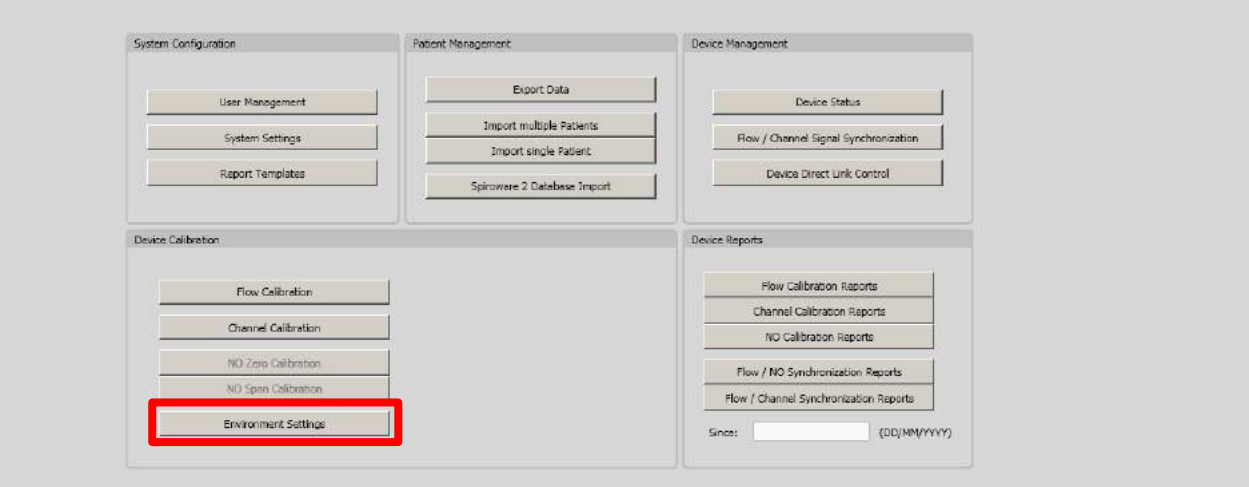
5.2.2 Enter Day of Test Dead Space Values

- Scroll to the ***Calibration*** header in System Settings
- Enter the **Pre-Cap Deadspace and Post-Cap Deadspace** values that correspond to equipment used at time of test for appropriate DSR Set # (Set 2 or Set 3, depending on which set was used for the test).
- Different studies have specific values
- Press **SAVE** before returning to the main menu

