STANDARD FORMS

4 ASTHMANET STANDARD FORMS

4.1 Standard Forms and Instructions

This section provides specific instructions needed to complete the AsthmaNet standard data collection forms. Most of these forms are entered into the study database and submitted to the DCC. The instructions for each form are in alphabetical order based on the form name found in the header of the form.

The following information is provided for each form: the purpose of the form, who completes the form, when the form should be completed, and form instructions. Each field on every form is identified by a 4-digit annotation number such as 1000. Some forms have fields identified with a ‘D’ following the 4 digits such as 1020D. These fields represent description fields. The recorded text should be entered into the AsthmaNet clinical data management system allowing a maximum of 100 characters. Most forms have a comments section (Question 6000) at the bottom of the form. The coordinator can record additional comments or information related to the form in this section. This information (maximum length of 250 characters) is entered into the AsthmaNet clinical data management system. If you are unable to find the specific information needed to complete a form, please contact the protocol-specific Primary Data Manager at (717) 531-3663.

10.1.1 Acute Asthma Assessment Questionnaire (AAAQ)

Purpose: To measure severity of asthma symptoms related to asthma exacerbations.

Who: The participant completes this form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

The Acute Asthma Assessment Questionnaire is a 7-question tool for participants ages 12 and older to report a 72-hour review of the severity of their asthma and the possible cause of an asthma exacerbation. This tool is used primarily to measure the duration and severity of asthma exacerbations.

Participant completed forms that are completed at study visits should always be reviewed by the coordinator upon completion. If a correction is noted, the participant should make the correction and initial and date next to the change. Coordinators should not alter participant completed forms.

The participant must complete the source documentation box (using 2 or 3 initials) on page 2 (Q1070 – Q1090). Enter the Date field in the database in the format mm/dd/yyyy. Enter the time field based on a 24-hour clock.

10.1.2 Additional Treatment Post Methacholine Challenge Testing (METHA_ADD_TRT)

Purpose: This form should be completed following methacholine challenge testing if the participant did not reverse to 90% of baseline FEV_1 after the standard reversal treatment of 2 or 4 puffs of albuterol.

Who: The Pulmonary Function Technician administers the additional treatment, pulmonary function tests, and completes the form.

When: If the participant's FEV_1 is not greater than the reference value after standard reversal from methacholine challenge testing.

Form Instructions:

Complete this form ***only*** if the participant needed additional treatment after the Methacholine Challenge procedure. The METHA_ADD_TRT form is always entered as a single form at the same visit as the METHA packet form.

If the technician completing the procedure is not certified and this procedure is being used as an observation session for certification, please complete the Supervisor ID located in the header on the METHA_ADD_TRT form with the ID of the certified technician who supervised the procedure. The Supervisor ID ***is*** entered into the database during data entry. Failure to complete the Supervisor ID when applicable could result in a protocol deviation.

Question 1000. If Q1000 is answered 'Yes', record the types of additional treatment used within the first hour post-challenge in Q1010-Q1060. If no additional treatments were used during this time period, skip to Q1110.

Question 1070. Record the participant's FEV_1 after additional treatment within the first hour. The FEV_1 value should come from the Post II Composite row of the MedGraphics Methacholine Report or, if the participant performed more than one maneuver after additional treatment, the row within the Post II section corresponding to the time of the first manuever.

Question 1090. Record the time based on a 24-hour clock (military time).

Question 1100. Determine if the participant's FEV_1 at this time is greater than or equal to the methacholine reversal reference value (B) in the gray box at the top of the METHA form. If the participant's FEV_1 is greater than or equal to the reference value, ***stop*** completing this form and continue with the remaining visit procedures. If the participant's FEV_1 is not greater than the reference value, continue on to Q1110.

Question 1110. If Q1110 is answered 'Yes', record the types of additional treatment used after one hour in Questions 1120-1190. If no additional treatments were used, continue on to Question 1200.

Questions 1200. Record the participant's final FEV_1 after all reversal treatment following methacholine challenge. The FEV_1 value should come from the Post II Composite row of the MedGraphics Methacholine Report or, if the participant performed more than one maneuver after additional treatment, the row within the Post II section corresponding to the time of the final maneuver.

Question 1220. Record the time based on a 24-hour clock (military time).

Question 1230. Determine if the participant's FEV_1 at this time is greater than or equal to the methacholine reversal reference value (B) in the gray box at the top of the METHA form. If the participant's FEV_1 is not greater than or equal to the reference value, ***have the study physician complete the source documentation box at the end of this form (Q1240-Q1260).*** If the physician's signature was obtained, enter a 1 in the database. Otherwise, leave the field blank during data entry. Enter the Date field in the database in the format mm/dd/yyyy.

The corresponding report for the METHA_ADD_TRT form is the MedGraphics Methacholine Final Report, abbreviated METHA_RPT. Refer to the protocol-specific MOP for details on when this report is used.

10.1.3 Additional Treatment Post Sputum Induction (SPUTUM_ADD_TRT)

Purpose: This form should be completed if the participant experienced > 10% fall from reference FEV_1 immediately after completion of sputum induction.

Who: The Pulmonary Technician administers the additional treatment, pulmonary function tests, and completes the form.

When: If the participant experienced a > 10% fall from reference FEV_1 immediately after completion of the sputum induction procedure.

Form Instructions:

Complete this form ***only*** if the participant experienced a greater than 10% fall from reference FEV_1 immediately after completing the sputum induction procedures. The SPUTUM_ADD_TRT form is always entered as a single form at the same visit as the SPUTUM packet form.

The Sputum Induction Reversal Reference Value is the value recorded for Q1030 on the Sputum Induction Checklist (SPUTUMCHK) form multiplied by .90.

Questions 1000 and 1010. The FEV_1 and FEV_1 (% predicted) can be found in the Post Composite row of the MedGraphics Spirometry Report. Record Q1000 to the nearest hundredth of a decimal.

Question 1020. Record the time based on a 24-hour clock (military time).

Question 1030. If Q1000 is less than the calculated sputum induction reversal reference value (found in the Clinic Use Only gray box at the top of this form), administer 2 puffs of albuterol, perform spirometry, and continue to complete the rest of the SPUTUM_ADD_TRT form. Otherwise, stop and continue with the remaining visit procedures.

Questions 1040 and 1050. The FEV_1 and FEV_1 (% predicted) can be found in the Post Composite row of the MedGraphics Spirometry Report. Be careful to select the row with the later time stamp since the best post test will be listed first regardless of the order in which tests were performed. Record the value for Question 1040 to the nearest hundredths of a decimal place.

Question 1060. Record the time based on a 24-hour clock (military time).

Question 1070. If Q1040 is less than the calculated sputum induction reversal reference value, answer ‘No’ and have the attending physician complete the source documentation box (Q1080-Q1100).

The corresponding report for the SPUTUM_ADD_TRT form is the MedGraphics Spirometry Final Report, abbreviated SI_RPT. Refer to the protocol-specific MOP for

details on when this report is used. To clarify that this Spirometry Final Report is listing maneuvers performed post-sputum induction, please add a comment to the ‘Post Test Comments’ section of the report.

10.1.4 Adult Asthma and Allergy History (ASTHMA_HX_ADULT)

Purpose: To record an overview of an adult participant's asthma history including family history, symptoms, triggers, allergies, and smoking history.

Who: An AsthmaNet coordinator interviews the participant while completing the form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

Questions 1000 and 1070. Have the participant give a best estimate of his/her age. If the participant reports 20.5 years, round up to the nearest whole year. If the participant was younger than 1 year old, record the participant's age as 00 years.

Questions 1090 – 1110. If the participant is adopted and does not know his or her biological parents and/or siblings, answer 'Don't Know.'

Question 1110. Record 'N/A' if the participant does not have any biological siblings.

Question 1120. Record 'N/A' if the participant does not have any biological children.

Questions 1140, 1150, 1160, and 1170. If the participant's asthma symptoms vary by season (Q1130), multiple seasons may be answered as 'Yes'; however, not all 4 seasons should be answered 'Yes.'

Questions 1180 – 1220 and 1260. If the participant answered 'none' to any of these questions, record '0' for the response.

Question 1300. In the scenario where a female participant has had a hysterectomy and no longer has a monthly menstrual cycle, she would not be able to correlate fluctuations in her asthma symptoms with her cycle anymore. Q1300 should be answered "Don't Know."

Question 1400. If Q1400 is answered 'Yes', please record a description for 'Other' in Q1400D.

Question 1410. If Q1410 is answered 'Yes', please record a list of medications for Q1410D.

Question 1420. If Q1420 is answered 'Yes', please record a list of foods for Q1420D.

Question 1460. If Q1460 is answered 'Yes', please record a description for 'Other' in Q1460D.

Questions 1570 – 1590. If the participant is adopted and does not know his or her biological parents and/or siblings, answer ‘Don’t Know.’

Question 1590. Record ‘N/A’ if the participant does not have any biological siblings.

Question 1600. Record ‘N/A’ if the participant does not have any biological children.

Question 1740. If Q1740 is answered ‘Yes’, skip to Q1760. Otherwise complete Q1750.

Questions 1750 and 1770. Calculate pack-years by multiplying the number of packs smoked per day by the number of years smoked at that quantity. One pack equals 20 cigarettes. Record the values to the nearest hundredths of a decimal.

Questions 1810 and 1820. Have the participant give a best estimate.

Questions 1830 and 1850. Have the participant give a best estimate. Month values should be rounded, as these fields only accept whole numbers. If the participant vaped or used a hookah for less than 6 months out of a year, round down to the nearest year. Six or more months of use should be rounded up to the next year. For example, if the participant has been vaping for 5 months, Q1830 should be answered ‘0’.

Questions 1860-1880. If the participant cannot remember the exact date, the month and year or the year only can be entered.

10.1.5 Adult Body Measurements (BODYMEAS_ADULT)

Purpose: To record the height, weight, and circumference measurements of an adult participant.

Who: An AsthmaNet coordinator completes the form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

Questions 1000 and 1010. The participant should remove shoes and heavy articles of clothing prior to taking these measurements. Calculate the participant body mass index (BMI) using the formula in the grey reference box and record the value. This value will not be entered into the study database.

Questions 1020 – 1040. The participant should be standing facing forward, with shoulders relaxed while taking these measurements using a plastic measuring tape.

For more information related to taking these measurements, please refer to Section 3 of the AsthmaNet General MOP.

10.1.6 Adult Methacholine Challenge Testing Checklist (METHACHK_ADULT)

Purpose: To determine if an adult participant is eligible to proceed with the diluent (solution #0) pulmonary function testing for the methacholine challenge testing.

Who: The Pulmonary Function Technician completes the form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

If the technician completing the procedure is not certified in methacholine challenge testing, a supervisory technician who is certified should monitor the technician and record his or her number in the Supervisor ID field at the top of the form. The Supervisor ID ***is*** entered into the database during data entry. Failure to complete the Supervisor ID when applicable could result in a protocol deviation.

Complete this form only if the participant is eligible according to the protocol-specific Pulmonary Procedure Checklist and successfully completed baseline spirometry session(s).

Question 1000. If Q1000 is answered 'Yes', answer Q1010 and have a physician sign the form.

Question 1020. If the physician's signature was obtained, enter a 1 in the database. Otherwise, leave the field blank during data entry.

Question 1050. Refer to the Concomitant Medications for Asthma/Allergy and Adverse Events (CMED) form and the Clinical Adverse Events (AECLIN) form.

Question 1060. The participant is ineligible to perform a methacholine challenge if the FEV_1 (% predicted) value recorded for Q1040 of the Spirometry Testing (SPIRO) form is less than 55% of predicted OR if the FEV_1 value recorded for Q1030 on the Spirometry Testing (SPIRO) form is less than 1.0 L.

Question 1070. Check 'N/A' if the participant is male or is a female that is post-menopausal, had a hysterectomy or a tubal ligation. A post-menopausal woman is defined as someone who has not had a regular period in over a year.

Question 1080. The participant is ineligible to proceed if his/her systolic blood pressure is > 200 mmHg or his/her diastolic blood pressure is > 100 mmHg.

Question 1100. If there is a reason the participant should not proceed with methacholine challenge testing that has not been captured on the form, explain in the space provided (Q1100D).

Question 1110. If the participant is deemed eligible, proceed to the Methacholine Challenge Testing using the Methacholine Challenge Testing (METHA) form. The participant is deemed ineligible for the diluent (solution #0) pulmonary function testing for the methacholine challenge if any of the shaded boxes are completed.

10.1.7 Allergy Skin Test Results (SKIN_TEST)

Purpose: To record whether or not the participant has a positive reaction to various allergens.

Who: An AsthmaNet coordinator certified to perform skin testing.

When: Refer to Visit Procedure Checklists.

Form Instructions:

Question 1000. Respond 'Yes' to Q1000 if (1) prior skin testing was performed by an AsthmaNet certified coordinator or technician and (2) prior skin testing occurred within the protocol-specific time limit. Protocol-specific time limits for reusing the SKIN_TEST form can be found in the Manual of Operations for each protocol. If Q1000 is answered 'No', proceed to Q1030.

Questions 1010 and 1020. If Q1000 is answered 'Yes', provide the date of the previous skin test in Q1010 and the ID of the coordinator who performed the skin test in Q1020. Stop here and continue with remaining visit procedures. Attach a photocopy of the previous skin test form (pages 1 through 4) to this form. Update the participant ID and visit in the header of pages 2, 3 and 4 to reflect the current participant ID and visit. At the time of data entry, enter Q1000 - Q1020 from this form and enter the rest of the data from the photocopied form (original skin test).

Question 1030. If any exclusionary medications were taken within the washout period, the participant is ineligible to complete the allergy skin testing at this visit. See Appendix 5 of the AsthmaNet General MOP for more information regarding exclusionary drugs for skin testing.

Question 1040. If the participant's most recent FEV_1% predicted is < 60%, the supervising physician must give permission to proceed with the skin testing procedure. The most recent FEV_1% predicted is the last spirometry maneuver completed prior to skin testing. If the supervising physician gives permission to proceed, record 'Yes' for Q1050 and obtain the physician's signature on Q1055. If the physician's signature was obtained, enter a 1 in the database. Otherwise, leave the field blank during data entry. If the supervising physician does not give permission to continue, the participant is ineligible to complete the allergy skin testing at this visit.

