Standard Operating Procedure:

Multiple Breath Nitrogen Washout

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

SIGNAL RE-ALIGNMENT 3.3.2

SIGNAL SYNCHRONIZATION USING DDC

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January 26, 2023

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1. What is Signal Alignment?

Signal alignment or synchronization refers to the temporal alignment of the flow, oxygen and carbon dioxide traces. 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 always 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 \uparrow and $[CO_2]$ decreases \checkmark Exhalation: $[O_2]$ decreases \checkmark and $[CO_2]$ increases \uparrow



Temporal alignment of flow, oxygen and carbon dioxide signals results in proper alignment that appear as smooth waveforms. Signal misalignment of $[O_2]$, $[CO_2]$, and flow results in a repeating pattern of peaks and dips in $[N_2]$ signal that are NOT apparent in the $[O_2]$ and $[CO_2]$ trace. These deflections can alter FRC calculation and measured CetN₂, 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 to ensure precise estimation and accurate calculation of gas concentration and volume.





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2. Signal alignment using Spiroware 3.2 and higher - Dynamic Delay Correction

Spiroware Software versions 3.2 and higher include a dynamic delay correction (DDC) algorithm that works in conjunction with the fixed delay correction, and results in improved signal synchronization.

The **fixed O₂ and CO₂ flow-to-signal offsets** (delay times) represent how much the O₂ and CO₂ signals must be shifted in time in order to align with the flow signal. These fixed values are established during the DDC Signal Synchronization maneuver.

In addition to the fixed offset values, the built-in algorithm uses the nafion tube volume determined during the synchronization maneuver to compensate for the change in gas transit time as the washout progresses. Travel (transit) time through the nafion tube increases as gas becomes **more viscous** with **higher O**₂ **concentrations.**

Washout	Approximate Gas Composition	Gas Viscosity	Travel Time
Start Washout	78% N ₂ / 17% O ₂ / 5% CO ₂	Low	Fast
End Washout	2% N ₂ / 93% O ₂ / 5% CO ₂	High	Slow

As gas viscosity increases, and the gas sample moves more slowly through the nation tube, the **required flow-to-signal offset** to align the gas and flow signals **increases.** DDC corrects for the change in gas sample transit time over the course of the washout.

Please Note: DDC Synchronization maneuver <u>replaces</u> the Fixed Delay Correction maneuver

DDC Synchronization Maneuver

The synchronization procedure using DDC is very similar to the previous fixed delay correction maneuver. The maneuver still requires stable breathing within volume targets and must be performed for each DSR Set. However, the DDC is performed **during pre-phase** while breathing **medical air** and the synchronization values are determined over **5 breaths instead of 10**.

Similarities	Differences
Requires stable breathing within targets	Performed during pre-phase while breathing medical air
Synchronization performed for each DSR Set	Synchronization values are determined over 5 breaths instead of 10

Fixed flow-to signal offsets and dynamic delay correction option are found under Flow-to-Signal Offsets in System Settings.

c . c .										
System Setti	ngs									
							H -			
DSK set Settings:										
Туре	Min. Calib. Flow Range [ml/ s]	Max. Calib. Flow Range [ml/ s]	Calib. Syringe volume [ml]	Vol. Detection Sens.	Pre-Cap. Deadspace [ml]	Post-Cap. Deadspace [ml]	Show flow / volume values in [ml]			
Set 1	90	110	100	2	2	3.5	✓			
Set 2	450	550	100	15	15	9.5				
Set 3	900	1100	1000	25	33.3	22				
Spirette	4000	5000	3000	50	25	25				
	Min. Bypass Flow [ml/s]	Max. Bypass Flow [ml/s]								
Set 1	180	250								
Set 2	550	850								
Set 3	900	1300								
Signal Corrections:										
Type	Comolo Elevy correction	O2 Response-Time	02 Baseanse Time [a]	MMss Response-Time	MMax Deseases Time [a]					
1,000	Sample How correction	correction	Oz Response-Time [s]	correction	ninss kesponser nine [s]					
Set 1	¥	⊻	0.03		0.035					
Set 2	¥	✓	0.03		0.03					
Set 3	¥	V	0.03	V	0.03					
Spirette			0.03		0.03					
Flow-to-Signal Offse	ts:									
	for measurements:			for A-File reloads:						
Туре	Flow to O2 Offset [s]	Flow to CO2 Offset [s]	Flow to MMss Offset [s]	Flow to O2 Offset [s]	Flow to CO2 Offset [s]	Flow to MMss Offset [s]	Dynamic Delay correction			
Set 1	0.63	0.05	0.73	0.55	0.05	0.73				
Set 2	0.689	0.072	0.77	0.3	0.045	0.3				
Set 3	0.2	0.02	0.2	0.2	0.02	0.2		Para	t to Defaul	te.
Spirette	0.69	0.07	0.8	0.69	0.07	0.8		Kead		
Number of washout breat	he for synchronization								Save	
Number of Washout breat	is for synchronization								Cancel	-

<u>Prior to beginning all testing</u>, a trained operator should have performed several 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 within the **Calibration** tab of the **System Settings**.