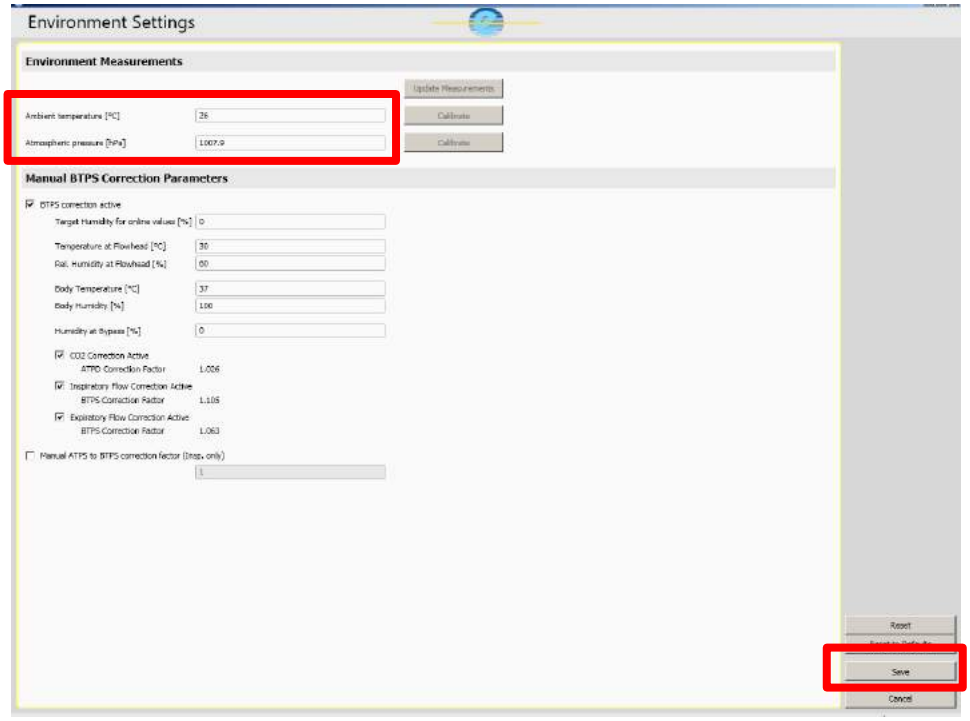


5.2.3 Enter Day of Test Environmental Conditions

6. From the **Administration** menu, select **Environment settings**

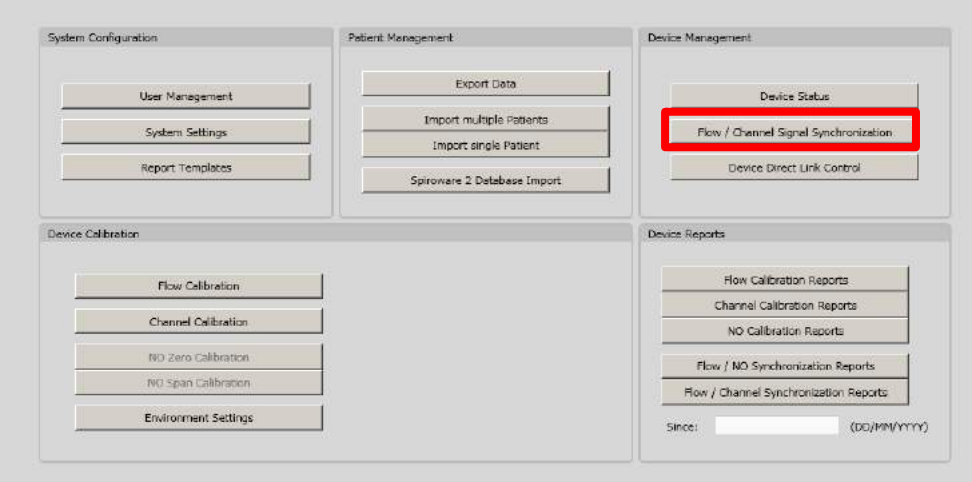


7. Enter the ambient Temperature and Pressure from the time of test, press **SAVE** before returning to the main menu.
    - Note – **do not** need to press Calibrate or Update Measurements

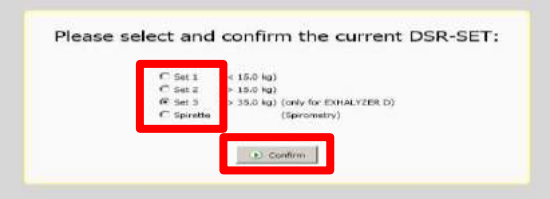


5.3 Perform Flow/Channel Signal Synchronization using existing data.

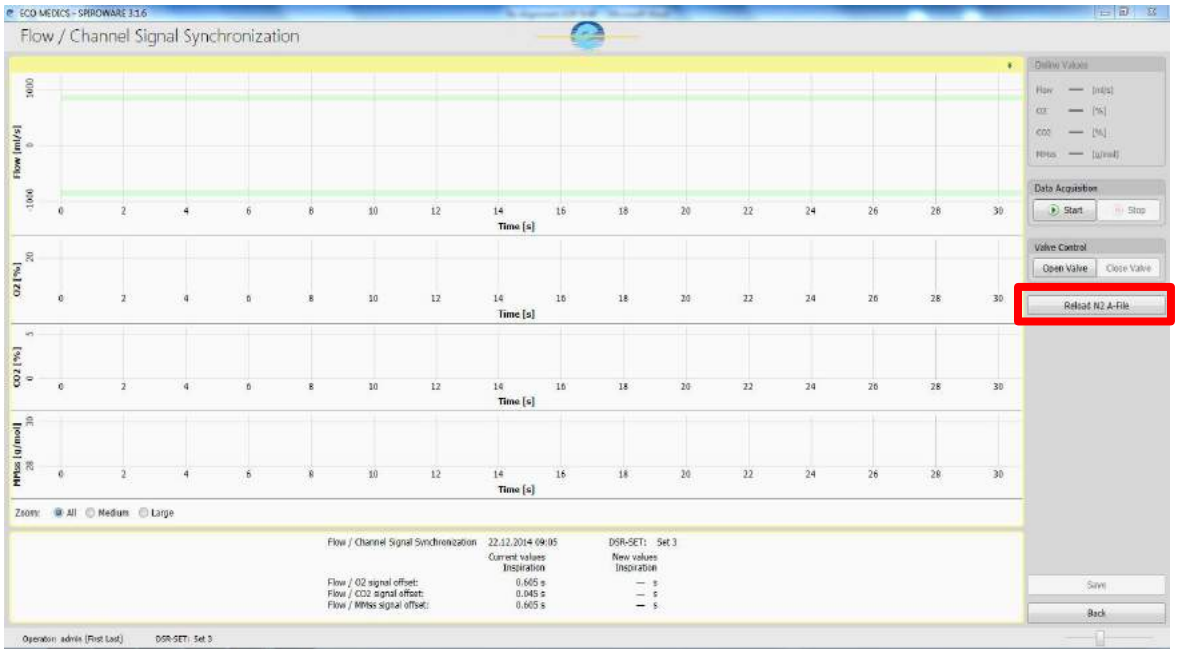
1. From the **Administration** menu, select **Flow/Channel Signal Synchronization**