Question 1060. If any of the shaded boxes are completed (Q1030 or Q1050), the participant is not eligible to proceed with allergy skin testing. Allergy skin testing may be rescheduled for the next visit (refer to protocol-specific MOP).

Question 1070. If the participant had a severe systemic reaction in the past to allergy skin testing, do not continue. Refer to the protocol-specific MOP for details on how to proceed.

Questions 1080 – 1100. Do not skin test a particular allergen if the participant has had a previous anaphylactic reaction to this allergen. Do not complete the 'reaction' questions (Q1430, Q1490, Q1550) for the corresponding allergen on the Allergy Skin Test Results (SKIN_TEST) form. Refer to the protocol-specific MOP for details on how to proceed.

Questions 1110 and 1120. Record the time based on a 24-hour clock (military time).There should be a 20-minute interval from the time the skin test sites were pricked (Q1110) and the time the participant's skin is evaluated (Q1120).

Questions 1130-1140. If the value of the positive control calculation (Q1130) is less than 3 mm (Q1140), the skin test is not valid. Do not complete the rest of the form. Refer to the protocol-specific MOP for details on how to proceed.

Questions 1150-1170. If the absolute value of the positive control calculation (Q1130) minus the negative control calculation (Q1150) is less than 3 mm (Q1170), the skin test is not valid. Do not complete the rest of the form. Refer to the protocol-specific MOP for details on how to proceed.

Questions 1190 – 1660. For each allergen, 1 – 16, indicate whether there was a positive reaction. A positive reaction is defined as a wheal size $\geq$ Q1180. Transfer the tracing of each wheal and record the longest diameter and the diameter at the perpendicular midpoint in mm. If the wheal is not measurable, record '0' for both diameters. The diameters should be recorded even if there was not a positive reaction. If a specific allergen will not be used (i.e. study participant has a known allergy to a specific food or other allergen), the Multi-Test arm should be broken off. The questions for that specific allergen should be left missing and any resulting errors pertaining to that allergen should be marked unresolvable with an appropriate comment.

For more information on skin testing procedures and definitions, see Appendix 5 of the AsthmaNet General MOP.

10.1.8 Asthma Bother Profile (ABP)

Purpose: To measure a participant's level of distress due to asthma.

Who: An AsthmaNet coordinator interviews the participant while completing the form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

The coordinator should read to the participant the information contained in the four bulleted items at the top of the questionnaire.

AsthmaNet will define retired as no longer performing any work for monetary payment. For example, an individual retires from their primary job, however still works part-time or is paid for consulting work, the answer to question Q1000 should be 'No'.

Question 1000. If Q1000 is answered 'Yes', complete Q1010; otherwise, skip to Q1020.

Question 1020. If Q1020 is answered 'Yes', complete Q1030; otherwise, skip to Q1040.

Question 1040. If Q1040 is answered 'Yes', complete Q1050; otherwise, skip to Q1060.

Question 1090. If Q1090 is answered 'Yes', complete Q1100 and Q1110; otherwise, skip to Q1110.

Question 1170. If Q1170 is answered 'Yes', complete Q1180, otherwise, skip to Q1190.

10.1.9 Asthma Control Questionnaire© (ACQ)

Purpose: To measure control of asthma symptoms during the past week.

Who: The participant completes this form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

AsthmaNet negotiated a license agreement with Dr. Elizabeth Juniper to use the Asthma Control Questionnaire© form in AsthmaNet studies. However, the original format of the form cannot be changed in any way. The header information including the Participant ID, Participant Initials, Visit, Visit Date, and Coordinator ID will be completed in the upper right hand corner of the form using the fillable PDF feature when preparing the visit packet.

This form should be completed before the participant undergoes spirometry.

Review the form after the participant or participant's parent/guardian has completed the form to ensure he/she circled a response for each question. Participant completed forms should always be reviewed by the coordinator upon form completion. If a correction is noted, the participant should make the correction and initial and date next to the change. Coordinators should not alter participant completed forms.

During data entry of this form, Questions 1 through 6 will be designated as (1) through (6) on the entry screen.

10.1.10 Asthma Control Questionnaire® (7 Question Version) (ACQ7)

Purpose: To measure control of asthma symptoms during the past week.

Who: The participant or participant's parent/guardian completes Questions 1 – 6, and the coordinator completes Question 7.

When: Refer to Visit Procedure Checklists.

Form Instructions:

AsthmaNet negotiated a license agreement with Dr. Elizabeth Juniper to use the Asthma Control Questionnaire© form in AsthmaNet studies. However, the original format of the form cannot be changed in any way. The header information including the Participant ID, Participant Initials, Visit, Visit Date, and Coordinator ID will be completed in the upper right hand corner of the form using the fillable PDF feature when preparing the visit packet.

Questions 1 through 6 should be completed by the participant before he/she undergoes spirometry. Instruct the participant not to complete Question 7.

Review the form after the participant or participant's parent/guardian has completed the form to ensure he/she circled a response for Questions 1 - 6. Participant completed forms should always be reviewed by the coordinator upon form completion. If a correction is noted in Questions 1-6, the participant should make the correction and initial and date next to the change. Coordinators should not alter participant completed questions.

If a correction is noted in Question 7, the coordinator may make the correction and initial and date next to the change. The participant is not required to make any corrections to Question 7 since it is coordinator-completed.

Question 7. After the participant has undergone spirometry, the coordinator should record the pre-bronchodilator FEV_1, FEV_1 predicted, and FEV_1 % predicted on the dotted lines next to Q7. *These values are not entered.* The coordinator should then circle the response corresponding to the range in which the participant's FEV_1 % predicted falls, from 0 (> 95%) to 6 (<50%); this value is entered.

During data entry of this form, Questions 1 through 7 will be designated as (1) through (7) on the entry screen.

10.1.11 Asthma Control Test™ (ACT)

Purpose: To determine how well the participant's asthma is controlled.

Who: Participant or Participant's Parent/Legal Guardian completes this form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

The AsthmaNet negotiated a license agreement with Quality Metric Incorporated to use the Asthma Control Test™ form in AsthmaNet studies. However, the original format of the form cannot be changed in any way. The header information including the Participant ID, Participant Initials, Visit, Visit Date, and Coordinator ID will be completed in the upper right hand corner of the form using the fillable pdf feature when preparing the visit packet.

Review the form after the participant or participant's parent/guardian has completed the form to ensure he/she marked a response (within the designated box) for each question. Ignore the scoring instructions at the bottom of the screen. The Asthma Control Test (ACT) will be scored using the data entered into the AsthmaNet data management system.

During data entry of this form, Questions 1 through 5 will be designated as Q1 through Q5 on the entry screen.

10.1.12 Asthma Quality of Life Questionnaire (AQLQ_12)

Purpose: To evaluate the participant's quality of life as a result of asthma.

Who: The participant completes this form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

AsthmaNet negotiated a license agreement with Dr. Elizabeth Juniper to use the Asthma Quality of Life Questionnaire© (AQLQ) form in AsthmaNet studies. However, the original format of the form cannot be changed in any way. The header information including the Participant ID, Participant Initials, Visit, Visit Date, and Coordinator ID will be completed across the header of the form using the fillable pdf feature when preparing the visit packet.

This version of the AQLQ is validated for individuals ages 12 and older. Participants are asked how their asthma has affected their lives over the ***last two weeks***. Instruct the participant to read each question carefully and circle the number corresponding to his or her best answer for each question. Directions on the questionnaire itself should be followed exactly.

This form should be completed before the participant undergoes spirometry. Standard questionnaires that collect information on a participant's perception of his/her asthma are administered before study procedures begin in order to avoid bias. The order of procedures on the Visit Procedure Checklist should be followed exactly.

Review the form after the participant has completed it to ensure that he/she clearly circled only one response for each question. Participant completed forms should always be reviewed by the coordinator upon form completion. If a correction is noted, the participant should make the correction and initial and date next to the change. Coordinators should not alter participant completed forms.

During data entry of this form, Questions 1 through 32 will be designated as (Q1) through (Q32) on the entry screen. All pages of this form must be presented to the participant, including the cover sheet. However, the cover sheet does not need to be forwarded to the DCC.

10.1.13 Asthma-Specific Work Productivity and Activity Impairment Questionnaire (WPAI_ASTHMA)

Purpose: To measure the effect of asthma on the participant's ability to work, attend classes, and perform regular daily activities.

Who: The participant completes this form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

The participant should answer the questions based on the past seven days, not including the day the participant is completing the form.

Question 1000. If Q1000 is answered 'Yes', the participant should complete Q1010, Q1020 and Question #4 (Q1030); otherwise skip to Q1040.

Questions 1010 and 1020. Record to the nearest tenths of a decimal.

Question 1040. If Q1040 is answered 'Yes', the participant should complete Q1050, Q1060 and Question #8 (Q1070); otherwise skip to Q1080.

Review the form prior to the participant leaving the clinic to ensure that the participant completed the form correctly. The participant should clearly circle one number for Questions 4, 8, and 9.

After the participant has completed the form, the AsthmaNet coordinator completes Q1030, Q1070, and Q1080 by recording the number the participant circled in the corresponding grey boxes.

To verify that the information recorded on this form is correct, have the participant initial (using 2 or 3 initials), date, and record the time in the source documentation box provided (Questions 1090-1110). Enter the Date field in the database in the format mm/dd/yyyy.

10.1.14 Asthma Symptom Utility Index (ASUI)

Purpose: To record how often asthma symptoms bothered a participant in the past 2 weeks.

Who: An AsthmaNet coordinator interviews the participant while completing the form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

Participants are asked questions about the severity and frequency of their asthma symptoms over the ***past two weeks.***

The coordinator should encourage the participant to be as precise as possible when reporting the number of days that he or she was bothered by asthma symptoms.

Question 1080. If the participant was bothered by side effects of his/her medication for one or more days, describe the side effects the participant experienced in Q1080D.

To verify that the information recorded on this form is correct, have the participant initial (using 2 or 3 initials), date, and record the time in the source documentation box provided on page 2 (Q1100-Q1120). Enter the Date field in the database in the format mm/dd/yyyy.

10.1.15 Childhood Asthma Control Test For Children 4-11 Years Old™ (CACT)

Purpose: To determine how well a pediatric participant's asthma is controlled.

Who: Participant and Participant's Parent/Legal Guardian complete this form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

AsthmaNet negotiated a license agreement with GlaxoSmithKline to use the Childhood Asthma Control Test™ (CACT) in AsthmaNet studies. However, the original format of the form cannot be changed in any way. The header information including the Participant ID, Participant Initials, Visit, Visit Date, and Coordinator ID will be completed across the header of the form using the fillable pdf feature when preparing the visit packet.

The pediatric participant completes Questions #1 - #4. If the child cannot read, the parent/guardian can ask the child the first four questions while showing him/her the happy/sad face pictures. The parent or guardian completes Questions #5 - #7. It is usually not necessary for the parent or guardian to score the form; however, the protocol-specific MOP should be consulted.

The child and/or parent/guardian may circle a response and/or complete the response in the Score box to the right of the question. If the response is only circled or the response is only written in the Score box, it is not required that both be completed.

The coordinator should not make edits to or complete the individual Score box for each question. If there is a discrepancy between what is circled and what is indicated in the Score box, request that the parent/guardian make the necessary correction(s) to the response and initial and date the correction. The coordinator may total the score at the bottom of the form or correct this total if the parent/guardian completes it in error. Review the form after the participant and the participant's parent/guardian have completed it to ensure that a response has been provided for each question.

If there is a discrepancy between what is circled and what is indicated in the Score box for an individual question, and the parent/guardian is not available in the clinic to make the correction to the form, the coordinator should enter the circled response in the database during entry of CACT.

During data entry of this form, Questions 1 through 7 will be designated as (1) through (7) on the entry screen.

10.1.16 Clinical Adverse Events (AECLIN)

Purpose: To record the details and events that occur each time a participant experiences a clinical adverse event.

Who: An AsthmaNet coordinator completes the form.

When: Refer to Visit Procedure Checklists.
Note: This form should also be completed if the participant or participant's guardian contacts study personnel to report a clinical adverse event outside of scheduled visits. This form should also be updated if the participant reports having an asthma/allergy or adverse event between visits. Questions on other forms may also prompt a coordinator to complete this form.

Form Instructions:

A clinical adverse event includes any new or worse than usual medical condition or inter-current illness the participant experiences during the course of the study. See Section 4 of the AsthmaNet General MOP for more information regarding adverse events.

At the first study visit, record all current events the participant experienced since signing the informed consent onto the Clinical Adverse Events (AECLIN) form. If a participant is not currently experiencing any adverse events, complete the information at the top right hand corner of the form and check the 'None' box.

At each subsequent visit, record all adverse events that have occurred since the previous visit. If a participant has not experienced any adverse events since the last visit, complete the information at the top right hand corner of the form and check the 'None' box. If any event is still ongoing at the current visit, leave the stop date and outcome blank and check the 'ONGOING at current visit' box (Q1040).

If the participant (or participant's guardian) contacts the clinic coordinator between visits, record the new adverse event on the AECLIN form completed at the last visit. This new adverse event should be updated in the Participant Data module within the data management application.

At each visit, review all ongoing events with the participant to acquire a stop date and outcome for each event. Ongoing events may be reviewed using the AECLIN form or the ongoing reports generated by the data management application. See Section 7 of the AsthmaNet General MOP for more information about Ongoing Adverse Events Reports.

At the participant's last study visit, review all ongoing events. If an event is ongoing at the final visit, leave the stop date and outcome blank and check the 'ONGOING at final visit' box.

A Clinical Adverse Events (AECLIN) form should be completed and entered for every study visit, even if the participant did not experience any adverse events at that visit.

Clinical Adverse Events forms should be data entered in the Participant Data module with the Entry Type of Concurrent (C) at the time the form is initiated. As the participant continues through the study and events are resolved, the updates should be recorded on the data collection form and then updated in the Participant Data module. Upon completion or early termination from the study, all Clinical Adverse Events forms should be sent to the DCC.

Question 1000. Describe the clinical adverse event. DO NOT complete the event number during form completion or prior to data entry. During data entry, record the number assigned by the module to each adverse event. This number will be a ***unique*** and ***chronological*** number assigned by the database. Number the form after all forms are completed to ensure related events are linked with the proper medication.

