



Multiple Breath Nitrogen Washout Testing Training and Qualification Requirements

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Multiple Breath Nitrogen Washout Testing Training and Qualification Requirements

MBW Central Training and Over-Reading Centre (CORC)

The CF Clinical Research Team at The Hospital for Sick Children, in collaboration with MBW researchers from around the world, have developed a testing manual (MBWN₂ Standard Operating Procedure) to facilitate standardized use of the Exhalzer D[®] Multiple Breath Nitrogen Washout (MBWN₂) system. The team has also developed an intensive hands-on training course and qualification process based on this manual to facilitate standardized data collection for multi-centre clinical trials. The training session is designed to facilitate making real-time decisions about test quality. To be qualified for MBW testing for clinical trials operators are required to 1) attend a one-day hands-on training session, 2) successfully complete a Post-Training knowledge test and 3) demonstrate ability to perform technically acceptable MBW tests. After all the components are successfully completed, the operator will be considered qualified for MBWN₂ testing. **Training and associated operator qualification are INDEPENDENT of specific trials and sponsors.**

For qualification inquiries please contact:

mbw.centre@sickkids.ca

1. MBWN₂ Training Session

Operators who will perform MBW measurements on clinical trial study participants should attend a one-day in person MBW training session. Prior to attending the one-day session, all participants are strongly encouraged to review the online MBW Pre-Training. *Please note:* some of the material presented in the online module will **not be** covered again during the one-day training session.

2. MBWN₂ Post-Training

Operators are required to complete the Post-Training knowledge test (80% pass mark required) within **2 weeks** of attending the training session. The knowledge test should be completed before MBW qualification tests are collected.

3. MBWN₂ Qualification Tests

MBW test feasibility improves as operators gain experience testing the target study population. After attending the training session and completing the knowledge test, each operator should perform qualification MBW tests to demonstrate ability to collect technically acceptable MBW data. *Qualification tests are required to be submitted within 3 months of attending the training session.* Subjects tested for qualification should be **representative of the age and disease (e.g. Cystic Fibrosis)** of the intended clinical trial study population. *Age groups can be considered as follows:*



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- **Adult/Paediatric: 6.0 years and older.** A total of 5 qualification tests should be performed by each operator wishing to be qualified.
- **Preschool: 2.5 - 5.9 years old.** Two operators working together must submit a total of 5 qualification tests; preschool subjects must be ≤ 5.9 years old.

***PLEASE NOTE:** Adult/paediatric qualification tests should be **submitted and approved** by the MBW Centre **before preschool qualification measurements are collected.**

If more than two operators per site wish to be qualified for preschool testing it is the operator's responsibility to ensure the above outlined minimum requirements are met.

3.1 Criteria for Successful Qualification

Each operator must receive a score of at least 80% on the knowledge test **AND** achieve the following:

- **Adult/Paediatric: 80% successful test occasions** per operator
 - Of the 5 qualification tests, operators should include **at least:**
 - **2 CF subjects**
 - **1 subject in the range of the study population** (e.g. paediatric site must successfully test at least 1 paediatric patient)
- **Preschool: 80% successful test occasions per pair** of operators
 - Of the 5 qualification tests, operators should include **at least:**
 - **2 CF subjects**
 - **1 subject must be < 4 years old**
 - Two operators seeking qualification should be present at all preschool test occasions
 - Each additional operator (over and above the initial two) will **require 80%** pass rate

***PLEASE NOTE:** Submissions of more than 5 qualification tests per operator and/or submissions that do not meet the above specifications for age and disease will not be evaluated.