Signal alignment should then be repeated (values recorded but not necessarily saved!) every week to verify that results are within +/-10 ms of previous characteristic delay times (See section Appendix 1).

2.1 Examples of Poor Signal Alignment

Poor signal alignment can be identified by repetitive deflections in the N₂ concentration trace.



The N₂ signal should return to zero between breaths, and provided gas calibration has been performed, should not be a negative value (dip below zero).



3. 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 the subject being tested may have a breathing pattern that is outside the range of values generated by operator synchronization.

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

4. Determining Correct Synchronization Values (delay times).

Determining correct delay times depends on why the original delay values were incorrect. Sometimes the correct delay settings are known but the incorrect values accidentally saved in system settings. Sometimes the delay values in system settings just need to be updated, for example nafion tube was changed so old values are no longer accurate. Sometimes, the subject being tested has a breathing pattern that is outside the typical range of values generated by operator synchronization.

Synchronization Values Known - See Section 5

Correct delay values are known but incorrect synchronization times were accidentally saved to system software settings need to be set back to usual settings. Correct values can be found in recorded in calibration log and used to re-run data (See Section 5).

Updated Synchronization Values Needed - See Section 5

Nafion tube was changed so usual settings are no longer correct. A new synchronization calibration needs to be performed to determine new characteristic delay values (See Appendix 1- How to perform Flow Channel Synch using DDC). Once correct values are known they can be used to re-run data (See Section 5).

Synchronization values Unknown – See Section 6

Trials were collected using the usual synchronization settings, but the signals were still misaligned. Generate subject specific delay values by **performing a** *Flow/Channel Signal Synchronization* with the subject's data (A-files) and use to re-run data (See Section 6).

5. Synchronization Values Known

If correct synchronization values are known, follow the following steps to re-run data.

5.1 Set General System Settings

- 1. Location of A-files (unprocessed data)
 - A-files can be found in the target directory indicated for 'File of unprocessed data' under the **Sensor** tab in **System Settings**.
 - New A-files will not be created by re-running data, but 'File of unprocessed data' should ALWAYS be selected.
 - 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

ECO MEDICS AG - SPIROWARE 3.3.1

System Settings		
Sensor		
CLD 88 sp is present on this machin	e	
Device supports auto calibration:	NO zero 🖌 NO	
Enabled tests:	FENO SB FENO MB Alveolar	
	✓ Nasal ✓ Offline	
 Exhalyzer D is present on this mach 	ine	
Device supports auto calibration	\checkmark	
Enabled tests:	N2 MBW N2 SBW DTG SBW	
	SF6 MBW He MBW	
Device with flow sensor only		Drive and folder
Serial port	v	location designated for
File of unprocessed data		A-files
Target directory	C:\Washout\3.3.1 Exports	
✓ File of BTPS and Delay Corrected Da	ata	
Target directory	C:\Washout\3.3.1 Exports	

- 2. Ensure orientation of the flow signal is correct and automatic start and stop are disabled.
 - Select the Multiple Breath Washin/out Tests tab in System Settings to confirm Show inspiration flow positive is selected.

Multiple Breath Washin/out Tests
 Show inspiration flow positive

• Click on the N2 Multiple Breath Washout tab in System Settings to confirm Automatic start and Automatic stop of the test are <u>NOT selected</u>.



5.2 Enter Correct *Flow to O₂ Offset* and *Flow to CO₂ Offset* values (synchronization values/delay times).

From the **Administration** menu navigate to **System Settings**. Scroll to flow-to-signal offsets under the **Calibration** tab.