If an adverse event needs to be removed, for example, adverse event #07, simply cross that row off and initial and date the form. DO NOT RENUMBER the form.

Question 1010. Identify the appropriate ICD9 code to describe the underlying condition or disease. Procedure codes should not be recorded.

A list of all ICD9 Codes used for AsthmaNet is available in an Excel spreadsheet on the AsthmaNet secure web site under the Application link.

A link to the list of ICD9 Codes also can be found during data entry and editing in the Participant Data module of the data management application.

A searchable list is also available during entry and editing by selecting the "ICD" button next to the Q1010 entry. Type in the ICD9 code or health problem or parts of the health problem and a list of matching ICD9 codes and descriptions will display for you to select.

If the coordinator is still unable to identify an ICD9 code, please call the Primary Data Manager at (717) 531-3663 for assistance.

Questions 1020 & 1030. If the adverse event is still present at the time of the current visit, leave the 'Data Stopped' blank (Q1030) and check the 'ONGOING at current visit' box (Q1040).

Questions 1050 and 1060. Record the Type and Severity of each adverse event.

Question 1070. A serious adverse event is defined as an event resulting in hospitalization, extension of a hospital stay, or death. Outpatient procedures, including outpatient surgery, and visits to the Emergency Department (ED) without further hospitalization are NOT considered serious adverse events. If the adverse event is serious, complete the Serious Adverse Event Reporting (SERIOUS) single form and fax it to the DCC within 72 hours at 717-531-4359.

Question 1080. Study drug(s) should be interpreted as blinded or unblinded study inhalers, tablets, capsules, or pills.

Question 1090. Study drug(s) should be interpreted as blinded or unblinded study inhalers, tablets, capsules, or pills. Indicate “Unchanged” if the change in study drug was made according to the protocol. Indicate “Altered” only if the change in study drug was related to a non-protocol reason (i.e., principal investigator decides to take participant off of the inhaler(s)). If Q1090 is answered ‘Altered’, complete the appropriate Change in Medications form.

Question 1100. Do not complete this question if the ‘Date Stopped’ is missing. If the outcome is death, a Serious Adverse Event Reporting (SERIOUS) single form should be completed.

Question 1110. If the participant requires hospitalization, complete the Serious Adverse Event Reporting (SERIOUS) single form and fax it to the DCC within 72 hours. Hospitalization is defined as admittance to the hospital and does not include Emergency Department (ED) visits where the participant is not admitted to the hospital or outpatient surgery/procedures. If the participant requires medication, please record it on the Concomitant Medications for Asthma/Allergy and Adverse Events (CMED) concurrent form.

Question 1120. If at the final visit with the participant there are event(s) still ongoing (i.e., no ‘Date Stopped’ recorded and ‘ONGOING at current visit’ was checked), be sure that the ‘ONGOING at final visit’ box is checked.

If it is unknown whether an event was stopped or ongoing at the participant’s termination (for instance, in the case of a participant who has been lost to follow-up), check the ‘ONGOING at final visit’ box. This will indicate that the event was still ongoing as of the last contact with the participant.

The AECLIN forms should not be submitted to the DCC until the participant has completed the study or has been terminated from the study.

If there are ‘Date Stopped’ data missing (i.e., an event has not ended), or other changes to the form need to be made, the site can make changes as needed through the Participant Data module and then send the forms to the DCC all at one time after the participant completes or terminates the study.

10.1.17 Cold History (COLD_HX)

Purpose: To record a participant's cold history over the past 12 months and the effect on his/her asthma.

Who: An AsthmaNet coordinator completes the form while interviewing the participant or participant's parent or guardian.

When: Refer to Visit Procedure Checklists.

Form Instructions:

Question 1000. If Q1000 is answered 'Other', record a description in Q1000D.

Question 1010. If the participant did not experience any respiratory tract infections/colds in the past 12 months, record '00'.

Question 1030. If Q1030 is answered 'No', do not complete the rest of the form.

10.1.18 Concomitant Medications for Asthma/Allergy and Adverse Events (CMED)

Purpose: To record any asthma/allergy and adverse event related concomitant medications that the participant uses during the study.

Who: An AsthmaNet coordinator completes the form.

When: Refer to Visit Procedure Checklists. **Note:** This form should be completed if the participant or participant's guardian contacts study personnel to report a concomitant medication used outside of scheduled visits. This form should also be updated if the participant reports taking an asthma/allergy or adverse event related concomitant medication between visits. Questions on other forms may also prompt a coordinator to complete this form.

Form Instructions:

At the first study visit, record all of the concomitant medications related to asthma/allergies and adverse events that the participant has taken since signing the informed consent. At each subsequent visit, record all of the concomitant medications related to asthma/allergies and adverse events that the participant has taken since the previous visit. Do not list routine use of study drugs or rescue medications. If a participant has not taken any asthma/allergy and adverse events related concomitant medications since the last visit, complete the information in the upper right hand corner of the form and check 'None'. If the participant is still taking a medication at the end of the current visit, leave the stop date blank and check the 'Ongoing at Current Visit' box.

At each visit, review all ongoing medications with the participant to acquire a stop date. Ongoing medications may be reviewed using the CMED form or ongoing records report generated by the data management application. See Section 7 of the AsthmaNet General MOP for more information on the Ongoing Medications Report.

At the participant's last study visit, review all ongoing medications. If the participant is still taking a medication at the final visit, leave the stop date blank and check the 'Ongoing at Final Visit' box.

A Concomitant Medications for Asthma/Allergy and Adverse Events (CMED) form should be completed for each participant in the study at each visit, even if the participant has not taken any concomitant medications since the last visit.
The Concomitant Medications for Asthma/Allergy and Adverse Events (CMED) forms should be data entered in the Participant Data module with the Entry Type of Concurrent (C) at the time the form is completed. As the participant continues through the study and medications are discontinued, the updates should be recorded on the

data collection form and then updated in the Participant Data module. Upon completion or early termination from the study, all CMED forms should be sent to the DCC.

Question 1000. Name of Medication**.** DO NOT complete the event number during form completion or prior to data entry. During data entry, record the number assigned in the module to each medication. This number will be a ***unique*** and ***chronological*** number assigned by the database.

If a medication needs to be removed, for example, medication #05, simply cross that row off and initial and date the form. DO NOT RENUMBER the form. Duplicate numbers are not to be used; each medication must have its own ***unique*** medication number.

If the participant contacts the coordinator between visits, record the new medication on the CMED form completed at the last visit. This new medication should be updated in the Participant Data module within the data management application.

If the medication is a combination drug, each component of the drug must be listed on the CMED form as a separate record. For example, Advair® would have two records entered on the CMED form; a record for fluticasone and a record for salmeterol.

Question 1010. Identify the appropriate drug code for the recorded medication. A list of drug codes can be found in an Excel spreadsheet on the AsthmaNet secure web site under the Application link. The drugs are listed as generic names. In addition, a Search Drug Codes link (that will display the same Excel spreadsheet) can be found during data entry and editing in the Participant Data module of the AsthmaNet data management application. A searchable list is also available during entry and editing by selecting the “D” button next to the Q1010 entry. Type in the medication name or a string of characters contained in the medication name and a list of matches will display with their corresponding drug codes. If the coordinator is still unable to find a corresponding drug code, please log into the AsthmaNet web site under Coordinator Resources: Forms and complete the Drug Code Request Form. Please complete your name, request date, the participant ID, and known information about the drug’s generic name, brand name, drug class or indication. Any questions/concerns should be directed to the asthmanet-drug_code_req@phs.psu.edu email alias.

Question 1020. If the medication is not related to an adverse clinical event, leave the event number missing, check the ‘N/A’ box and enter a zero into the database. If the medication is related to an adverse event, complete the event number from the AECLIN form after the AECLIN form has been entered and the Adverse Event number is assigned.

Question 1030. If the dose of medication is tapered across time, the dose that is listed should be the dose that is administered on the first day the medication is taken.

Questions 1040, 1050, and 1055. A list of codes for the units (Q1040), frequency (Q1050), and route (Q1055) are located on the AsthmaNet secure website under

Standard Forms/Reference/Units, Frequency, and Route Codes for Concomitant Medications (CMED_REF).

When recording the dose, units, and frequency of a medication, it is important to record the amount of the drug taken using weight or volume, if applicable. Do not record medication dosages in quantities (e.g., puffs).

Q1030 should always record the strength of the medication. If the participant or parent/guardian does not know the strength of the medication, the coordinator can go to the PDR (pdr.net) to get the information.

For example, a search on pdr.net for diphenhydramine, will return several results. The product label for Children's Benadryl Allergy Liquid will indicate 12.5 mg per 5 ml (5ml = 1 tsp). If the participant or parent/guardian indicates 1 tsp was taken, 12.5 would be recorded in Q1030 and '1' for milligrams would be recorded in Q1040.

If the participant was prescribed ceritizine, 1ml = 1mg (5 ml = 1 tsp) or 5mg per tsp. So if the participant or parent/guardian indicates 1 tsp was taken, 5 would be recorded in Q1030 and '1' for milligrams would be recorded in Q1040.

If the participant was prescribed 80 micrograms of beclomethasone, 80 would be recorded in Q1030 and '2' for micrograms would be recorded in Q1040.

Q1040 should always record the unit of measurement however there are specific responses that are required for the following medication categories.

Category	**Acceptable Response**
Antihistamine	Code 1 (mg) or 2 (mcg)
Corticosteroid	Code 1 (mg) or 2 (mcg)
Beta-2 Adrenergic Agonist	Code 1 (mg) or 2 (mcg)
Anticholinergic Agent	Code 2 (mcg)
Leukotriene Modifier	Code 1 (mg)
Xanthine Derivative	Code 1 (mg)

Indicate the correct codes for each medication listed on the form. If any code cannot be found, log into the AsthmaNet web site under Coordinator Resources: Forms and complete the Drug Code Request Form. Please complete your name, request date, the participant ID, and known information about the drugs generic name, brand name, drug class or indication. Any questions/concerns should be directed to the asthmanet-drug_code_req@phs.psu.edu email alias.

If a medication is a tapered dose, Q1050 should be recorded as ‘taper dose’ for the record.

At the time of entry, the medication number (Q1000) should be written on the form as it appears on the entry screen.

Question 1060. The ‘Start Date’ field (Q1060) must be completed. For any medications the participant started prior to signing the informed consent, record the informed consent date as the ‘Start Date’.

Questions 1070, 1080, and 1090. If the participant is still taking a medication at the time of the visit, leave the ‘Stop Date’ (Q1070) blank and check the ‘Ongoing at current visit’ box (Q1080).

Question 1090. If at the final visit with the participant there is a medication(s) still ongoing (i.e., no ‘Date Stopped’), check the ‘Ongoing at final visit’ to close out the record.

If it is unknown whether a medication was stopped or ongoing at the participant’s termination (for instance, in the case of a participant who has been lost to follow-up), check the ‘Ongoing at final visit’ box. This will indicate that the medication was still being taken as of the last contact with the participant.

Send all CMED forms to the DCC once a participant completes the study or terminates. When collating and mailing this form to the DCC, all Concomitant Medications for Asthma/Allergy and Adverse Events (CMED) forms completed for a participant should be **paper clipped** together as one form. These forms should be arranged in visit number order. Once all forms are completed for a participant, complete the ‘Form Page __ of __ ’ field at the bottom center of each page. For example, if twenty-one Concomitant Medications for Asthma/Allergy and Adverse Events (CMED) forms are completed, the first form should be numbered ‘Form Page 1 of 21’, the second as ‘Form Page 2 of 21’, and so on respectively regardless of visit number assignment.

For more information on recording concomitant medications, see the Concomitant Medications discussion in Section 7 of the AsthmaNet General MOP.

10.1.19 Effects of a Child's Asthma Flare-up on the Parents (PARENT_QOL)

Purpose: To measure the effects on the parent's quality of life when a child suffers an asthma flare-up.

Who: A child's parent or legal guardian completes the form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

Questions Q1000 – Q1210. Shade in one circle for each question.

Question 1220. If the parent/legal guardian did not miss any work or regular planned activities to take care of his/her child, record '00'.

Question 1230. If the parent/legal guardian wan not about to perform his/her work or regular planned activities at all, record '000'.

Question 1250. If Q1250 is answered 'Other', record a description in Q1250D.

10.1.20 Exhaled Nitric Oxide (ENO)

Purpose: To record the outcome measures from the participant's Exhaled Nitric Oxide collection.

Who: The ENO Technician completes the form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

If the technician in charge of the procedure is not ENO certified, a supervising technician, who is certified, should monitor the technician and record his or her ID number in the Supervisor ID field at the top of the form. In addition, this field needs to be entered into the database in the (Sup ID) field.

Exhaled Nitric Oxide must be performed prior to spirometry testing. Refer to Appendix 8 of the AsthmaNet General MOP for more information on ENO collection.

Question 1030. If NO concentration indicated on report is "<5," enter this as "5" in the database. These fields on the data entry screen will not accept the "<" symbol.

Question 1040. Record time eNO started based on a 24-hour clock (military time).

10.1.21 GIS Consent Tracking Form (GIS)

Purpose: To record information on the participant's consent to the Ancillary Geographic Information System (GIS) study.

Who: An AsthmaNet coordinator completes the form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

Question 1000. Reference the participant's GIS consent document for the current study. Record the date the consent was signed in Q1000.

Question 1010. Reference the participant's GIS consent document for the current study. If the participant and/or his/her guardian consented to allow the use of his/her home address for GIS analysis, answer this question 'Yes.' Otherwise, answer this question 'No.'

Participant/Guardian Source Documentation. After all data is recorded on the GIS form, the participant or his/her guardian should be asked to review all information and initial and date the source documentation box to verify the accuracy of the information. *Source documentation is necessary even if consent for GIS participation was not granted.*

10.1.22 Home Environment Questionnaire (HEQ)

Purpose: To record the characteristics of the participant's home environment.

Who: An AsthmaNet coordinator interviews the participant or participant's parent/ legal guardian while completing the form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

If the participant's parent or guardian is completing the form for a child, point out to him/her that the reference 'you' in the questions is the child who is the study participant.

'House' is defined as the place where the participant lives most of the time. If the participant does not have a bed or bedroom, he/she should answer questions related to characteristics of the bedroom based on the place where he/she sleeps.

Question 1000. Check only one box. If Q1000 is answered 'Other', Q1000D should be completed.