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3.2 Protocol for Qualification Tests

1. Tests should be performed according to the MBWN₂ Standard Operating Procedure. Preschool tests should be performed according to the study specific MBW SOP.
2. Spiroware version 3.1.6.17312/3 (May 2014) must be used
3. Each test occasion submitted should represent a discrete subject.
4. Operator should aim to collect three good quality trials per test occasion.
5. Poor quality trials should be marked as excluded in Spiroware by the operator.
6. Data collected for studies that have been over-read by the CORC cannot be used as qualification test submissions

3.3 Criteria for a Successful Test

A successful MBWN₂ test will consist of at least two acceptable trials. Acceptable trials are defined as having:

1. No evidence of leak
2. No evidence of coughing, laughing or talking
3. No evidence of signal misalignment
4. No evidence of inadequate time between trials
5. Clear satisfaction of end of test criteria
6. Grossly normal tidal breathing pattern*

*Operators should aim to demonstrate ability to encourage subjects to breathe in a relaxed tidal breathing pattern. Only trials with grossly distorted breathing pattern will be deemed unacceptable for breathing pattern alone.

3.4 Feedback

Feedback will include comments and suggestions aimed to emphasize and support good practice and offer suggestions on improvement. Feedback will be provided to the operator on the quality of each transmission **within 10 business days of receiving files in the correct format (see Appendix 1)**. Official qualification report will only be provided when all qualification tests have been collected/sent by the operator. However, operators can request initial feedback for their first qualification test submission. Please note, during times when multiple operators are qualifying to be part of a clinical trial, delays can be expected in receiving feedback.

3.5 Unsuccessful Qualification

Due to the unique and varied circumstances for unsuccessful qualification, this will be addressed on a case by case basis. If an operator does not meet qualification requirements on the first attempt, they may be asked to submit additional MBWN₂ qualification test occasions for evaluation. The additional



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test occasions should be collected by the operators whose original submissions were unsuccessful. Under circumstances where additional traces are also unsuccessful, further training may be required.

3.6 Training and Qualification of Additional Operators:

New operators can register for an upcoming training session at a cost of \$800.00 CAD which covers the training course and subsequent certification.

We will only review qualification trials for operators who have not attended a training session if they have been trained on site by an existing trained and certified operator at their institution. The existing operator must be experienced in testing and have demonstrated thorough understanding of test procedure through a record of 80% success rate from at least 50 test occasions in the study population. It is the responsibility of the site to submit evidence of 50 successful test occasions to the MBW Centre for consideration. Documentation of successful test occasions can be found in the study specific quality control reports sent by the MBW Centre. Qualification trials do not count towards the 50 successful test occasions.

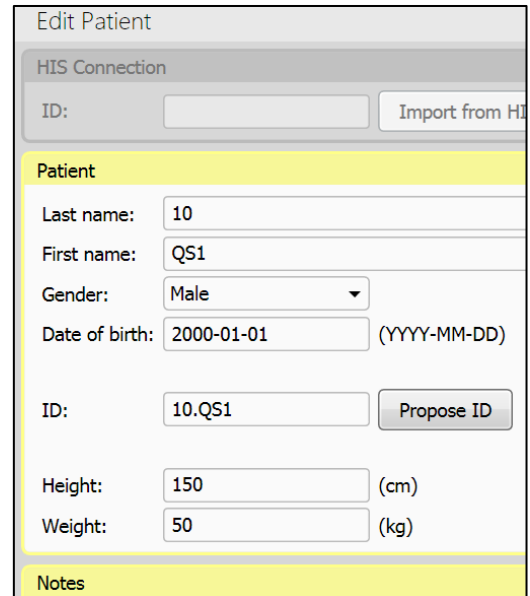
New operators who are trained by an existing operator at their site must collect and submit 5 qualification test occasions with 4/5 successful test occasions and successfully complete the knowledge test in order to become certified for testing. Qualification tests may be submitted to the central over-reading centre at any time. The cost of knowledge test administration and certification is \$400.00 CAD per submission.