- Enter the correct fixed delay values (not necessarily the values shown here) corresponding to DSR (Set 2 or 3) in the Flow to O₂ Offset, Flow to CO₂ Offset, and Flow to MMss Offset fields in 'for A-File reloads'.
 - Note: If signal misalignment occurred during the test occasion, DON'T use the values from the A-Files.
- 2. Ensure that "Number of washout breaths for synchronization" is set for 5 breaths.
- 3. Ensure Dynamic Delay Correction is selected for all DSR Sets.
- 4. Press **SAVE** before returning to the main menu



5.3 How to Re-Run A-Files to Correct Signal Misalignment.

- 1. On the Select a Patient page, highlight the subject whose data needs to be re-run.
- 2. Once highlighted, press "Reload A-file(s)"
- 3. Make sure that All Files is selected.
- 4. Find the A-files to be re-run. All A-files can be selected together.
- 5. Press "Open".

ECO MEDICS AG - SPIROWARE 3.3.1							– 0 ×
Select a Patient							
Filter: (1)							
Patient List				1		U	Register New Patient
Patient Number 🔶 Last Name First Name	Date of Birth La	st test date Search tag	g(s)				Patient History
1005_454_016_5 Test 1234	01.09.2007 18	.08.2020 12:14					C la p in J
							Eult Patient
C Open					×		New Test
← → ∽ ↑ 📙 « Summer Students 20	021 > James Lynch > 1005_454_016_	5	 S S	Search 1005_454_016_5			Reload FENO A-File
						2	Reload A-File(s)
Organize 👻 New folder				8== 🔻 🛄			
h Music 🔷 Name	Date modified	Туре	Size				
Pictures 1005 454 016 5	spx 2020-08-18 12:42 PM	SPX File	229 KB				
Videos A-20200818-121	111-1005 2020-08-18 12:14 PM	Text Document	1,600 KB				
🔛 Local Disk 📄 A-20200818-121	1942-1005 2020-08-18 12:22 PM	Text Document	1,698 KB	Λ			
Translation A-20200818-122	2630-1005 2020-08-18 12:27 PM	Text Document	482 KB	4			
Public (\\F	2801-1005 2020-08-18 12:31 PM	Text Document	1,698 KB				
🛖 fratjen (\\c 🗸						1	
				F1 (4.4)	2		
File name: A-2020081	18-121111-1005_454_016_5-N2MultiBre	thWashoutTest-Set3" "A-	20200818 V All	Files (*.*)	<u> </u>		
				Open 👻 Canc	el	J	
				_			
				5			
				-			

6. Select Use settings from A-File(s) except offsets and press Confirm.

When selecting 'Settings from A-File(s)', the corresponding system settings inside each A-File will be used. If an A-File does not contain any system settings (1st line in A-File), the current system settings will be used for this A-File.
When selecting 'Current settings', all system settings inside the A-File(s) are ignored and the current system settings will be used.
When selecting 'Settings from A-File(s) except offsets', the corresponding system settings inside each A-File without the Flow-to-Signal offsets will be used. Instead the Flow-to-Signal offsets for Reloads of the current system settings will be used.
 use settings from A-File(s)
 Use settings from Arriel(s) except onsets
Confirm

7. Select the appropriate **DSR set** (same set as used at time of test) and press **Confirm**. If a mask setup was used on the day of test, ensure that the correct mask is chosen before clicking confirm.

Please selec	t and confirm the current DSR-SET:
	Set 1 (< 15.0 kg) 9 Set 2 (> 15.0 kg) Set 3 (> 35.0 kg) (only for EXHALYZER D) Spirette (Spirometry)
G	✓ Mask: Set2 - Black - bacteria filter - Mask 1512 ∨
	() Confirm

- 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-run 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 will now be visible in the subject file. **DO NOT DELETE THE ORIGINAL DRAFT FILE!**
 - 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 6

6. Synchronization Values Unknown

6.1 Set General System Settings to Perform Flow/Channel Signal Synchronization

- 1. Location of A-files (unprocessed data)
 - A-files can be found in the target directory indicated for 'File of unprocessed data' under the **Sensor** tab in **System Settings**.
 - New A-files will not be created by re-running data, but 'File of unprocessed data' should ALWAYS be selected.
 - 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

e	ECO MEDICS AG - SPIROWARE 3.	3.1					
	System Settings						<u> </u>
	Sensor						
	CLD 88 sp is present on this machin	ne					
	Device supports auto calibration:	NO zero	✓ NO				
	Enabled tests:	✓ FENO SB	FENO MB	✓ Alveolar			
		✓ Nasal	✓ Offline				
	 Exhalyzer D is present on this mach 	ine					
	Device supports auto calibration	\checkmark					
	Enabled tests:	N2 MBW	N2 SBW	DTG SBW			
		SF6 MBW	He MBW			Г	
	Device with flow sensor only						Drive and folder location
	Serial port			~		\sim	designated for A-files
	✓ File of unprocessed data					L	
	Target directory	C:\Washout	3.3.1 Exports		\swarrow		
	File of BTPS and Delay Corrected Da	ata					
	Target directory	C:\Washout	3.3.1 Exports				

- 2. Ensure orientation of the flow signal is correct and automatic start and stop are disabled.
 - Select the Multiple Breath Washin/out Tests tab in System Settings to confirm Show inspiration flow positive is selected.