Questions 1010 and 1020. Record the years and months the participant has lived in the current house. For example, if the participant has lived in the current house for 5 years and 2 months, record 5 for the Q1010 and 2 for Q1020. If unsure of the number of months or years, estimate to the nearest number of years and months.

Question 1090. If Q1090 is answered 'No' or 'Don't Know', skip to Q1170.

Question 1160. If Q1060 is answered 'Yes', complete Q1160D.

Question 1170. If Q1170 is answered 'No', skip to Q1260.

Question 1250. If Q1250 is answered 'Yes', complete Q1250D.

Question 1260. If Q1260 is answered 'No', skip to Q1350.

Question 1340. If Q1340 is answered 'Yes', complete Q1340D.

Question 1410. If Q1410 is answered 'Other', complete Q1410D.

Question 1420. If Q1420 is answered 'Other', complete Q1420D. If Q1420 is answered 'None', skip to Q1440.

Question 1440. If Q1440 is answered 'No', skip to Q1460.

Question 1460. If Q1460 is answered ‘Other’, complete Q1460D. If Q1460 is answered ‘None’, skip to Q1480.

Question 1480. If Q1480 is answered ‘No’, skip to Q1570.

Questions 1490 – 1550. Enter ‘00’ if no pets of a particular type live in the household. If there is one or more pet of a particular type, check whether this (these) pet(s) are Indoor, Outdoor, or Both.

Question 1620. If Q1620 is answered ‘Yes’, complete Q1620D.

If the participant is 6 years of age or older, STOP HERE and complete the source documentation box. The source documentation must be completed even if Q1630 – Q1700 are skipped based on the age of the participant.

Questions 1630 – 1700. These questions should be completed only if the participant is 5 years of age or younger.

Question 1630. If Q1630 is answered ‘Yes’, complete Q1640.

Question 1650. If Q1650 is answered ‘No’, do not complete Q1660 – Q1700. The source documentation box must be completed even if Q1660 – Q1700 are not completed due to the skip pattern.

Review the form prior to the participant leaving the clinic to ensure that the participant completed the form correctly.

The participant or participant’s parent/legal guardian must complete the source documentation box (using 2 or 3 initials) on page 5 (Q1710 and Q1720). Enter the Date field in the database in the format mm/dd/yyyy.

10.1.23 Household Socio-economic Information (HOUSEHOLD_SEI)

Purpose: To record the socio-economic information of the participant's primary household.

Who: The participant or participant's parent/legal guardian completes the form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

If the participant is a college student living away from home during the school year, the questions pertain to the parents' household.

For all other participants, 'Household' is defined as the place where the participant lives most of the time.

Question 1000. If Q1000 is answered 'Other', record a description in Q1000D.

Questions 1010 and 1020. The participant or participant's parent/legal guardian may refuse to answer these questions. Be sure to select the 'Decline to answer' option instead of leaving the question missing. Q1030 should be answered even if the participant or participant's parent/legal guardian declined to answer Q1020.

Review the form prior to the participant leaving the clinic to ensure that the participant completed the form correctly.

10.1.24 ImmunoCAP Results (IMMUNOCAP)

Purpose: To record a participant's ImmunoCAP results of one or more allergens.

Who: An AsthmaNet coordinator completes the form.

When: When allergy skin testing cannot be performed for one or more allergens.

Form Instructions:

ImmunoCAP Testing should be performed instead of allergy skin testing if the participant previously had a severe systemic reaction to allergy skin testing. Complete the testing for all allergens on the Allergy Skin Test Results (SKIN_TEST) form.

ImmunoCAP Testing should be performed if the participant has a history of or existing allergy to milk, egg, or peanut. The AsthmaNet coordinator certified in performing skin testing should not skin test for the food(s) that the participant is allergic to. Record the ImmunoCAP result(s) for the specific food(s) the participant had a reaction to.

ImmunoCAP Testing can be performed if the participant used any medications listed in the skin test section of the AsthmaNet General MOP within the exclusionary periods and an allergy skin test cannot be rescheduled.

Upon the discretion of the physician, based on interfering eczema, dematographisms, etc., ImmunoCAP Testing should be performed for both the food and aeroallergens on the Allergy Skin Test Results (SKIN_TEST) form.

Questions 1000 – 1130. If multiple values are received for a particular allergen, refer to the protocol-specific MOP as to how to record these values.

Upon receipt of the lab report, complete the ImmunoCAP Results (IMMUNOCAP) form as a single form at the same visit where the allergy skin testing was/should have been performed. Attach a Data Processing Cover Sheet (DPCS) to the form and send the single form to the DCC after data entry. Store the original lab report with a copy of the IMMUNOCAP form in the participant's study file at the clinical site.

The IMMUNOCAP form and original lab report will be reviewed at AsthmaNet site visits.

10.1.25 Pre-Bronchodilator IOS (IOS_PRE)

Purpose: To record the outcome measurements from the pre-bronchodilator IOS procedure.

Who: The Pulmonary Technician completes the form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

If the technician in charge of the procedure is not certified in IOS testing, a supervising technician who is certified should monitor the technician and record his or her ID number in the Supervisor ID field at the top of the form. The supervisor ID number should be entered in the post test comments section of the test session. The Supervisor ID ***is*** entered into the database during data entry. Failure to complete the Supervisor ID when applicable could result in a protocol deviation.

The protocol-specific pulmonary procedure checklist (PULMONARYCHK) needs to be completed to determine eligibility before performing Pre-Bronchodilator Testing (IOS_PRE). Please refer to the protocol-specific MOP.

If a procedure needs to be rescheduled, complete a new Pre-bronchodilator IOS form with the current date. Do not enter the old Pre-bronchodilator IOS form into the study database and do not send it to the DCC. Only enter and submit (to the DCC) the most recent Pre-bronchodilator IOS form. However, all completed forms, the old original Pre-bronchodilator IOS form and the current photocopy of the Pre-bronchodilator IOS form should be filed in the subject's study file.

Question 1000. Record the time based on a 24-hour clock (military time).

Questions 1010-1080. These values will be obtained from the Act1 column on the Jaeger system IOS report.

Questions 1090-1160. These values will be obtained from the Act2 column on the Jaeger system IOS report.

Questions 1170-1240. These values will be obtained from the Act3 column on the Jaeger system IOS report.

Question 6000. This section is provided for the Clinic Coordinator to complete if the form requires addition comments or information. This question is data entered into the database.

Always print two copies of the Pre-bronchodilator IOS report from the Jaeger system.

If the form is a packet form, clip one report to the back of the visit packet and forward to the DCC (after data entry and resolution of entry errors). Place the report with the photocopy of the visit packet in the participant's study folder.

If the form is a single form, clip a report to the back of the single form and forward it to the DCC with a Data Processing Cover Sheet (DPCS) attached. Place the report with the copy of the single form in the participant's study folder.

During data entry for a visit packet or single form that contains the Pre-bronchodilator IOS procedure, you will need to acknowledge whether or not the Pre-bronchodilator IOS report is being submitted to the DCC. These reports are referred to as Tracking Forms in the AsthmaNet data entry application. When you reach the end of the visit packet data entry or single form data entry, possible reports related to that visit packet/single form will be listed with the default, 'Yes' (this report is being submitted) selected. Select 'No' if a particular report is not being forwarded to the DCC. If all other data entry procedures for this visit packet/single form are completed, select 'Save Data'.

See Section 2.21 in the AsthmaNet General Mop for more information regarding these procedures.

See Appendix 9 of the AsthmaNet General MOP for more information regarding Pre-bronchodilator IOS procedures.

10.1.26 Maximum Reversibility Testing (MAXREV)

Purpose: To record the maximal improvement in FEV_1 following albuterol treatment.

Who: The Pulmonary Function Technician completes the form.

When: Refer to Visit Procedure Checklists.

Complete this form ***only*** if the participant ***is eligible*** according to the protocol-specific Pulmonary Procedure Checklist (PULMONARYCHK) and ***successfully completed*** baseline spirometry sessions(s) (SPIRO).

Form Instructions:

If the technician in charge of the procedure is not certified in spirometry testing, a supervising technician who is certified should monitor the technician and record his or her ID number in the Supervisor ID field at the top of the form. The supervisor ID number should be entered in the post test comments section of the test session. The Supervisor ID ***is*** entered into the database during data entry. Failure to complete the Supervisor ID when applicable could result in a protocol deviation.

Administer 4 puffs of albuterol, wait 10 to 15 minutes, then perform spirometry and continue with Q1000.

Questions 1000, 1010, 1050, 1060, 1110, 1120. Record the time based on a 24-hour clock (military time).

Questions 1030 and 1040. These values should come from the Post 4 Composite row of the MedGraphics Max Reversibility Report. Record the value for Q1030 to the nearest hundredths of a decimal.

Administer 2 puffs of albuterol, wait 10 to 15 minutes, then perform spirometry and continue with Q1050.

Questions 1070 and 1080. These values should come from the Post 2 (6) Composite row of the MedGraphics Max Reversibility Report. Record the value for Q1070 to the nearest hundredths of a decimal.

Question 1090. This field will accept both positive and negative values. When applicable, note the negative sign in front of the value on the form. The calculated value will be rounded to the nearest tenth of a decimal.

Question 1100. Refer to the percent difference in Q1090. If the percent difference is $\leq$ 5.0%, the test should be stopped and Q1150 should be completed. If not, administer 2

puffs of albuterol, wait 10 to 15 minutes, then perform spirometry and continue with Q1110-Q1140.

Questions 1130 and 1140. These values should come from the Post 2 (8) Composite row of the MedGraphics Max Reversibility Report. Record the value for Q1130 to the nearest hundredths of a decimal.

The corresponding report for the MAXREV form is the MedGraphics Maximum Reversibility Final Report, abbreviated MAXREV_RPT. Refer to the protocol-specific MOP for details on when this report is used.

Photocopy the Max Reversibility Report. If the form is a packet form, clip the original report to the back of the packet and forward it to the DCC. Place the copy in the participant's study folder. If the form is a single form, clip the original to the back of the single form and forward it to the DCC with a Data Processing Cover Sheet (DPCS) attached. Place the copy in the participant's study folder.

10.1.27 MEMS®6 Monitor Quality Control (MEMSQC)

Purpose: To determine if the MEMS®6 monitor is functioning properly at each visit.

Who: A MEMS®6 monitor certified technician performs the procedure and completes the form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

Enter and send the MEMS®6 Monitor Quality Control (MEMSQC) form for both failed and successful MEMS®6 monitor trials to the DCC.

If the participant forgets his/her MEMS®6 monitor, do not complete a MEMS®6 Monitor Quality Control (MEMSQC) form. Indicate on the Visit Procedure Checklist that the participant forgot his or her MEMS®6 monitor. During data entry, register MEMS®6 Monitor Quality Control (MEMSQC) form as missing. If the participant brings in his or her MEMS®6 monitor at a later date (other than the visit date), use the later date as the visit date for the MEMSQC form. This form should then be entered as a single form.

When completing the MEMS®6 Monitor Quality Control (MEMSQC) form between visits, specify the last visit number completed and the current date in the upper right hand corner of the MEMS®6 Monitor Quality Control (MEMSQC) form. This form should be entered as a single form.

Question 1000. There should be a serial number recorded on the cap of each MEMS®6 monitor.

Question 1010. At each visit, record the date the MEMS®6 monitor information was read.

Question 1020. Respond ‘Yes’ to Q1020 if the MEMS®6 monitor being issued is new to the participant; then indicate the reason the ‘old’ MEMS®6 monitor is no longer being used by checking the appropriate box in Q1030. If the ‘old’ MEMS®6 monitor is being reissued, respond ‘No’.

Question 1030. Respond ‘First Issuing’ at the first study visit since this is the first time the participant is receiving the device. If at later visits the participant is given a new device, do not respond ‘First Issuing’, instead indicate the appropriate reason why a new device was given to the participant. If Q1030 is answered ‘Other’, complete Q1030D.

Questions Q1040-1060. Alerts regarding battery expiration, battery voltage, and used memory will appear when reading MEMS®6 cap for the first time. This should be done

prior to dispensing MEMS®6 cap for use. If no alerts appear, expiration, voltage, and memory are adequate and Q1040-Q1060 should be answered No.

Question 1070. If any of the gray boxes were checked in Q1040, Q1050 or Q1060, then the monitor did not pass quality control.

For more details on the quality control testing procedures for the MEMS®6 monitor, see the MEMS®6 Monitor Quality Control discussion in the MEMS®6 Monitor manual, Appendix 5 of the AsthmaNet General MOP.

When collating and mailing this form to the DCC, all MEMSQC forms completed for the same participant on the same day should be organized together in the order in which they were tested.

Example: Two MEMS®6 monitors were tested and both failed the quality control testing. As a result, a third MEMS®6 monitor was tested and it passed the quality control testing. The forms should be ordered as follows: The MEMSQC form for the 'old' MEMS®6 monitor tested should be the first page. The MEMSQC form for the 'second' MEMS®6 monitor should be the second page. The MEMSQC form for the 'third' MEMS®6 monitor tested should be the third page.

Complete the 'Form Page __ of __' fields at the bottom center of the form for each MEMS®6 monitor tested. For example, if three MEMS®6 monitors are tested, the first MEMSQC form should be numbered 'Form Page 1 of 3', the second as 'Form Page 2 of 3', and the third as 'Form Page 3 of 3'.

10.1.28 Methacholine Challenge Testing (METHA)

Purpose: To record outcome measurements from the methacholine challenge procedure.

Who: The Pulmonary Function Technician administers the methacholine and pulmonary function tests and completes the form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

Complete this form ***only*** if the participant has ***successfully completed*** either the Pediatric Methacholine Challenge Testing Checklist (METHACHK_PED) or the Adult Methacholine Challenge Testing Checklist (METHACHK_ADULT).

If the technician completing the procedure is not certified and this procedure is being used as an observation session for certification, please complete the Supervisor ID located in the header on the METHA form with the ID of the certified technician who supervised the procedure. The Supervisor ID ***is*** entered into the database during data entry. Failure to complete the Supervisor ID when applicable could result in a protocol deviation.

The Supervisor ID should be entered in the Post Test Comments area of the MedGraphics system. Refer to Appendix 4 of the AsthmaNet General MOP for detailed instructions on certification of technicians in methacholine challenge testing.