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Appendix 1: Spiroware File Naming

Only de-identified subject files will be accepted by the MBW Centre. Studies submitted as MBWN₂ qualification tests should use the following naming scheme:

- Last Name: Site Number
 - Site number will be assigned by the MBW Centre.
- First Name: Qualification Subject Study Number
 - Please assign each qualification subject a discrete study number (ie. QS1 – QS10)
- ID: Site Number. Qualification Study Number (e.g. 10.QS1)
- Date of birth: please enter as accurately as IRB allows.
- Height and weight: please enter accurate measurements from day of test. Obtain measurements as you would for a study participant



Edit Patient	
HIS Connection	
ID:	<input type="text"/> <input type="button" value="Import from HIS"/>
Patient	
Last name:	<input type="text" value="10"/>
First name:	<input type="text" value="QS1"/>
Gender:	<input type="text" value="Male"/>
Date of birth:	<input type="text" value="2000-01-01"/> (YYYY-MM-DD)
ID:	<input type="text" value="10.QS1"/> <input type="button" value="Propose ID"/>
Height:	<input type="text" value="150"/> (cm)
Weight:	<input type="text" value="50"/> (kg)
Notes	

**If you do not have a Qualification Subject Study Number, please contact the MBW Centre
(mbw.centre@sickkids.ca)**

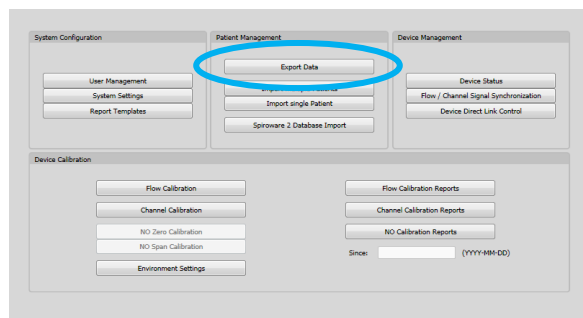
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Appendix 2: Data Export

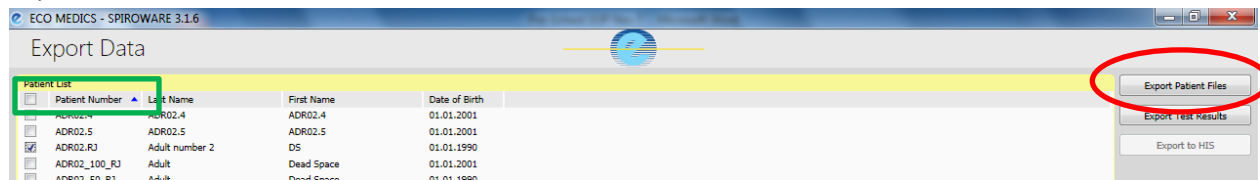
Sites **MUST** use Spiroware software version (3.1.6.17312/3 (May 2014)) for data collection

*Any site who does not have this software version should contact Eco Physics.

*****Files MUST be saved as DRAFT prior to export from Spiroware*****



This will bring up the entire patient list; all files are selected by default. If you do not wish to export all patient files in the database uncheck **Patient Number** (square) and then select the files you wish to export.



- Select **Export Patient Files** in upper right corner of the Export Screen (circle).
- Select a pre-existing folder or make a new folder to store exported .spx files and press ok.
- Once complete a confirmation will appear in the **Export Log** at the bottom of the export data page.

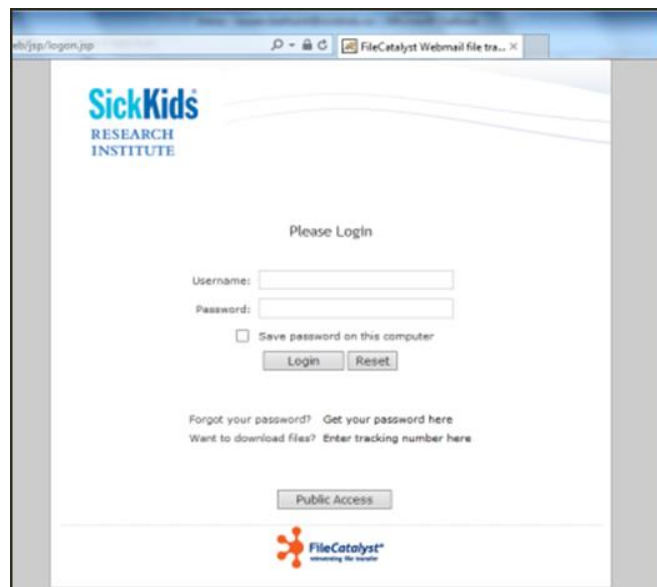
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Appendix 3: Data Transfer

Exported .spx files from all sites will be submitted for over-reading via a secure file transfer protocol (FTP) hosted by The Hospital for Sick Children, or study specific FTP equivalent.