2. Select Set 2 or Set 3 depending on which DSR Set was used for testing – press **Confirm**



3. Select "**Reload N_2 A-Files**"

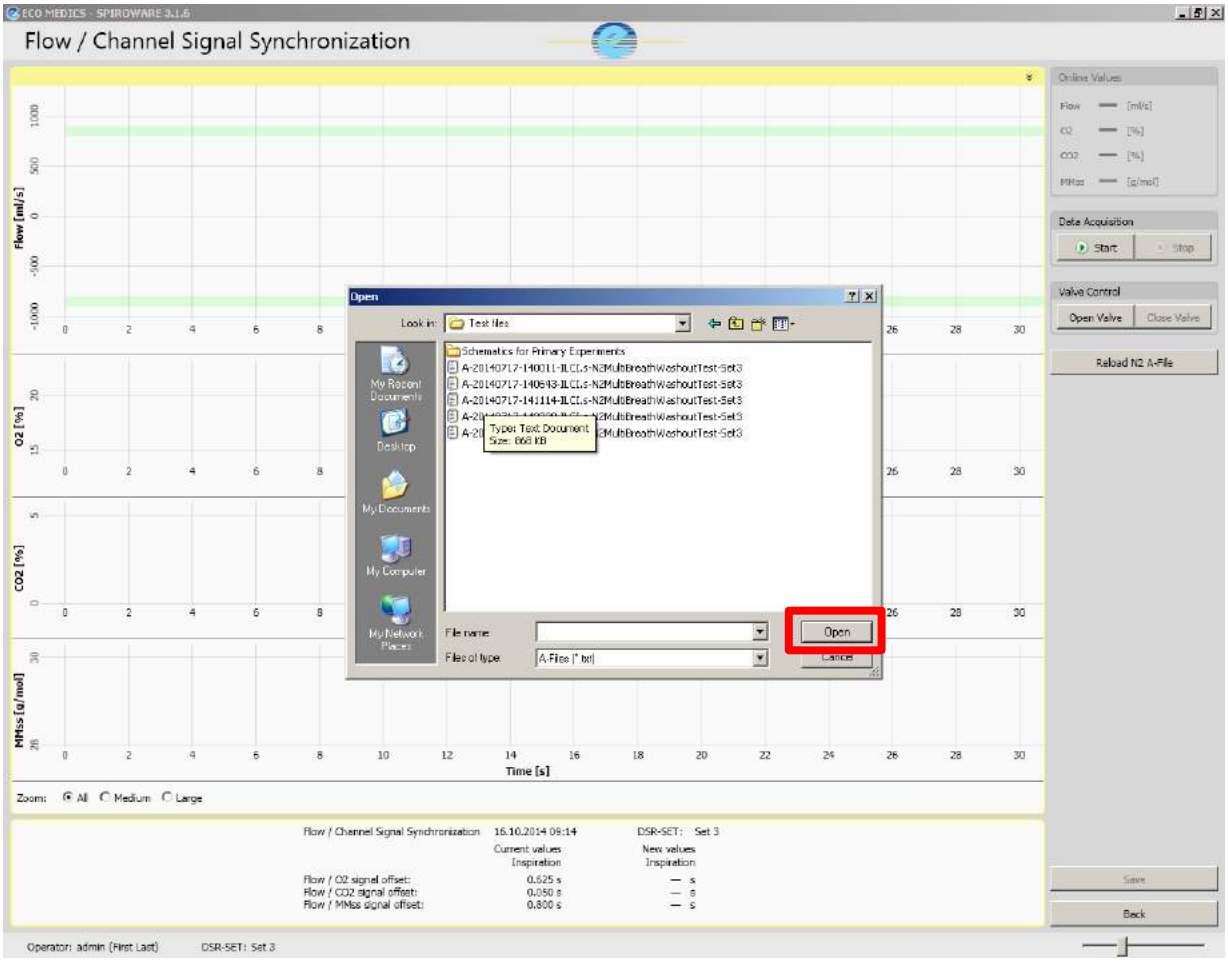


4. Select an A-file to be used to generate new delay values.

When selecting an A-file to use for synchronization please ensure the following:

- ✓ **The first 10 breaths are tidal breaths; no irregular breaths**
- ✓ **The transition from exhalation to inspiration is smooth; no hesitations**