The Methacholine Reference Reversal Reference Value is the value recorded for Q1030 on the Spirometry Testing (SPIRO) form X .90.

Question 1000. This value should come from the Diluent or Diluent II (if necessary) Composite row of the Methacholine Report. Record the value for Q1000 to the nearest hundredths of a decimal.

Question 1010. If the participant's FEV_1 dropped $\geq$ 20% at the diluent stage(s), record 'Yes' for Q1010 and record '0' for Q1050. See Appendix 2 in the AsthmaNet General MOP for more information.

Question 1020. Record the concentration of the Challenge/Max stage of the MedGraphics Methacholine Report. Record the value for Q1020 to the nearest ten thousandths of a decimal.

Question 1030. Record the FEV_1 from the Composite Challenge/Max row of the MedGraphics Methacholine Report. Record the value for Q1030 to the nearest hundredths of a decimal.

Questions 1040 and 1050. If a PC_{20} was achieved, it will be printed on the last page of the MedGraphics Methacholine Report under the graph as 'PC='.

- If the participant's FEV_1 does not drop 20% or more after all concentrations of solution are administered during the methacholine challenge, answer Q1040 as 'No' and leave the PC_{20} value (Q1050) blank.
- If the challenge is stopped prematurely for any reason, answer Q1040 as 'No' and leave the PC_{20} value (Q1050) blank.
- Occasionally it may be necessary to recompute a PC_{20} value recorded by the methacholine software. When a problem occurs during a methacholine challenge, note the circumstances in the comments associated with the challenge so that the overreader may adjust the grade accordingly. Contact the protocol-specific scientific coordinator at the DCC and notify the overreader. The scientific coordinator will compute the PC_{20} and send the new value to the technician and the overreader via e-mail. The technician should submit a copy of the e-mail documentation along with the data collection form with the corrected value.

Question 1050. Record the value for Q1050 to the nearest hundredths of a decimal.

Question 1060. Record the time based on a 24-hour clock (military time).

Question 1070. Record the post-albuterol FEV_1 after standard reversal from methacholine. This value should come from the Post Composite row of the MedGraphics Methacholine Report. Record the value for Q1070 to the nearest hundredths of a decimal.

Question 1080. Record the time based on a 24-hour clock (military time).

Question 1090. To calculate the methacholine reversal reference value (B) in the gray box, round the calculation from Question A X 0.9 to the hundredths of a decimal. (Example: if the value is 1.2576, record the value in (B) as 1.26). The FEV_1 value used in Question A in the grey box should be obtained from Q1030 on the Spirometry Testing (SPIRO) form. If Question 1090 is answered 'Yes', STOP HERE and continue with the remaining visit procedures. Otherwise, proceed to the Additional Treatment for Methacholine Challenge Testing (METHA_ADD_TRT) form.

Photocopy the methacholine report from the MedGraphics system. Clip the original report to the visit packet that will be forwarded to the DCC (after data entry and resolution of entry errors). File the copy of the report in the participant's study file.

The corresponding report for the METHA form is the MedGraphics Methacholine Final Report, abbreviated METHA_RPT. Refer to the protocol-specific MOP for details on when this report is used.

10.1.29 Paediatric Asthma Quality of Life Questionnaire™ (PAQLQS)

Purpose: To measure a pediatric participant's quality of life living with asthma.

Who: An AsthmaNet coordinator completes the form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

AsthmaNet negotiated a license agreement with Dr. Elizabeth Juniper to use the Paediatric Asthma Quality of Life Questionnaire© in AsthmaNet studies. However, the original format of the form cannot be changed in any way. The header information including the Participant ID, Participant Initials, Visit, Visit Date, and Coordinator ID will be completed across the header of the form using the fillable pdf feature when preparing the visit packet. **Note:** Do **NOT** complete the Name, Number, and Dates of Completion fields at the top of the Response Sheet. The participant's name is a HIPAA identifier and should never be listed on any documentation forwarded to the DCC.

PAQLQ(S) is a 23-question tool validated for ages 7-17 years. It has a 1-week recall. The interviewer-administered version will be used for AsthmaNet studies. Participants are asked to think about how their asthma has affected them during the previous week and to respond to each of the 23 questions on a 7-point scale. Scales are shown on blue and green response cards provided by Dr. Juniper. The coordinator should present the appropriate card for each question as it is administered. Directions for questionnaire administration on page 1 of the form must be followed exactly.

As stated in the directions, parents should not be present during the interview. The participant's own experiences that should be evaluated. Some parents may want to influence this evaluation and some children may want to look to the parent for guidance.

Show the blue and green response cards to the participant and explain the options. For children who can read, ask them to read aloud each of the response options. For younger children, read through each of the responses with them. Make sure the child understands the concept of grading from 1 (extremely bothered/all of the time) to 7 (not bothered/none of the time).

As the questions are administered, record the numeric answer to each in the 1st column on the response sheet (page 5 in the questionnaire packet with page number 4 on it).

This form should be completed before the participant undergoes spirometry. Standard questionnaires that collect information on a participant's perception of his/her asthma symptoms are administered before study procedures begin in order to avoid bias.

During data entry of this form, Questions 1 through 23 will be designated as (Q1) through (Q23) on the entry screen. All pages of the questionnaire must be present during administration of the questionnaire, but only the Response Sheet (Page 5 in the questionnaire packet) should be forwarded to the DCC with the visit packet. A new questionnaire should be administered at each study visit (i.e. the Response Sheet is not reused as its 4-column structure implies). Record all responses in the 1st Response column only.

10.1.30 Pediatric Long Physical Exam (LEXAM_PED)

Purpose: To record a pediatric participant's height, weight, parental height, evidence of oral candidiasis, and physical findings.

Who: An AsthmaNet coordinator completes Page 1 of this form. Page 2 is completed by a licensed medical practitioner.

When: Refer to Visit Procedure Checklists.

Form Instructions:

For more information related to performing a long physical exam, please refer to Section 3 of the AsthmaNet General MOP.

Questions 1010 – 1050. The biological parents' heights should be captured only once during a protocol. This should be attempted at the first visit and at every subsequent visit until the fields are completed. If the fields are all completed at the first study visit, the fields should be left blank for subsequent visits.

Question 1100. Plot this value on gender- and age-appropriate growth charts. See protocol-specific MOP for further details.

Question 1110. If Q1110 is answered 'No', please specify the reason why it was unacceptable in Q1120.

Question 1130. Plot this value on gender- and age-appropriate growth charts. See protocol-specific MOP for further details.

Question 1140. If Q1140 is answered 'Yes', complete the Clinical Adverse Events (AECLIN) form.

Only the responses from Page 1 and the Comments from Page 3 (Q6000) are entered into the study database.

The source documentation box is completed on Page 2 by a licensed medical practitioner verifying he/she completed Page 2 of the physical exam.

10.1.31 Pediatric Methacholine Challenge Testing Checklist (METHACHK_PED)

Purpose: To determine if a pediatric participant is eligible to proceed with the diluent (solution #0) pulmonary function testing for the methacholine testing.

Who: The Pulmonary Function Technician completes the form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

If the technician completing the procedure is not certified in methacholine challenge testing, a supervisory technician who is certified should monitor the technician and record his or her number in the Supervisor ID field at the top of the form. The Supervisor ID ***is*** entered into the database during data entry. Failure to complete the supervisor ID when applicable could result in a protocol deviation.

Complete this form only if the participant is eligible according to the protocol-specific Pulmonary Procedure Checklist and successfully completed baseline spirometry session(s).

Question 1000. If Q1000 is answered 'Yes', Q1010 must be completed.

Question 1020. If the physician's signature was obtained, enter a 1 in the database. Otherwise, leave the field blank during data entry.

Question 1030. If Q1030 is answered 'Yes', Q1040 must be completed.

Question 1050. Refer to the Concomitant Medications for Asthma/Allergy and Adverse Events (CMED) form and the Clinical Adverse Events (AECLIN) form.

Question 1060. The participant is ineligible to perform a methacholine challenge if the FEV_1 (% predicted) value recorded on the Q1040 of the Spirometry Testing (SPIRO) form is less than 70% of predicted.

Question 1070. Check 'N/A' if the participant is male or is a female that has not started menses.

Question 1080 and 1090. A participant who is 12 years old or older is ineligible to proceed if his/her systolic blood pressure is > 200 or his/her diastolic blood pressure is > 100. If the participant is less than 12 years old, he/she is ineligible to proceed if his/her systolic blood pressure is > 180 or his/her diastolic blood pressure > 90.

Question 1100. If there is a reason the participant should not proceed with methacholine challenge testing that has not been captured on the form, explain in the space provided (Q1100D).

Question 1110. If the participant is deemed eligible, proceed to the Methacholine Challenge (METHA) form. The participant is deemed ineligible for the diluent (solution #0) pulmonary function testing for the methacholine challenge if any of the shaded boxes are completed.

10.1.32 Pediatric Respiratory Assessment Measure (PRAM)

Purpose: To measure the respiratory assessment of a pediatric participant.

Who: An AsthmaNet coordinator completes the form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

Questions 1000 and 1010. Record the time based on a 24-hour clock (military time).

10.1.33 Pediatric Short Physical Exam (SEXAM_PED)

Purpose: To record a pediatric participant's height, weight, evidence of oral candidiasis, and physical findings.

Who: An AsthmaNet coordinator completes this form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

For more information related to performing a short physical exam, please refer to Section 3 of the AsthmaNet General MOP.

Questions 1070, 1080, 1090 and 1100. Record to the nearest tenths of a decimal.

Question 1100. Plot this value on gender- and age-appropriate growth charts. See protocol-specific MOP for further details.

Question 1110. If 'No' is checked, please record the reason why it was unacceptable in Q1120.

Question 1130. Plot this value on gender- and age-appropriate growth charts. See protocol-specific MOP for further details. Record to the nearest tenth of a decimal.

Question 1140. If 'Yes' is recorded, complete the Clinical Adverse Events (AECLIN) form.

Only the responses from Page 1 and the Comments recorded on Page 2 (Q6000) are entered into the study database.

The coordinator completing the form should complete the source documentation box on Page 2.

10.1.34 Pediatric Asthma and Allergy History (ASTHMA_HX_PED)

Purpose: To record an overview of a pediatric participant's asthma history including family history, symptoms, triggers, allergies, and smoking history.

Who: An AsthmaNet coordinator interviews the participant or participant's parent/ legal guardian while completing the form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

Questions 1000 and 1010. Record the participant's age using both the years and months fields. For example, if the participant was 2 years, 3 months old when chest symptoms suggesting asthma first appeared, record '2' for Q1000 and '3' for Q1010. If the participant was 2 years old, record '2' for Q1000 and '0' for Q1010.

Questions 1070 and 1080. Record the participant's age using both the years and months fields. For example, if the participant was 2 years, 3 months old when asthma was first diagnosed, record '2' for Q1070 and '3' for Q1080. If the participant was 2 years old, record '2' for Q1070 and '0' for Q1080.

Questions 1090 – 1120. If the participant is adopted and does not know his or her biological parents and/or siblings, answer 'Don't Know.'

Question 1110. Record 'N/A' if the participant does not have any biological siblings.

Question 1120. Record 'N/A' if the participant does not have any biological children.

Questions 1140, 1150, 1160, and 1170. If the participant's asthma symptoms vary by season, multiple seasons may be answered as 'Yes'; however, not all 4 seasons should be answered 'Yes.' At least one 'Yes' should be checked.

Questions 1180 – 1240. If the participant or participant's guardian answered 'none' to any of these questions, record '00' for the response.

Question 1250. If Q1250 is answered 'No', skip to Q1290.

Question 1400. If Q1400 is answered 'Yes', record a description in Q1400D.

Question 1410. If Q1410 is answered 'Yes', list the medicines in Q1410D.

Question 1420. If Q1420 is answered 'Yes', list the food in Q1420D.

Question 1460. If Q1460 is answered 'Yes', record a description in Q1460D.

Question 1480. Record the participant's age using both the years and months fields. For example, if the participant was 2 years, 3 months old when the participant first had eczema, record '2' for Q1480 and '3' for Q1490. If the participant was 2 years old, record '2' for Q1480 and '0' for Q1490.

Question 1510. If Q1510 is answered 'None', skip to Q1570.

Questions 1570 – 1600. If the participant is adopted and does not know his or her biological parents and/or siblings, answer 'Don't Know.'

Question 1590. Record 'N/A' if the participant does not have any biological siblings.

Question 1600. Record 'N/A' if the participant does not have any biological children.

Question 1610. If Q1610 is answered 'No' or 'Don't Know', skip to Q1650.

Questions 1650 – 1680. These questions are related to a child's exposure to smokers in the household from birth to 5 years of age.

Questions 1690 – 1720. These questions are related to a child's exposure to smokers in the household at the present time.

10.1.35 Pediatric Quality of Life Inventory (5-7) (PEDSQL)

Purpose: To measure a pediatric participant's general quality of life.

Who: Participant's Parent/Legal Guardian completes this form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

AsthmaNet negotiated a license agreement with MAPI Research Trust in France to use the Pediatric Quality of Life Inventory™ (PedsQL) Parent Report for Young Children (Ages 5-7) in AsthmaNet studies. However, the original format of the form cannot be changed in any way. The header information including the Participant ID, Participant Initials, Visit, Visit Date, and Coordinator ID will be completed across the header of the form using the fillable pdf feature when preparing the visit packet.

This version of the PedsQL is a 23-question tool validated for ages 5-7. It has a 1-month recall. The participant's parent or guardian is asked to think about how the participant has been during the previous month and to respond to each of the 23 questions on a 5-point scale (0 = never to 4 = almost always). The form should be presented to the parent/guardian with all pages, including the instruction sheet. The parent/guardian should complete the form by circling clearly one answer to each question.

Review the form after the participant's parent/guardian has completed it to ensure he/she clearly circled only one response (within the designated box) for each question. Participant/guardian completed forms should always be reviewed by the coordinator upon form completion. If a correction is noted, the participant's parent/guardian should make the correction and initial and date next to the change. Coordinators should not alter participant completed forms.

During data entry of this form, the questions will be designated PHYSICAL_1 – PHYSICAL_8, EMOTIONAL_1 – EMOTIONAL_5, SOCIAL_1 – SOCIAL_5, and SCHOOL_1 – SCHOOL_5.