Study Data Submission Process – FTP Site

- The MBW Centre will set-up an FTP account for each site.
 - This requires the e-mail address of the designated user from each site
- Upon creation of the FTP account, Username and Password will be sent to the designated user
- Navigate to FTP site – <https://ritftp.research.sickkids.ca>
- Log in with assigned Username and Password
- User can then change password at first login



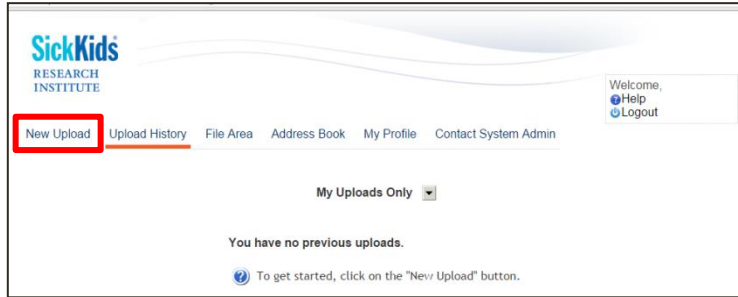
If you have trouble, please contact the MBW Centre:

mbw.centre@sickkids.ca

[Please DO NOT email researchhelpdesk@sickkids.ca](mailto:researchhelpdesk@sickkids.ca)

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1. Select 'New Upload'



The screenshot shows the SickKids Research Institute user interface. The 'New Upload' button in the top navigation bar is highlighted with a red box. Other navigation options include 'Upload History', 'File Area', 'Address Book', 'My Profile', and 'Contact System Admin'. A 'Welcome' message with 'Help' and 'Logout' links is visible in the top right. Below the navigation bar, there is a 'My Uploads Only' dropdown menu and a message stating 'You have no previous uploads.' with a link to get started by clicking the 'New Upload' button.

2. Enter the Recipients' emails

Email: mbw.centre@sickkids.ca



The screenshot shows the 'New Upload' form in the SickKids Research Institute user interface. The 'New Upload' button in the top navigation bar is highlighted with a red box. The form contains the following fields and options:

- Recipient's Email:** A text input field containing 'mbw.centre@sickkids.ca', highlighted with a red box. A red asterisk and the text '(Up to a maximum of 10)' are visible next to the field.
- Short Note:** A large text area for entering a note.
- Notify when download occurs?:** A radio button option set to 'Yes (Edit My Profile)'.
- Download Password:** A text input field with a red asterisk and the text 'required field' below it.

At the bottom of the form, there are three buttons: 'Upload Files', 'Cancel', and 'Finish'.

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3. Enter 'Short Note'

Please include the following in the **Short Note** section:

1. Name of subject file uploaded (i.e. 10.QS1).
2. Confirm whether MBW testing has been performed according to testing protocol outlined in study specific SOP.
3. Any deviations to equipment or test procedure should be clearly indicated.

The screenshot shows the 'SensitiveData Transfer' form on the SickKids Research Institute website. The form includes a navigation bar with 'New Upload', 'Upload History', 'Address Book', 'My Profile', and 'Contact System Admin'. A 'Welcome' message with 'Help' and 'Logout' links is in the top right. The main content area is titled 'Please enter the following information:' and contains the following fields:

- SensitiveData Transfer**: You must contact the recipients by phone or SMS and give them the password. You **MUST NOT** send the password in an email. Emails are not secure.
- Recipient's Email (Up to a maximum of 10)**: mbw.centre@sickkids.ca
- Short Note**: 10.QS1, 10.QS2, 10.QS3, etc. MBW testing has been performed according to testing protocol outlined in SOP.
- Notify when download occurs?**: Yes (Edit My Profile)
- Download Password**: (empty)

Buttons at the bottom include 'Upload Files', 'Cancel', and 'Finish'. A red box highlights the 'Short Note' field.