5. Press Open – the file will automatically start running

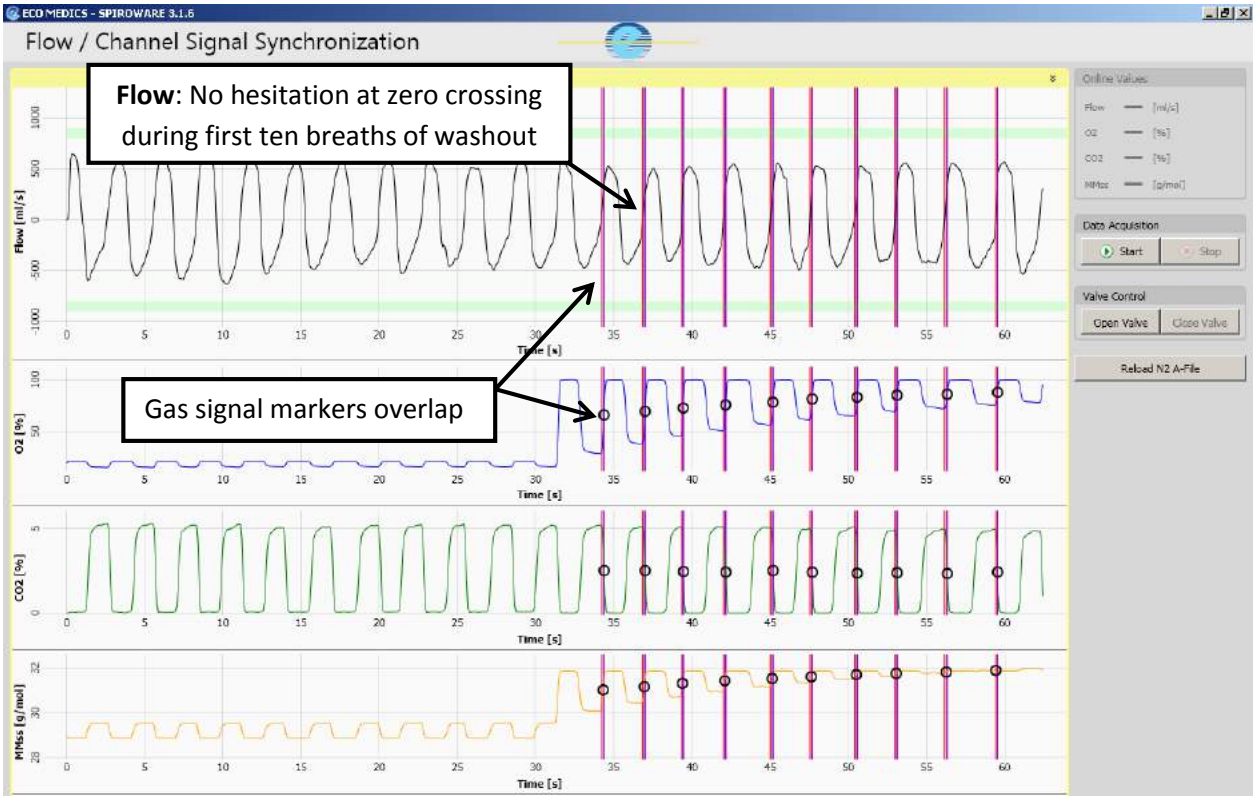


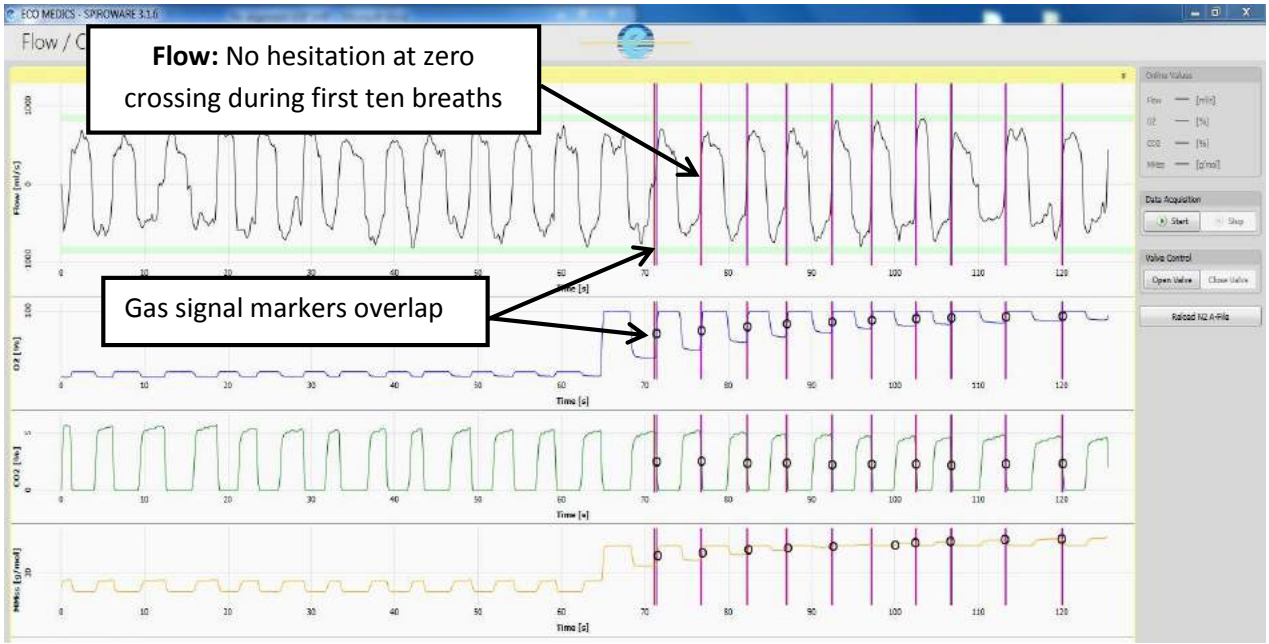
5.3.1 How do I know if the synchronization is acceptable?