10.1.36 Perceived Stress Scale (PSS_10)

Purpose: To measure the participant's perceived level of stress during the last month.

Who: The participant completes the form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

Questions 1000 – 1090. The participant should only check one box for each question.

Review the form prior to the participant leaving the clinic to ensure that the participant completed the form correctly.

To verify that the information recorded on this form is correct, have the participant initial (using 2 or 3 initials), date, and record the time in the source documentation box provided (Q1100, Q1110 and Q1120). Enter the Date field in the database in the format mm/dd/yyyy.

10.1.37 Post-Advair® (2 puffs) Spirometry Testing (PADVAIR_SPIRO)

Purpose: To record the outcome measurements from the participant's pulmonary function testing after 2 puffs of Advair® were administered.

Who: The Pulmonary Function Technician completes the form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

If the technician completing the procedure is not certified in spirometry testing, a supervisory technician who is certified should monitor the technician and record his or her number in the Supervisor ID field at the top of the form. The Supervisor ID ***is*** entered into the database during data entry. Failure to complete the Supervisor ID when applicable could result in a protocol deviation.

Administer 2 puffs of Advair®, wait 1 hour, then perform spirometry and continue with Q1010.

Questions 1000 and 1010. Record the time based on a 24-hour clock (military time).

Questions 1020-1060. These values should come from the MedGraphics Spirometry Final Report, Post Composite row. Record the values for Q1020 and Q1030 to the nearest hundredths of a decimal. Record the value to the nearest hundredths of a decimal.

The corresponding report for the PADVAIR_SPIRO form is the MedGraphics Spirometry Final Report, abbreviated PADVAIR_RPT. Refer to the protocol-specific MOP for details on when this report is used.

Photocopy the Spirometry Report from the MedGraphics system. Clip the original report to the back of the packet and forward it to the DCC. Place the copy in the participant's study folder.

See Appendix 1 of the AsthmaNet General MOP for more information regarding spirometry procedures.

10.1.38 Post-Albuterol (2 puffs) Spirometry Testing (PALB2_SPIRO)

Purpose: To record the outcome measurements from the participant's pulmonary function testing after 2 puffs of albuterol were administered.

Who: The Pulmonary Function Technician completes the form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

If the technician completing the procedure is not certified in spirometry testing, a supervisory technician who is certified should monitor the technician and record his or her number in the Supervisor ID field at the top of the form. The Supervisor ID ***is*** entered into the database during data entry. Failure to complete the Supervisor ID when applicable could result in a protocol deviation.

Administer 2 puffs of albuterol, wait 10 to 15 minutes, then perform spirometry and continue with Q1000.

Questions 1000 and 1010. Record the time based on a 24-hour clock (military time).

Questions 1020-1060. These values should come from the MedGraphics Spirometry Report, Post Composite row. Record the values for Q1020 and Q1030 to the nearest hundredths of a decimal. Record the value to the nearest hundredths of a decimal.

The corresponding report for the PALB2_SPIRO form is the MedGraphics Spirometry Final Report, abbreviated SPIRO_RPT. Refer to the protocol-specific MOP for details on when this report is used.

Photocopy the Spirometry Report from the MedGraphics system. Clip the original report to the back of the packet and forward it to the DCC. Place the copy in the participant's study folder.

See Appendix 1 of the AsthmaNet General MOP for more information regarding spirometry procedures.

10.1.39 Post-Albuterol (4 puffs) Spirometry Testing (PALB4_SPIRO)

Purpose: To record the outcome measurements from the participant's pulmonary function testing after 4 puffs of albuterol were administered.

Who: The Pulmonary Function Technician completes the form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

If the technician completing the procedure is not certified in spirometry testing, a supervisory technician who is certified should monitor the technician and record his or her number in the Supervisor ID field at the top of the form. The Supervisor ID ***is*** entered into the database during data entry. Failure to complete the Supervisor ID when applicable could result in a protocol deviation.

Administer 4 puffs of albuterol, wait 10 to 15 minutes, then perform spirometry and continue with Q1000.

Questions 1000 and 1010. Record the time based on a 24-hour clock (military time).

Questions 1020-1060. These values should come from the MedGraphics Spirometry Final Report, Post Composite row. Record the values for Q1020 and Q1030 to the nearest hundredths of a decimal. Record the value to the nearest hundredths of a decimal.

The corresponding report for the PALB4_SPIRO form is the MedGraphics Spirometry Final Report, abbreviated SPIRO_RPT. Refer to the protocol-specific MOP for details on when this report is used.

Photocopy the Spirometry Report from the MedGraphics system. Clip the original report to the back of the packet and forward it to the DCC. Place the copy in the participant's study folder.

See Appendix 1 of the AsthmaNet General MOP for more information regarding spirometry procedures.

10.1.40 Post-Ipratropium (4 puffs) Spirometry Testing (PIPRA4_SPIRO)

Purpose: This form records outcome variables from the participant's post-ipratropium pulmonary function testing.

Who: The Pulmonary Function Technician completes the form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

If the technician in charge of the procedure is not certified in spirometry testing, a supervisory technician who is certified should monitor the technician and record his or her ID number in the Supervisor ID field at the top of the form. The Supervisor ID ***is*** entered into the database during data entry. Failure to complete the Supervisor ID when applicable could result in a protocol deviation.

Administer 4 puffs of ipratropium, wait 10 to 15 minutes, then perform spirometry and continue with Q1000.

Question 1000 and 1010. Record the time based on a 24-hour clock (military time).

Questions 1020 - 1060. These values should come from the MedGraphics Spirometry Final Report, Post Composite row. Record the values for Q1020 and Q1030 to the nearest hundredths of a decimal.

The corresponding report for the PIPRA4_SPIRO form is the MedGraphics Spirometry Final Report, abbreviated PIPRA4_RPT. Refer to the protocol-specific MOP for details on when this report is used.

Photocopy the Spirometry Report from the MedGraphics system. Clip the original report to the back of the packet and forward it to the DCC. Place the copy in the participant's study folder.

See Appendix 1 of the AsthmaNet General MOP for more information regarding spirometry procedures.

10.1.41 Prior Asthma/Allergy Treatment (PRIOR_TRT)

Purpose: To record a participant's medications used to treat asthma or allergies over the last 12 months.

Who: An AsthmaNet coordinator completes the form while interviewing the participant or participant's parent/legal guardian.

When: Refer to Visit Procedure Checklists.

Form Instructions:

Question 1000. If Q1000 is answered 'Other', record a description in Q1000D

Questions 1010 – 1910. Record 'Don't Know' if the participant does not know or is unsure if he or she has used the medication listed during the past 12 months. If the participant did use the medication during the past 12 months but does not know the exact date the medication was last taken, prompt the participant for the month and the year. If the participant cannot recall the day, leave the day blank; if the participant cannot recall the month, leave the month and day blank.

When entering these dates during data entry, the month, day, and year are each represented by a separate entry field. The first box represents the month. Only enter the month into this box. The leading zeros can be left out. The second box represents the day. Only enter the day of the month into this box. The leading zeros can be left out. The third box represents the year. Only enter the year into this box. The year must be entered as four digits. For example, when entering 01/10/2010, enter 01 or 1 into the first box, enter 10 into the second box, and enter 2010 into the third box.

Partial dates can also be entered during data entry for these fields by leaving the box for the unknown information blank. If the day is missing, the month and year can be entered. If both the month and day are missing, the year can be entered. If at least the year is not known, change the leading question to Don't Know.

Question 1050. If none was used, record '000'.

Question 1430. If Q1430 is answered 'Yes', complete Q1470, Q1480 and Q1490.

Question 1470. Refer to the Prior Asthma/Allergy Treatment Form (PRIOR_TRT_CARD) Reference Card to find the corresponding code for the inhaled steroid taken. If the inhaled steroid taken is not listed, record '999' and specify the name of the medication in Q1470D.

Question 1500. If Q1500 is answered 'Yes,' complete Q1535, Q1540, and Q1550.

Question 1535. Refer to the Prior Asthma/Allergy Treatment Form Reference Card (PRIOR_TRT_CARD) to find the corresponding code for the nebulized steroid taken. If the nebulized steroid taken is not listed, record '99' and specify the name of the medication in Q1500D.

Question 1560. If Q1560 is answered 'Yes,' complete Q1600, Q1610, and Q1620.

Question 1600. Refer to the Prior Asthma/Allergy Treatment Form (PRIOR_TRT_CARD) Reference Card to find the corresponding code for the inhaled steroid/long-acting beta-agonist taken. If the medication taken is not listed, record '9999' and specify the name of the medication in Q1600D and complete Q1610 and Q1620.

Question 1830. If Q1830 is answered 'Yes,' record the name(s) of the other medication(s) used during the past 12 months to treat asthma or allergies in Q1830D.

Question 1870. If Q1870 is answered 'Yes,' record the indication that oral steroids were used during the past 12 months for something other than asthma in Q1870D.

Question 1910. If Q1910 is answered 'Yes,' record the indication that injectable steroids were used during that past 12 months for something other than asthma in Q1910D.

10.1.42 Prior Conditions for Adult Participants (PRIOR_COND_ADULT)

Purpose: To record an adult participant's prior diseases, illnesses, conditions, and surgeries by bodily system.

Who: An AsthmaNet coordinator completes the form while interviewing the participant.

When: Refer to Visit Procedure Checklists.

Form Instructions:

Questions 1000 – 1120. Record a 'Yes' or 'No' for each question. Do not leave a question missing. For each question where a 'Yes' is recorded, provide a description of the disease, illness, condition, or surgery in the corresponding row. The descriptions (Q1000D – Q1120D) will be entered into the study database.

10.1.43 Prior Conditions for All Participants (PRIOR_COND_ALL)

Purpose: To record a participant's prior diseases, illnesses, conditions, and surgeries related to skin, ears, nose, and throat, lungs, stomach or intestines, and sleep disorders.

Who: An AsthmaNet coordinator completes the form while interviewing the participant or participant's parent/legal guardian.

When: Refer to Visit Procedure Checklists.

Form Instructions:

Question 1000. If Q1000 is answered 'Other', record a description in Q1000D.

Questions 1010, 1060, 1110, 1130, 1150, 1170, and 1180. If 'Yes' is recorded for these questions, provide a description of the disease, illness, condition, or surgery in the corresponding row. The descriptions (Q1010D, Q1060D, Q1110D, Q1130D, Q1150D, Q1170D and Q1180D) will be entered into the study database.

10.1.44 Serious Adverse Event Reporting Form (SERIOUS)

Purpose: To record the details of each serious adverse event.

Who: An AsthmaNet coordinator completes the form in collaboration with the Principal Investigator.

When: A clinical adverse event, laboratory adverse event, or significant asthma exacerbation is deemed serious.

Form Instructions:

The Serious Adverse Event Reporting Form (SERIOUS) is a single form only.

A serious adverse event is defined as an event resulting in hospitalization, extension of a hospital stay, or death.

A Serious Adverse Event Reporting Form (SERIOUS) should be completed and faxed to the DCC at (717) 531-4359 within 72 hours of notification of a serious adverse event. Relevant source documents (ER records, clinic notes, discharge summary, etc.) and related data collection forms (copies of the Clinical Adverse Events form [AECLIN] and the Concomitant Medications for Asthma/Allergy and Adverse Events [CMED]) should also be faxed to the DCC.

If the form is completed between visits, specify the number of the last visit completed and the date the form is completed.

Questions 1010 and 1010D. Describe the serious adverse event concisely (Q1010D) and identify the appropriate ICD9 code (Q1010). If the serious adverse event was related to a clinical adverse event, record the same description, ICD9 code, and date as on the Clinical Adverse Events (AECLIN) form. This will allow the DCC to link the serious adverse event to the respective clinical adverse event.

A list of all ICD9 Codes used for AsthmaNet is available in an Excel spreadsheet on the AsthmaNet secure web site under the Application link. A link to the list of ICD9 Codes also can be found during data entry and editing in the Participant Data module of the data management application. If the coordinator is still unable to identify an ICD9 code, please call the protocol-specific Primary Data Manager at (717) 531-3663 for assistance.

Question 1020. When answering this question, keep in mind that the term “study drug” refers to any medications given out as part of the study. Please refer to the protocol specific MOP for additional guidance.

Questions 1030 and 1040. Please refer to the protocol-specific MOP for guidance in determining the time interval between the last administration of the study drug and the adverse event.

Question 1050-1180. These questions outline the criteria for determining whether or not an event was serious. If the participant does not meet at least one of these criteria, do not complete this form.

Question 1070. If Q1070 is answered 'No', skip to Q1100. Otherwise, complete Q1080 and Q1090.

Question 1180. If Q1180 is answered 'Yes', describe the 'Other' in Q1180D.

Question 1190-1220. These questions outline the criteria for determining what may have caused the serious adverse event. At least one of the items must be answered 'Yes.'

Question 1210. If Q1210 is answered 'Yes', describe the concurrent medication in Q1210D.

Question 1220. If Q1220 is answered 'Yes', describe the other condition or event in Q1220D.

Questions 10 and 11. These questions do not get data entered.

REPORTING INVESTIGATOR section on page 3 should be completed for all serious adverse events. The AsthmaNet principal investigator should complete the Name, Signature and Date section below the comments.

See Section 4 of the AsthmaNet General MOP for more information regarding adverse events.

10.1.45 Sinonasal Questionnaire (SNQ)

Purpose: To record the frequency of sinonasal symptoms the participant has had over the last 3 months.

Who: The participant completes the form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

Questions 1000 – 1040. The participant should only check one box for each symptom.

Review the form prior to the participant leaving the clinic to ensure that the participant completed the form correctly.

To verify that the information recorded on this form is correct, have the participant initial (using 2 or 3 initials), date, and record the time in the source documentation box provided (Q1050 – Q1070). Enter the Date field in the database in the format mm/dd/yyyy.

10.1.46 Spirometry Testing (SPIRO)

Purpose: To record the outcome measurements from the participant's pre-bronchodilator spirometry procedure.

Who: The Pulmonary Function Technician completes the form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

The protocol-specific pulmonary procedure checklist (PULMONARYCHK) needs to be completed to determine eligibility before performing Spirometry Testing (SPIRO). Please refer to the protocol-specific MOP.