\bigcirc	Multiple Breath Washin/out Tests
\checkmark	Show inspiration flow positive

• Click on the N2 Multiple Breath Washout tab in System Settings to confirm Automatic start and Automatic stop of the test are <u>NOT selected</u>.



- 3. From the Administration menu navigate to System Settings. Scroll to flow-to-signal offsets under the Calibration tab.
 - Ensure Dynamic Delay Correction is selected for all DSR Sets.
 - Ensure Number of breaths for synchronization is set to 5 breaths.

Flow-to-Signal Offsets:								
	for measurements:			for A-File reloads:				
Туре	Flow to O2 Offset [s]	Flow to CO2 Offset [s]	Flow to MMss Offset [s]	Flow to O2 Offset [s]	Flow to CO2 Offset [s]	Flow to MMss Offset [s]	Dynamic Delay correction	
Set 1	0.63	0.05	0.73	0.63	0.05	0.73	\checkmark	
Set 2	0.689	0.072	0.77	0.645	0.045	0.74	\checkmark	
Set 3	0.651	0.084	0.757	0.645	0.045	0.74	\checkmark	Report to Defaulte
Spirette	0.69	0.07	0.8	0.69	0.07	0.8		Reset to Defaults
Number of washout breaths for s	synchronization 5		ר					Save
							v	Cancel

6.2 Perform Flow/Channel Signal Synchronization Using Existing Data.

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

iystem Configuration	Patient Management	Custom Configuration
User Management	Export Data	Masks
Custom Cottines	Import multiple Patients	Madantian
System Securitys	Import single Patient	medications
Report Templates	Delete multiple Patients	Sensor Descriptions
Normative Values	Spiroware 2 Database Import	Comments
Device Calibration	Device Management	Device Reports
		Flow Calibration Reports
Environment Settings	Device Status	Channel Calibration Reports
Flow Calibration		Flow / Channel Synchronization Reports
Channel Calibration	Plow / Channel Signal Synchronization	Change Log Report
Tracer Gas Calibration	Device Direct Link Control	Login Report
		Since: (YYYY-MM-DD)

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



- 3. Select "Reload N₂ A-File"
- 4. Make sure that A-Files is selected.
- 5. Find the A-file to be used to generate new delay values.
- 6. Press "Open".
- 7. The synchronization will begin automatically once you click "Open." When you believe the subject is in a comfortable breathing pattern during the pre-phase, click **"Start Synch."**

CO3 S	MEDICS	AG - SPIROWARE 3.3.1											- 0	\times
Flow / Channel Signal Synchronization														
_		5	,								×	Oplino Valuar		
8												Elow	[ml/s]	
Ħ												02	- [%]	
5												CO2	- [%]	
/ <u></u>		📀 Open						×	1			MMss	[g/mol]	
Flov		← → ▼ ↑ _ « Summer Students 2021 → James Lynch → 1005_454_016_5 V ♂ Ø Ø Search 1005_454_016_5										Synchronization Type		
-1000	0	Organize 🔻 New folder 👔 🐨 🛄 👔 26 28 30								30	 N2 (fixed delay correction) SF6 (fixed delay correction) 			
-		👌 Music 🔷	Name	Date modified	Туре	Size						Tidal Breat	ing (dyn. delay con	rection)
- ²		E Pictures	A-20200818-121111-1	005 2020-08-18 12:14 PM	Text Document	1,600 KB	5					Data Acquisition		
2 [%		🚰 Videos	A-20200818-121942-1	- 2020-08-18 12:22 PM	lext Document	1,698 KB	J					Start	💿 Sto	p
Ŭ	0	🎬 Local Disk	A-20200818-122630-1	005 2020-08-18 12:27 PM	Text Document	482 KB			26	28	30		_	
		🛖 Translation	A-20200818-122801-1	005 2020-08-18 12:31 PM	Text Document	1,698 KB						Synchronization	Contro 7	
[96		🛖 Public (\\F										Start Sync.		
0.02		🛫 fratjen (\\c 🗸				_						R	eload A-File	
0	0		File name: A-20200818-1211	11-1005_454_016_5-N2MultiBre	athWashoutTest-Set3	A-F	iles (*.txt)	~	4	28	30			-
_ @	-					6	Open 😽 🤇	Cancel					2	
/mol													5	
28 [0														
MM	0	2 4	6 8	10 12	14 16 Time [s]	18 20	22	24	26	28	30			
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			c).	nw / Channel Signal Synchronization	11.08.2021.14:53	DSR cat: Sat ?					_	Same	r A-File Reloade	
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				on / minus agear offseti	0.7575	-,							Back	