Acceptable:

- ✓ Flow tracing clearly crosses zero during transition between inspiration and expiration for the first ten breaths of the washout.
- ✓ All gas signal marker lines (blue, red) overlap for the first ten breaths of the washout.

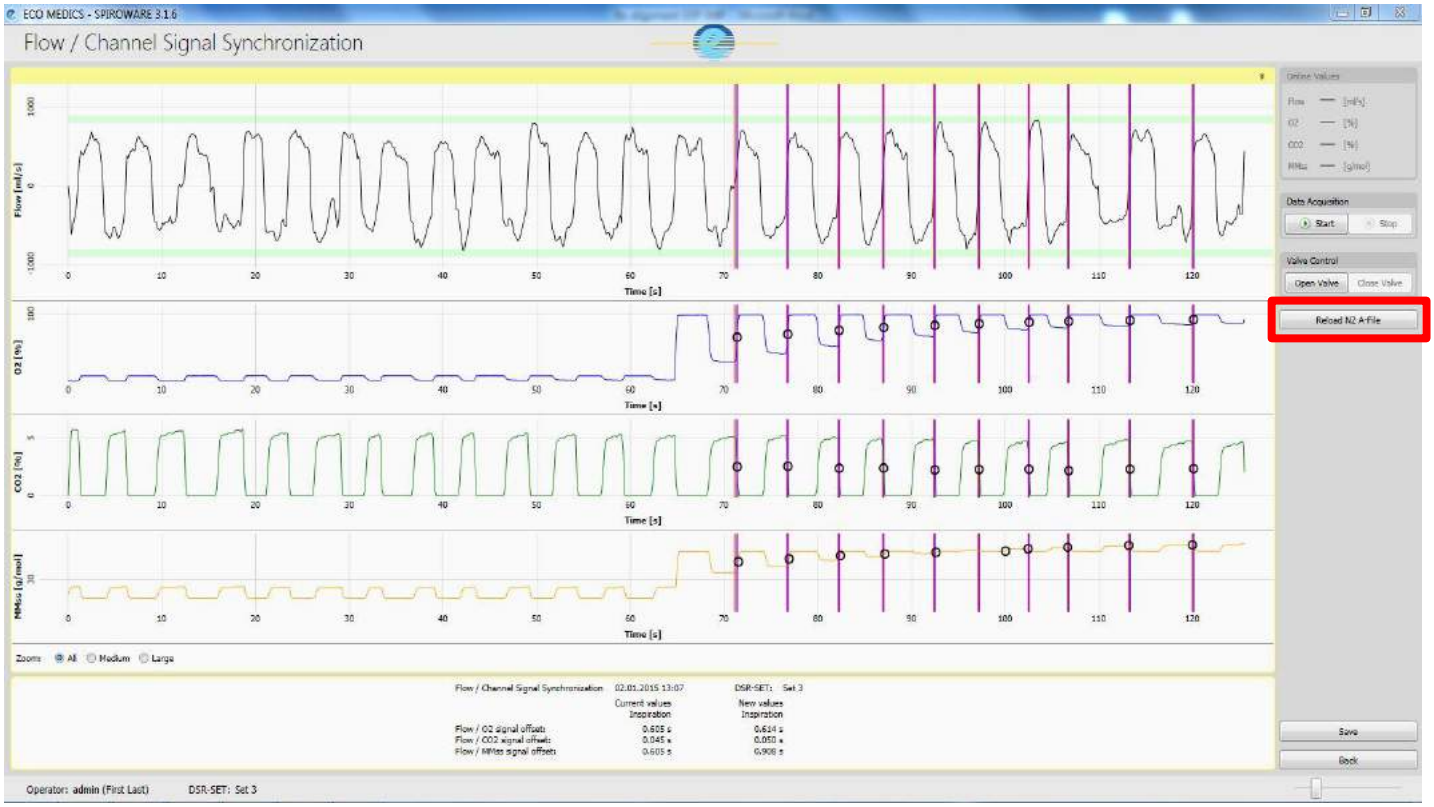