If the technician completing the procedure is not certified and this procedure is being used as an observation session for certification, please complete the Supervisor ID located in the header on the SPIRO form with the ID of the certified technician who supervised the procedure. The Supervisor ID ***is*** entered into the database during data entry. Failure to complete the Supervisor ID when applicable could result in a protocol deviation.

The Supervisor ID should be entered in the Post Test Comments area of the MedGraphics system. Refer to Appendix 1 of the AsthmaNet General MOP for detailed instructions on certification of technicians in spirometry testing.

If the participant is deemed ineligible to proceed with the pulmonary function testing, the participant's pulmonary function testing should be rescheduled within the visit window. On the day of the rescheduled procedure, complete a new Spirometry Testing (SPIRO) form with the **current date**. Do not enter the old form into the study database and do not send it to the DCC. Only enter and submit the most recent form. However, all completed forms, the old original form and the current photocopy of the form should be filed in the participant's study file.

Question 1010. Record the time based on a 24-hour clock (military time).

Questions 1020-1060. These values should come from the Spirometry Report, Pre Composite row. Record the values for Q1020 and Q1030 to the hundredths of a decimal.

Question 1060. Record the value for Q1060 to the hundredths of a decimal.

The corresponding report for the SPIRO form is the MedGraphics Spirometry Final Report, abbreviated SPIRO_RPT. Refer to the protocol-specific MOP for details on when this report is used.

Photocopy the Spirometry Report from the MedGraphics system. If the form is a packet form, clip the original report to the back of the packet and forward it to the DCC. Place the copy in the participant's study folder. If the form is a single form, clip the original report to the back of the single form and forward it to the DCC with a Data Processing Cover Sheet (DPCS) attached to the front. Place the copy in the participant's study folder.

If methacholine challenge is completed, the Spirometry Testing Report (SPIRO_RPT) should be marked 'No' in the database. The Methacholine Challenge Report (METHA_RPT) should be marked 'Yes' in the database. The spirometry session data is included on the Methacholine Challenge Report (METHA_RPT) and a separate Spirometry Testing Report (SPIRO_RPT) does not need to be printed.

If post-albuterol (4 puffs) spirometry testing is completed, the Spirometry Testing Report (SPIRO_RPT) should be marked 'No' in the database. The Post-Albuterol (4 puffs) Spirometry Testing Report (PALB4_RPT) should be marked 'Yes' in the database. The spirometry session data is included on the Post-Albuterol (4 puffs) Spirometry Report (PALB4_RPT) and a separate Spirometry Testing Report (SPIRO_RPT) does not need to be printed.

If post-ipratropium (4 puffs) spirometry testing is completed, the Spirometry Testing Report (SPIRO_RPT) should also be marked 'No' in the database. The Post-Ipratropium (4 puffs) Spirometry Testing Report (PIPRA4_RPT) should be marked 'Yes' in the database. The spirometry session data is included on the Post-Ipratropium (4 puffs) Spirometry Testing Report (PIPRA4_RPT) and a separate Spirometry Testing Report (SPIRO_RPT) does not need to be printed.

See Appendix 1 of the AsthmaNet General MOP for more information regarding spirometry procedures.

10.1.47 Spirotel® Quality Control (SPIROTELQC)

Purpose: To determine if the spirotel® device is functioning properly at each visit.

Who: A spirotel® certified AsthmaNet coordinator performs the procedure and prints the form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

The Spirotel® Quality Control (SPIROTLQC) form will be generated automatically by the spirotel® software during the calibration testing procedure. See Appendix 6 of the AsthmaNet General MOP.

Only enter the SPIROTELQC form for the turbine and spirotel combination that passed calibration for the study visit and was sent home with the participant.

If the participant forgets his/her spirotel®, indicate on the Visit Procedure Checklist that the participant forgot his or her spirotel®. During data entry, register the Spirotel® Quality Control (SPIROTELQC) form as missing. If the participant brings in his or her spirotel® at a later date (other than the visit date) or between visits, the visit date on the SPIROTELQC report will pre-populate with the date the quality control testing was performed . This form should then be entered as a single form with the last visit number completed and the current date in the upper right hand corner.

Question 1000. Enter this date into the database in the format mm/dd/yyyy.

Questions 1040 – 1080. Record these values to the nearest hundredth of a decimal.

10.1.48 Sputum Induction (SPUTUM)

Purpose: To record information about the sputum induction procedure.

Who: A sputum induction technician completes the form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

A technician must be certified in sputum induction in order to complete this form.

Question 1000. Do not complete Q1000 if this is the first time the participant is attempting sputum induction for a given study or if the sample was not adequate at a prior attempt. If the participant has previously attempted sputum induction at other study visits, and the sample was adequate, the duration at the current visit should not exceed the duration of the first adequate sample.

Questions 1010 and 1020. Record the time based on a 24-hour clock (military time).

Question 1030. Record duration of sputum induction at this visit. If monitoring with FEV_1 was necessary during sputum induction, the time spent on spirometry should not be counted in the duration. Subtract any time spent on spirometry from the total time of the sputum induction procedures to obtain the correct value for Q1030. The duration at the current visit (Q1030) should not exceed the duration of the first time the sample was adequate, as reported in Q1000.

Question 1040. If the duration of the induction did not last for at least 4 minutes at the visit, answer Q1040 ‘No’.

Question 1050. Record to the nearest tenth of a decimal.

Question 1060. The technician responsible for processing should determine if the volume is adequate for processing.

Question 1070. If either of the shaded boxes are completed (Q1040 or Q1060), the sample is not adequate and should not be processed. Answer Q1070 ‘No’ and **DO NOT** complete the Sputum Induction Lab (SPUTLAB) form.

If Q1070 is answered ‘Yes’, the sample should be processed.

Questions 1080 and 1090. The FEV_1 and FEV_1 (% predicted) and Time can be found in the Pre Composite row of the MedGraphics Spirometry Report. Record Q1080 to the nearest hundredth of a decimal.
Question 1100. Record the time based on a 24-hour clock (military time).

Question 1110. The percent difference field will accept both positive and negative values. When applicable, note the negative sign in front of the value on the form. The calculated value will be rounded to the nearest tenth of decimal.

Question 1120. Otherwise, continue with remaining visit procedures. If Question 1120 is answered 'Yes', proceed to the Additional Treatment for Sputum Induction (SPUTUM_ADD_TRT) form. Otherwise, continue with remaining visit procedures.

The corresponding report for the SPUTUM form is the MedGraphics Spirometry Final Report, abbreviated SI_RPT. Refer to the protocol-specific MOP for details on when this report is used. To clarify that this Spirometry Final Report is listing maneuvers performed post-sputum induction, please add a comment to the 'Post Test Comments' section of the report.

10.1.49 Sputum Induction Checklist (SPUTUMCHK)

Purpose: To determine whether the participant is eligible to proceed with sputum induction procedures.

Who: A sputum induction technician completes the form.

When: Refer to Visit Procedure Checklists.

Complete this form ***only*** if the participant ***is eligible*** according to the protocol-specific Pulmonary Procedure Checklist (PULMONARYCHK) and ***successfully completed*** baseline spirometry session(s) (SPIRO).

Form Instructions:

A technician must be certified in sputum induction in order to complete this form.

Question 1000. Only complete this question if the participant completed a methacholine challenge at this visit. Refer to Q1090 on the Methacholine Challenge Testing (METHA) form to answer this question OR Q1100 or Q1230 on the Additional Treatment Post Methacholine Challenge Testing (METHA_ADD_TRT) form.

Question 1010. If 'No', the participant is ineligible to proceed with sputum induction procedures. If 'Yes', the supervising physician must sign Q1020.

Question 1020. During data entry, enter a '1' for Q1020 if a signature is present, otherwise leave Q1020 blank.

Question 1030. If the participant completed a Methacholine Challenge at this visit, this value is Q1070 on the Methacholine Challenge Testing (METHA) form or Q1070 or Q1200 on the Additional Treatment Post Methacholine Challenge Testing (METHA_ADD_TRT) form. If the participant did not complete a Methacholine Challenge at this visit, this value comes from either Q1030 on the Post-Albuterol (4 puffs) Spirometry Testing (PALB4_SPIRO) form, Q1030 on the Post-Albuterol (2 puffs) Spirometry Testing (PALB2_SPIRO) form or Q1070 or Q1130 on the Maximum Reversibility Testing (MAXREV) form.

Question 1040. For post methacholine challenge procedures, refer to Appendix 7, Section IV, B in the AsthmaNet General MOP for instructions on how to calculate the FEV_1% predicted. Otherwise, refer to the FEV_1% predicted value recorded on the form related to Q1030 above.

Question 1060. If 'Yes', record an explanation in Q1060D.

Question 1070. If answered ‘Yes’, the participant is eligible, to proceed with sputum induction. If any of the shaded boxes are completed, the participant is not eligible to proceed with sputum induction procedures.

10.1.50 Sputum Induction Lab Values (SPUTLAB)

Purpose: To record information about slide processing.

Who: A sputum processing technician completes the form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

A technician must be certified in sputum induction processing in order to complete this form.

Question 1000. Record the date the sample was processed. During data entry, please enter the date in the format mm/dd/yyyy.

Question 1010. Record the time based on a 24-hour clock (military time).

Question 1020. Record to the nearest tenth of a decimal.

Question 1030. Compare Q1020 on the Sputum Induction (SPUTUM) form to Q1010 on the Sputum Induction Lab Values (SPUTLAB) form. If the time difference is greater than 4 hours, record ‘No” and mark the samples as excluded in the Biological Sample Tracking module.

10.1.51 The RAND Impact of Asthma on Quality of Life Questionnaire SF-12 (RAND_IAQL_12)

Purpose: To evaluate the participant's quality of life as a result of asthma.

Who: The participant completes this form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

The RAND Impact of Asthma on Quality of Life Questionnaire (RAND_IAQL) was developed by Cathy Sherbourne and other researchers funded by NHLBI to be a freely available new system for measuring the impact of asthma on quality of life. The original item bank contains 65 items. AsthmaNet will employ the 12-item short form (RAND_IAQL_12). The authors of the questionnaire will use data collected in AsthmaNet studies to help validate their instrument against other well-known questionnaires such as the Asthma Quality of Life Questionnaire (AQLQ) developed by Liz Juniper and her colleagues. The questionnaire will be validated for participants who are ages 12 and older.

For the RAND_IAQL_12, participants are asked how their asthma has affected the quality of their lives in various areas over the ***last four weeks***. Instruct the participant to read each question carefully and mark the one box corresponding to his/her best answer for each question.

This form should be completed before the participant undergoes spirometry at the visit. Adhere to the procedure order on the Visit Procedure Checklist.

Review the form after the participant has completed it to ensure that he/she marked a response (within the designated box) for each question. Participant completed forms should always be reviewed by the coordinator upon form completion. If a correction is noted, the participant should make the correction and initial and date next to the change. Coordinators should not alter participant completed forms.

To verify that the information recorded on this form is correct, have the participant initial (using 2 or 3 initials), date, and record the time in the source documentation box provided (Questions Q1120 – Q1140). Enter the Date field in the database in the format mm/dd/yyyy. Enter the time field based on a 24-hour clock.

10.1.52 Urine Pregnancy Test (PREG_TEST)

Purpose: This form is completed for female participants ages 6 years and older. It assists in determining if a female participant is eligible to enter the study and perform methacholine challenges at the applicable visits.

Who: An AsthmaNet coordinator completes the form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

This form must be completed for **all** female subjects ages 6 and older, regardless of whether they are able to bear children and regardless of whether they will perform a methacholine challenge during the study. Refer to previous PREG_TEST forms completed for the participant (if available) for the current protocol to verify reproductive status.

For more detailed discussion on pregnancy testing, refer to Section 3 of the General MOP.

Question 1000. If the participant is pre-menarche, skip Q1010-Q1040 and have the parent/guardian complete the source documentation box (Q1050-Q1060).

Question 1010. If it has been at least one year since the participant's last menses, or she had a complete hysterectomy, Q1010 should be answered Yes.

Question 1040. The answer to Q1040 is based on the results of an in-office urine pregnancy test. This test must be performed if the participant is able to bear children (i.e., none of the answers to Q1000-Q1030 is completed as 'Yes'). A history of infertility does not qualify the participant as 'Unable to bear children'. In these circumstances, a urine pregnancy test should be performed, assuming none of Q1000-Q1030 is completed 'Yes'.

If any of the shaded boxes in Q1000-Q1030 are checked, the participant is considered unable to bear children. In this case, no pregnancy test is required. The participant or participant's legal guardian still should complete the source documentation box to acknowledge the validity of the recorded data.

For more specific details pertaining to whether a coordinator should permit the participant to continue in the study, refer to the protocol-specific eligibility criteria.

To verify that the participant or participant's legal guardian was informed of the test results and present at the time this form was completed, have the participant or participant's legal guardian record her/his initials (using 2 or 3 initials) and

date (Q1050, Q1060) in the source documentation box at the bottom of the form. During data entry, please enter in the format of the date as mm/dd/yyyy.

10.1.53 Wisconsin Upper Respiratory Symptom Survey – 21 Daily Symptom Report (WURSS_21)

Purpose: To record a participant's daily upper respiratory symptoms when he or she is experiencing a cold.

Who: A participant or participant's parent/legal guardian completes the form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

The AsthmaNet did not receive permission from the creator of this form to alter the format of the form. Therefore, the WURSS-21 form does not include the standard AsthmaNet header and footer information or 4-digit annotation for each question.

Participants in studies using the WURSS-21 form will be given several copies of the form. Pre-fill the participant's ID and initials prior to distributing the forms to the participant. The participants should follow the instruction sheet, Wisconsin Upper Respiratory Symptom Survey-21 (WURSS-21) Instructions (WURSSINST) when completing the WURSS-21 form. The participant should complete a form each day he/she has a cold and stop completing this form when he/she has answered the first question on the form, 'How sick do you feel **today**?" as "**Not sick**" for <u>two days in a row</u>. The participant must complete the 'Date' field on each form he or she completes. The participant should return all completed forms at the next study visit. Review the WURSS-21 forms completed by the participant to verify that the participant recorded a valid and unique date on each form. At each visit, determine if the participant should be given more WURSS-21 forms.