6.2.1 How Do I Know if the Synchronization is Acceptable?

Acceptable:

- ✓ Flow tracing clearly crosses zero during transition between inspiration and expiration for 5 breaths of the pre-phase; no hesitations (see below).
- ✓ All gas signal marker lines (blue, red) overlap for 5 breaths of the pre-phase
- ✓ 5 tidal pre-phase breaths with no irregular breaths

Example of Acceptable Synchronization



Example of Unacceptable Synchronization



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Only values generated from acceptable synchronization should be saved. If the first A-file is unacceptable select **"Reload N2 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.

Once an acceptable trial is found, press <u>save for A-file Reloads</u>; the newly generated numbers will then be saved in System Settings. These values will be used for A-file re-run but will not overwrite settings used for data collection.



6.3 How to Re-Run A-Files Once New Delay Times Have Been Generated.

Now that the new delay values have been saved to system settings, the operator may proceed with rerunning files to correct signal misalignment.

- 1. On the Select a Patient page, **highlight** the subject whose data needs to be re-run.
- 2. Once highlighted, press "Reload A-file(s)"
- 3. Make sure that All Files is selected.
- 4. Find the A-files to be re-run. All A-files can be selected together.
- 5. Press "Open".

CO MEDICS	AG - SPIROWARE 3.3.1									- 0 ×
Select a	a Patient				<u></u>					
Filter:		(1)								
Patient List					_	7			5	Register New Patient
Patient Number	r 🔺 Last Name	First Name	Date of Birth L	ast test date Search	tag(s)					Patient History
1005_454_010	_5 Test	1234	01.09.2007 1	0.00.2020 12.14						Edit Patient
	🖉 Open						×			New Test
	$\leftarrow \rightarrow \sim \wedge$	« Summer Students 2021 > Jame	es Lynch > 1005 454 016	5 5	Š Š V	Search 1005 454	016 5			Reload FENO A-File
			,	-					2	Reload A-File(s)
	Organize 🔻 New	/ folder							2	L
	👌 Music \land	Name	Date modified	Туре	Size					
	Pictures	1005 454 016 5.spx	2020-08-18 12:42 PM	SPX File	229 KB					
	Videos	A-20200818-121111-1005	2020-08-18 12:14 PM	Text Document	1,600 KB					
	🎬 Local Disk	A-20200818-121942-1005	2020-08-18 12:22 PM	Text Document	1,698 KB	4				
	🛨 Translation	A-20200818-122630-1005	2020-08-18 12:27 PM	Text Document	482 KB					
	🛖 Public (\\F	A-20200818-122801-1005	2020-08-18 12:31 PM	Text Document	1,698 KB					
	🛫 fratjen (\\c 🗸				_					
		File name: "A-20200818-121111-10	005 454 016 5-N2MultiBr	eathWashoutTest-Set3"	"A-20200818 V	ll Files (*.*)	~	3		
						One la	Consel	5		
						Open 🔻	Cancer			
					Г					
						5				

6. Select Use settings from A-files except offsets and press Confirm.



7. Select the **DSR set** to be used and press **Confirm**. Use the same set as the time of test. If a mask setup was used on the day of test, ensure that the correct mask is chosen before clicking confirm.

Please select and confirm the current DSR-SET:
 Set 1 (< 15.0 kg) ● Set 2 (> 15.0 kg) Set 3 (> 35.0 kg) (only for EXHALYZER D) Spirette (Spirometry)
Set2 - Black - bacteria filter - Mask 1512 💙
() Confirm

- 8. 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.
- 9. Once the re-run 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.
- 10. 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!**
 - 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.
- 11. If alignment is still not corrected go back to Section 6.2, select a new A-file from that participant for the signal synchronization, and try to Re- Run the test occasion again. Continue to go back and try different A-files for the participant until mis-alignment has been corrected.