Examples of acceptable synchronization

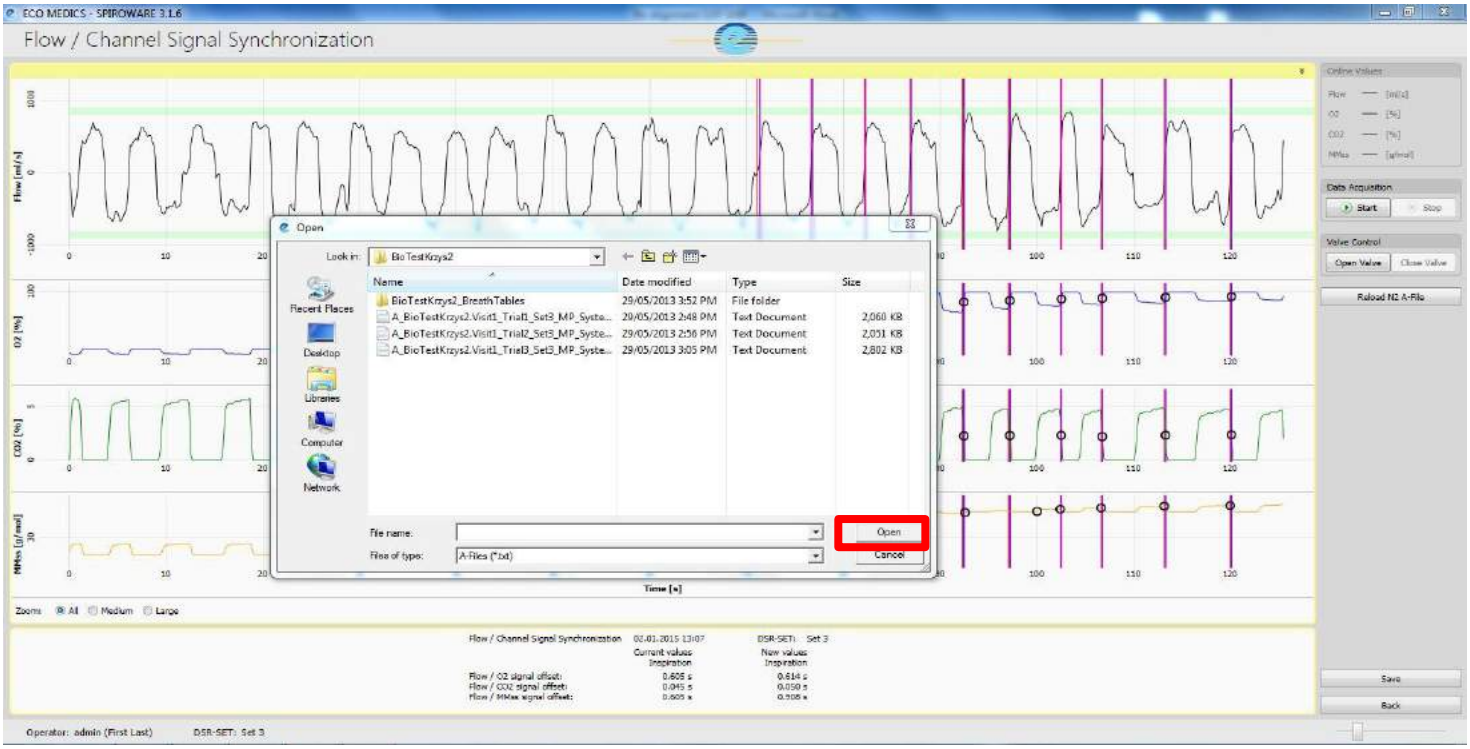




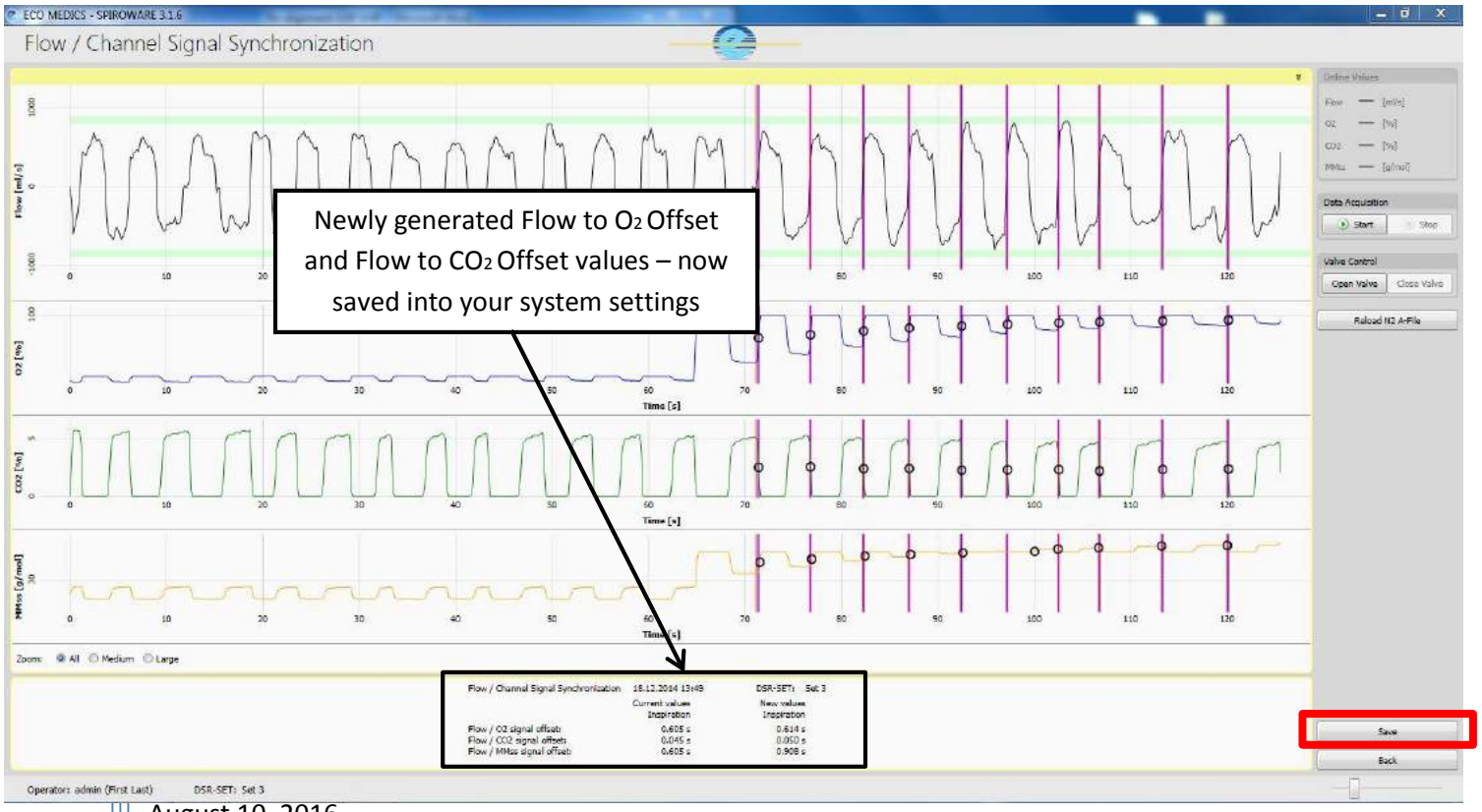
Examples of unacceptable synchronization

8. Only values generated from acceptable synchronization should be saved. If the first A-file is unacceptable select "**Reload N_2 A-file**" again