4. Enter Password

- mbwcentre

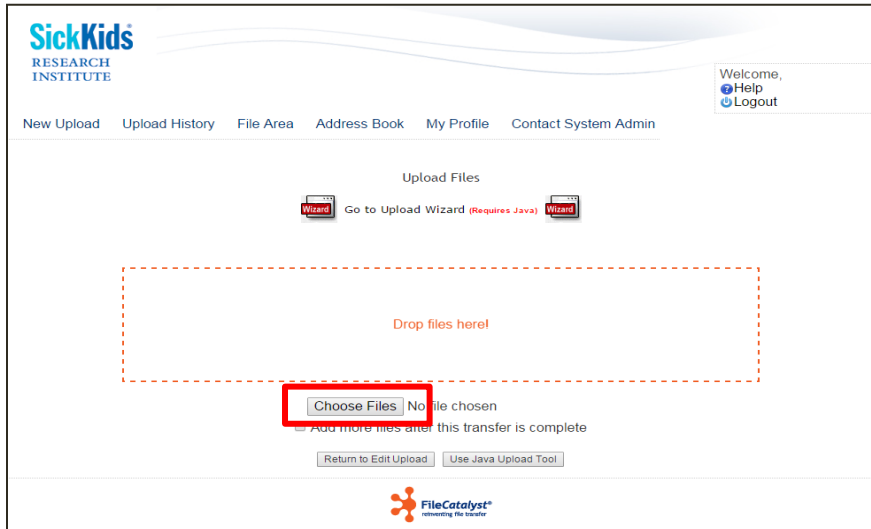
The screenshot shows the 'SensitiveData Transfer' form on the SickKids Research Institute website. The form includes a navigation bar with 'New Upload', 'Upload History', 'Address Book', 'My Profile', and 'Contact System Admin'. A 'Welcome' message with 'Help' and 'Logout' links is in the top right. The main content area is titled 'Please enter the following information:' and contains the following fields:

- SensitiveData Transfer**: You must contact the recipients by phone or SMS and give them the password. You **MUST NOT** send the password in an email. Emails are not secure.
- Recipient's Email (Up to a maximum of 10)**: mbw.centre@sickkids.ca
- Short Note**: 10.QS1, 10.QS2, 10.QS3, etc. MBW testing has been performed according to testing protocol outlined in SOP.
- Notify when download occurs?**: Yes (Edit My Profile)
- Download Password**: mbwcentre

Buttons at the bottom include 'Upload Files'. A red box highlights the 'Download Password' field.

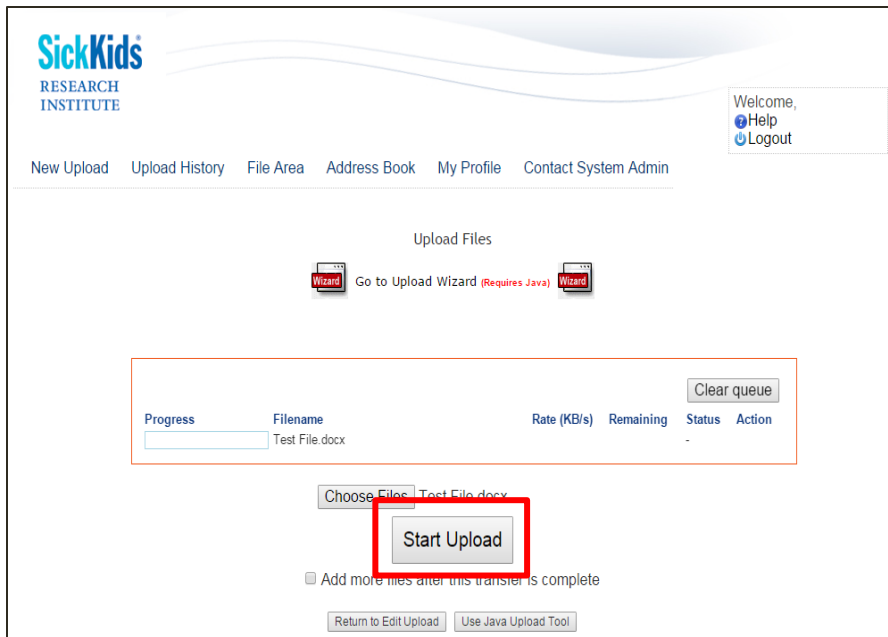
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5. Select 'Choose Files'