7. Appendix 1 – How to perform flow/channel synch using DDC

7.1 Flow/Gas Signal Synchronization (MBWN2 SOP section 5.4)

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 several 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 2.1, Signal Synchronization Troubleshooting).

7.2 Set up equipment for Flow/Gas Signal Synchronization (MBWN2 SOP section 5.4.1)

- 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).
- 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.

7.3 Perform Signal Synchronization (MBWN2 SOP section 5.4.2)

- > 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, System Settings and select the Calibration tab.
- Confirm that the correct post gas sampling-point (Post-Cap.) dead space volume is listed in the DSR Set Settings for the appropriate DSR Set to be used for synchronization and testing (Figure 1).
- 3. Confirm number of washout breaths for synchronization is set to 5 (Figure 1).
- 4. Confirm Dynamic Delay Correction is enabled (checked)

CO MEDICS A	G - SPIROWARE 3.3	.2						_		×
System S	ettings			-0						
							• •			
DSR set Settings	:						^			
Туре	Min. Calib. Flow Range [ml/s]	Max. Calib. Flow Range [ml/s]	Calib. Syringe volume [ml]	Vol. Detection Sens.	Pre-Cap. Deadspace [ml]	Post-Cap. Deadspace [ml]	e Show flow / volume values in [ml]			
Set 1	90	110	100	2	2	3.5				
Set 2	450	550	1000	15	33.3	9.5				
Set 3	900	1100	1000	25	33.3	22				
Spirette	4000	5000	3000	50	25	25				
	Min. Bypass Flow [ml/s]	Max. Bypass Flow [ml/s]								
Set 1	180	250								
Set 2	550	850								
Set 3	900	1300								
Cignal Connection	-									
-	Sample Flow	02 Response-Time	02 Response-Time	MMss Response-	MMss Response-					
Туре	correction	correction	[s]	Time correction	Time [s]					
Set 1	✓	✓	0.03	~	0.035					
Set 2	\checkmark	\checkmark	0.03	✓	0.03					
Set 3	\checkmark	\checkmark	0.03	✓	0.03					
Spirette			0.03		0.03					
Flow-to-Signal O	ffsets:									
for measurements:				for A-File reloads:						
Туре	Flow to O2 Offset [s]	Flow to CO2 Offset [s]	Flow to MMss Offset [s]	Flow to O2 Offset [s]	Flow to CO2 Offset [s]	Flow to MMss Offset [s]	Dynamic Delay correction			
Set 1	0.63	0.05	0.73	0.63	0.05	0.73				
Set 2	0.689	0.076	0.767	0.685	0.08	0.762				
Set 3	0.668	0.089	0.77	0.661	0.078	0.766		Porot	to Default	
Spirette	0.69	0.07	0.8	0.69	0.07	0.8		Neset	to berault	
Number of warbout h	reaths for synchronize	tion E							Save	
Number of Washout t	a course for synchroniza	5					~ [Cancel	
									an icei	

Figure 1. Post gas sampling-point dead space values, values entered here will be applied to raw data.

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



Figure 2. Administration Menu; Flow/Channel Signal Synchronization

- 7. Wearing nose clips, place mouth on mouthpiece and begin tidal breathing through the system; press **Start** (Figure 3).
- C ECO MEDICS AG SPIROWARE 3.3.1 Ø × Flow / Channel Signal Synchronization 1000 00 fml/s 1000 8 10 24 26 28 02 [%] 28 02 [%] 8 B All O Medium O Large 05.08.2021 12:01 DSR set: Set 3 0.665 s 0.074 s 0.768 s 0.675 s 0.079 s 0.777 s Flow / O2 signal offset: Flow / CO2 signal offset: Flow / MMss signal offset
- 8. As soon as breathing pattern is stable, select Start Sync. (Figure 3).



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.

- 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 to align with flow. Values are displayed at the bottom of the screen.
- 10. Confirm that the values for O₂ are between 0.500 and 0.800s and that the values for CO₂ are between 0.040 and 0.070s
 - O₂ and CO₂ delay times are influenced by sample flow rate and to some extent properties of the respective gas analyzers and, in the case of O₂, 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.
- 11. Atypical delay times (see above) should prompt investigation.
- 12. Record delay times and ambient conditions, these values may be required to review data at a later date.