to load the subject's next A-file. You can do this as many times as needed until an acceptable trial is found.





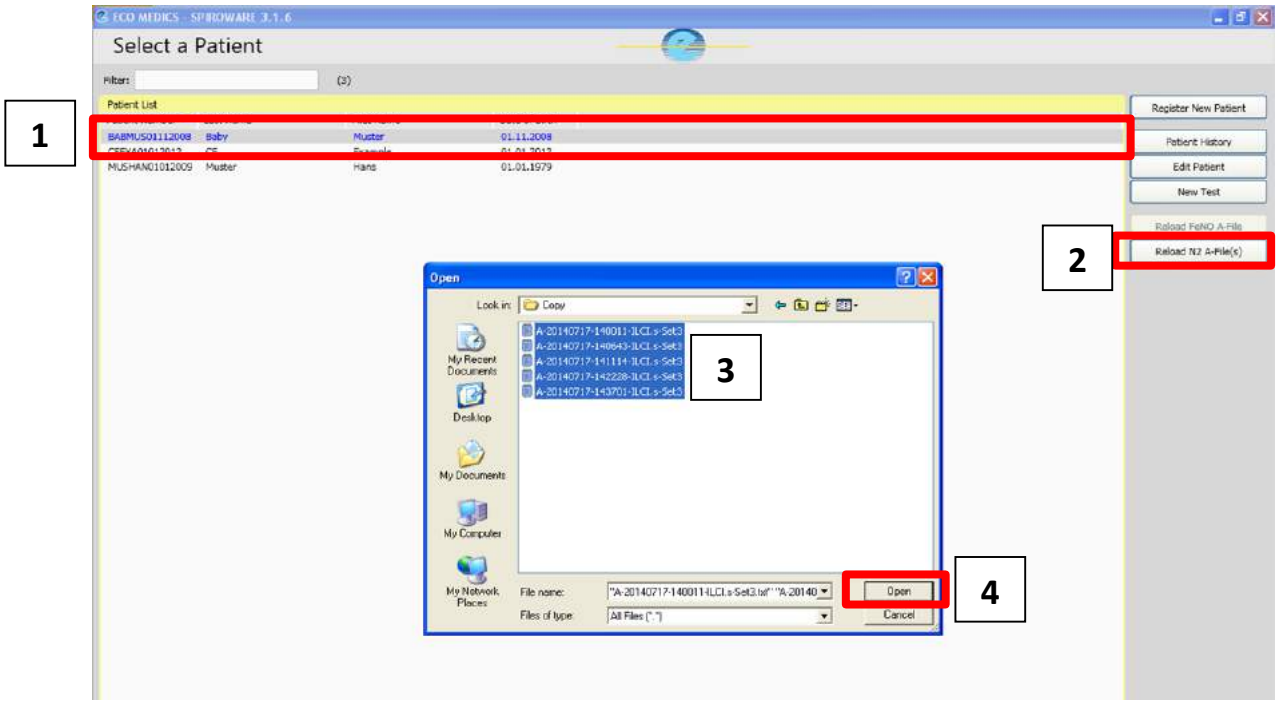
9. **Once an acceptable trial is found, press <u>save</u>; the newly generated numbers will then be saved in System Settings.**