6. Select the .spx file(s) to upload

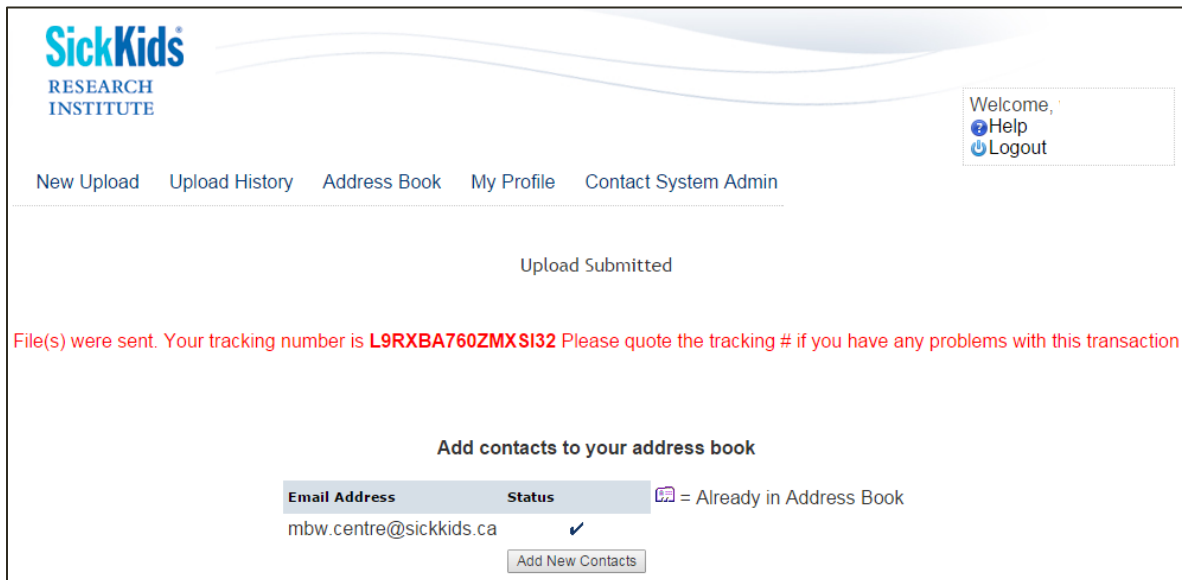
7. Select 'Start Upload'



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8. Upload Confirmation

- Tracking number should be saved for site records



The screenshot shows the SickKids Research Institute website interface. At the top left is the SickKids Research Institute logo. On the top right, there is a user menu with 'Welcome,' 'Help', and 'Logout' options. Below the logo, there is a navigation bar with links for 'New Upload', 'Upload History', 'Address Book', 'My Profile', and 'Contact System Admin'. The main content area displays 'Upload Submitted' in the center. Below this, a red message states: 'File(s) were sent. Your tracking number is L9RXBA760ZMXSI32 Please quote the tracking # if you have any problems with this transaction'. Further down, there is a section titled 'Add contacts to your address book' which contains a table with two columns: 'Email Address' and 'Status'. The table has one row with the email 'mbw.centre@sickkids.ca' and a checkmark in the status column. To the right of the table, there is a legend: a purple icon followed by '= Already in Address Book'. Below the table is an 'Add New Contacts' button.

Email Address	Status
mbw.centre@sickkids.ca	✓

Sites will receive:

- A confirmation e-mail from the FTP service that the file has been uploaded.
 - Tracking number should be saved for site records.
- E-mail notification from the FTP service when the file has been downloaded by the MBW Centre should be received within 48 hours of submission. If confirmation is not received sites should confirm that the correct e-mail address was entered into the 'Recipient E-mail' field on the FTP software.



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Appendix 4: Spioware Version Date

The Spioware version can be found at the bottom of the Administration menu.