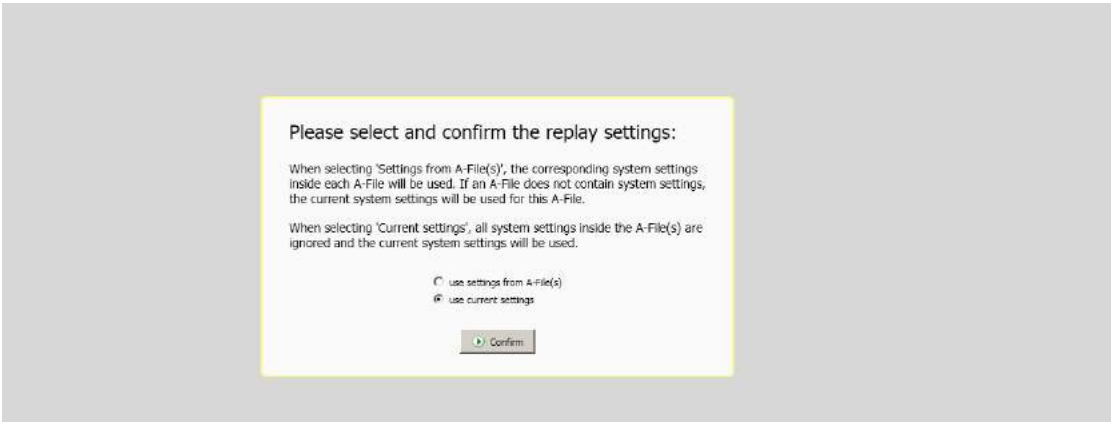
5.4 How to re-run A-files once new delay times have been generated.

Now that all of the system and environmental settings have been restored to day of test and the new delay values have been saved to system settings the operator may proceed with re-running files to correct signal mis-alignment.

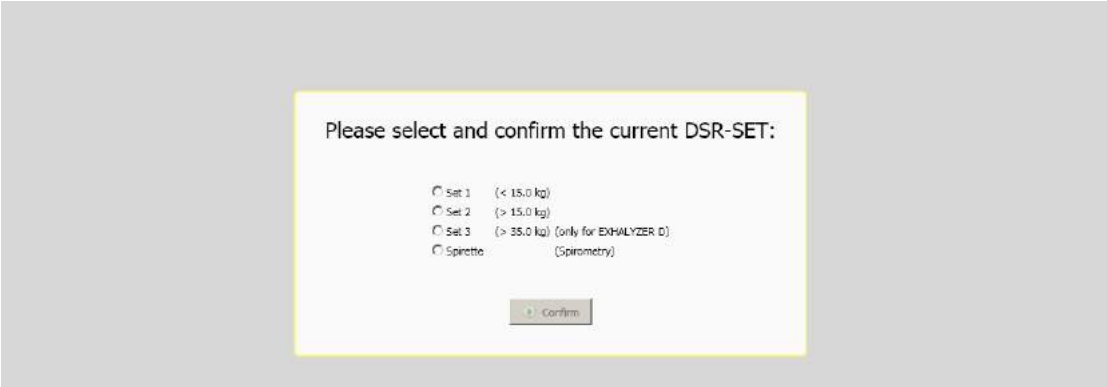
5. On the Select a Patient page, **highlight** the subject whose raw data files will be re-run
6. Press **Reload N_2 A-file(s)**
7. Find the files for be re-run **(can select all at once)**
8. Press **Open**.



10. Select **Use current settings** and press **Confirm.**



11. Select the **DSR set** to be used and press **Confirm**. Use the same set as the time of test.



- The rerun will then begin and the A-files will automatically re-play in sequence, once the re-run is complete the software will stop automatically.

- **Once the re-un is complete, navigate to the Analysis Page (exactly the same as during a live test) and be sure to SAVE AS DRAFT before leaving the test occasion or the results will not be saved.**

- In addition to the draft file saved at the time of test, a second draft file, with the date of the re-run, will now be visible in the subject file. **DO NOT DELETE THE ORIGINAL DRAFT FILE!**

12. Prior to submitting the corrected file for analysis check that the signals have now been aligned by opening the draft file, and scrolling through each trial inspecting for evidence of signal misalignment.

- If alignment is still off, repeat synchronization procedure using a different A-file