Ask the participant if he or she is still experiencing cold symptoms. It is possible that a participant will experience a cold that won't be resolved at the time of a study visit. The participant should return the completed WURSS-21 forms at the time of the current visit and get more to keep at home in case they are needed. The participant will continue to complete WURSS-21 forms until the cold has resolved. The participant should return the balance of the completed forms at the next study visit to complete the 'cold packet'. The cold packet will get entered with the next visit's data. Ex: If a cold starts between visits 5 and 6 and is ongoing at the time of visit 6, the participant will turn in any completed forms at visit 6. These will be held in the participant's folder. He/she will continue to complete WURSS-21 forms until the cold is resolved. The balance of the forms will be turned in at visit 7. The entire cold packet will get entered with visit 7 data.

Note: It is possible that a participant could have more than one cold between visits, so there may be multiple 'cold packets' with the same visit number on them (but with a number of days or weeks separating the two cold events).

When the cold packet is complete and ready to be entered, record the Coordinator ID and Visit at the top of each form. The data entry screen in the Participant Data module will contain the full or shortened text of each question for easy reference. Enter the code for each question response corresponding to the circle the participant filled in. For example, if the participant filled in the circle under 'Very mild' for 'Runny nose', then enter a '1' for this question.

The codes for the responses to the last question, '**Compared to yesterday**, I feel that my cold is …' are displayed on the data entry screen under the question text: 1 = Very much better; 2 = Somewhat better; 3 = A little better; 4 = The same; 5 = A little worse; 6 = Somewhat worse; and 7 = Very much worse.

The Participant Data module will not allow you to enter more than one form with the same 'Date' for a Visit.

When a cold is reported, add a record to the AECLIN form using a code such as 460. (acute nasopharyngitis [common cold]), 465.8 (acute upper respiratory infections of other multiples sites), or 465.9 (acute upper respiratory infections of unspecified site). The end date for the record should be the calendar date prior to the two "Not sick" records (where 'How sick do you feel today' = 0). If only one "Not sick" record is present, use the calendar date prior to that record. If no "Not sick" records are present, use the participant reported stop date.

4.2 STANDARD ADMIN FORMS AND INSTRUCTIONS

This section provides specific instructions needed to complete the AsthmaNet standard administrative forms. These forms are not entered into the study database and most are not submitted to the DCC. The instructions for each form are in alphabetical order based on the form name.

The following information is provided for each form: the purpose of the form, who completes the form, when the form should be completed, and form instructions. If you are unable to find the specific information needed to complete a form, please contact the protocol-specific Primary Data Manager at (717) 531-3663.

10.1.54 Adult Long Physical Exam (LEXAM_ADULT)

Purpose: To record the results of an adult participant's routine physical exam.

Who: An AsthmaNet coordinator completes the form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

This form is an administrative form for clinical site use only. The data will not be entered into the study database.

Questions 1 – 3. Refer to Section 3 of the AsthmaNet General MOP for more information related to recording these measurements.

Question 4. If Q4 is answered 'Yes', complete the Clinical Adverse Events (AECLIN) form.

Questions 5 – 15. A licensed medical practitioner should determine whether the current findings are normal or abnormal. If abnormal, a comment should be provided.

To verify that the information collected on this form is correct, the attending physician should sign, print name, date and indicate the time of the form completion in the source documentation box provided on page 2.

For use only at the clinical site – DO NOT forward this form to the DCC.

This form will be reviewed during AsthmaNet site visits.

10.1.55 Adult Short Physical Exam (SEXAM_ADULT)

Purpose: To record the results of an adult participant's brief physical exam.

Who: An AsthmaNet coordinator completes the form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

This form is an administrative form for clinical site use only. The data will not be entered into the study database.

Questions 1 – 4. Refer to Section 3 of the AsthmaNet General MOP for more information related to recording these measurements.

To verify that the information collected on this form is correct, the coordinator should sign, print name, date and indicate the time of the form completion in the source documentation box.

For use only at the clinical site – DO NOT forward this form to the DCC.

This form will be reviewed during AsthmaNet site visits.

10.1.56 Adult Participant Contact Information (CONTACT_ADULT)

Purpose: To record pertinent participant identification information for all adults so that the AsthmaNet coordinator will know how and when to easily contact the participant.

Who: The participant completes the form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

This form ***must*** be completed at the first study visit. At subsequent study visits, update this form as indicated on the Visit Procedure Checklists.

For use only at the clinical site – DO NOT forward this form to the DCC.

This form will be reviewed during AsthmaNet site visits.

10.1.57 Asthma Control Questionnaire© Score (ACQ_SCORE)

Purpose: To determine the participant's average ACQ score.

Who: A coordinator completes this form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

From each question on the Asthma Control Questionnaire© form, transcribe the number directly into the appropriate field on the ACQ_SCORE form. Add the 6 scores and record this value in the 'Total' field. Divide the 'Total' by 6 to obtain the 'Average Score'.

10.1.58 AsthmaNet Research Drug Destruction Log (DRUG_DEST_LOG)

Purpose: Verify that all study drug at a clinical center has been destroyed.

Who: An AsthmaNet coordinator completes the form.

When: A new destruction log must be completed for each date that study medication is destroyed. Drug can be destroyed during the study or at study end.

Form Instructions:

The table information (columns) including the Participant ID number, Drug Description, Drug Identification Number/Lot #, Quantity Destroyed, Returned, and Expired should be completed for each date that study medication is destroyed.

Print and sign name, date and coordinator ID when form is completed. E-mail the log to: AsthmaNet-drugs-supplies@phs.psu.edu.

10.1.59 AsthmaNet Room Temperature Monitoring Record

Purpose: Monitor the room temperature where AsthmaNet study drug is stored.

Who: An AsthmaNet coordinator completes the form.

When: Daily.

Form Instructions:

Please complete all columns on a daily basis. If you do not have a thermometer that monitors humidty, leave columns blank.

Print and sign name, date and coordinator ID when form is completed. E-mail the log to: AsthmaNet-drugs-supplies@phs.psu.ed.

10.1.60 AsthmaNet Satisfaction Questionnaire (SATQX)

Purpose: This form gives a participant or participant's parent/legal guardian the opportunity to provide the AsthmaNet research staff with feedback related to his/her (or child's) participation in an AsthmaNet study.

Who: The participant or participant's parent/legal guardian completes the form.

When: The last study visit.

Form Instructions:

This form should be distributed to the participant during the termination visit or last visit of the study. If the participant does not return to the clinic site for a last visit, then the coordinator should mail the form to the participant with a self-addressed postage paid envelope for him/her to return it to the DCC.

Before distributing the form to the participant, the coordinator should record the protocol number and site number of the site distributing the form in the right-hand corner of the form and complete Question 1000 indicating the study status of the participant at the time of his/her termination.

Please remind the participant that no PHI (names, telephone numbers) should be written on the SATQXs.

This form is to be completed voluntarily, and all responses will be confidential. After the participant or participant's parent/legal guardian completes the form, he/she should seal it in the pre-addressed envelope and send it to the DCC. The site should not have access to the completed SATQX form, however if a completed SATQX is received at the site, the form should be placed immediately in a pre-addressed envelope and mailed directly to the DCC.

Pre-addressed and stamped envelopes will be provided to the clinical sites. Please contact the DCC if you run out of prepaid envelopes.

10.1.61 Concomitant Medications for Non-Asthma Drugs (CMED_NON)

Purpose: To record all concomitant medications not related to the treatment of asthma and allergy symptoms or adverse events that the participant takes after signing the informed consent.

Who: An AsthmaNet coordinator completes the form.

When: Refer to Visit Procedure Checklists. Note that this form should also be completed if the participant or participant's parent/legal guardian reports a non-asthma/allergy-related concomitant medication between visits. Questions on other forms may also prompt a coordinator to complete this form.

Form Instructions:

Medications for concurrent medical problems not related to asthma or allergies should be recorded here. Examples would include antihypertensives, thyroid medications, calcium supplements, vitamins, influenza vaccines, aspirin for cardioprotection, and lipid-lowering agents. Most of these medications will be those that participants are taking at the time of signing the informed consent/participant assent at study entry and continue through the study.

Note that some studies impose numerous restrictions on the use of non asthma-related medications for study entry. Many drugs have required washout periods prior to enrollment. Others are allowed throughout the study, but should be withheld prior to certain procedures (e.g., methacholine challenge testing and skin testing). See the Exclusionary Drugs reference card (EXCLDRUG) for each study for the appropriate study for a complete list. It is extremely important that drug washout periods be strictly enforced and that concomitant medications be monitored diligently throughout each study.

Use of herbal remedies (for asthma and non-asthma conditions) and other alternative therapies should be recorded on the CMED_NON form, as no drug codes are available for these treatments.

At the first visit, a CMED_NON form should be started for a participant by completing the Participant ID and the Participant Initials at the top of the form. For each medication, record the medication name, start date, stop date (if applicable), whether the participant is continuing on the medication at the end of the study (if applicable), and the reason the participant is taking the medication.

For any medications the participant started prior to signing the informed consent, record the informed consent date as the 'Start Date'.

At each subsequent visit, update the form. Indicate any new medications started and any old medications that were stopped since the last visit. If the participant is still taking a medication at the end of the study, leave the stop date blank and check the “Ongoing at end of study’ box. This should be the only time the stop date is not completely filled in. If the participant does not take any concomitant medications that are unrelated to asthma, allergies, or adverse events during the entire study, check the ‘None’ box.

In the event that an approved AHFS drug code cannot be entered into the database from the CMED form, it may be recommended by the DCC to record the drug on the CMED_NON form for record keeping purposes.

This form is not entered into the database and should not be sent to the DCC.

10.1.62 Data Processing Cover Sheet (DPCS)

Purpose: This form assists the clinical site and the DCC with the tracking of all data collection packets/forms from the time of collection at the clinical site to the final processing at the DCC.

Who: Clinical center and DCC personnel complete the form.

When: This form is completed each time a data processing activity is performed.

Form Instructions:

Complete the Participant ID number, Participant initials, Visit number, and packet/form code of the packet/form being processed. The person completing the data processing activities (reviewing and collating of the forms) should record the current date and his or her 4-digit interviewer/technician ID number for each activity.

Important:

When preparing copies of the Data Processing Cover Sheets (DPCS), please use the original document that can be printed from the AsthmaNet website. Photocopies should not be made from a copy of the DPCS. All forms are now scanned at the DCC and placed in an electronic archive. The quality of the print greatly diminishes when a photocopy of a photocopy is made, this may cause the form not to be scanned correctly.

When filling out the Data Processing Cover Sheets (DPCS) remember:

- ALL information must be handwritten or pre-filled on the DPCS
-Write in the Visit number in the Visit number space provided
-Write the form name in the form name space provided

******If the practice above is not followed, the DCC may send the DPCS form back to your site to be recreated correctly.***

Clip the Data Processing Cover Sheet (DPCS) to each visit packet and each single form before any data processing activity.

10.1.63 Diskus® Inhalation Technique Checklist (TECH_DISKUS)

Purpose: To record information related to the assessment of the participant's Diskus® inhalation technique.

Who: The AsthmaNet coordinator or Pulmonary Function Technician completes the form.

When: When a Diskus® is first dispensed to a participant and as indicated on the Visit Procedure Checklists.

Form Instructions:

When the participant demonstrates the use of the Diskus®, evaluate whether his or her performance on each step was wrong or correct. Calculate the participant's score by adding the total points. Record the participant's score on the form in the designated area.

If the score is less than 10, retrain the participant and complete a new form. Be sure to complete the page numbers at the bottom of the form: 'Page _ of _'. Store all completed forms in the participant's study folder.

For use only at the clinical site – DO NOT forward to the DCC.

This form will be reviewed during AsthmaNet site visits.

10.1.64 DOSER™ Tracking Log (DOSER_LOG)

Purpose: To track the Dosers™ used in AsthmaNet studies.

Who: An AsthmaNet coordinator completes the log.

When: The log is updated every time a Doser™ is dispensed or returned or a problem is experienced with a device.

Form Instructions:

In the Balance column of the first row of the log, record the total number of Dosers™ available for distribution at your site. When completing each subsequent row, subtract one from the Balance column. If a returned Doser™ is put back into the pool of Dosers™ for distribution to future participants, add one to the Balance column in the next available row.

A row must be completed in the Doser™ Tracking Log, every time a Doser™ is distributed to a participant in an AsthmaNet study. When a Doser™ is dispensed, record the Doser™ ID number, participant ID, the date dispended, and the dispenser's initials on the log. Unique identifying numbers should be assigned to and permanently marked on the Dosers™ sequentially from 001 to 999 at each site. You can record the Wake Up date of the Doser™ on the log to determine if you should dispense a returned Doser™ to another study participant. Dosers™ have a one year lifetime starting from the day they are "woken up" for the first time. Note that multiple participants can use a given Doser™ over the course of a study. However, in most studies, each device will be assigned to one participant during its lifetime. See Section 2 of the protocol-specific MOP for more information regarding the Doser™.

When a Doser™ is returned, record the date returned, the collector's initials, and comments if the participant experienced any problems with the device.

To organize multiple pages of the DOSER_LOG, complete and update the 'Page _ of _' at the bottom of each page.

This log will be reviewed during AsthmaNet site visits.

10.1.65 GIS Address Tracking Form (GIS_ADDRESS)

Purpose: To record the participant's home addresses during study participation for GIS tracking purposes.

Who: An AsthmaNet coordinator completes the form.

When: When GIS consent has been obtained and as indicated on the Visit Procedure Checklists.

Form Instructions:

When the participant has consented to allow the use of his/her home address for GIS analysis by researchers at the University of Pittsburgh, the GIS Consent Tracking Form (GIS) should be completed in conjunction with the GIS Address Tracking Form (GIS_ADDRESS).

Apt: Addresses should include Apartment Number, when applicable.

Zip Code: Zip Code should be recorded as the 9-digit zip code, if the last four digits are known. Otherwise, record the 5-digit zip code.

At Enrollment: Record the participant's current home address and dates of occupancy, if known, in the section titled "Address at Enrollment in Protocol." This address is entered in the GIS spreadsheet for the protocol to be submitted to the University of Pittsburgh.

At subsequent visits as indicated on the visit procedure checklists: the participant should be asked for updated home address information. Record new address information if the participant has resided there for at least 4 weeks or plans to remain there indefinitely. If the participant indicates that he/she is residing at an address temporarily (i.e., less than 4 weeks), do not record this address on the form.

Subsequent addresses are recorded in the next available spot in the section titled "Subsequent Address(es) during Study Participation."

If the participant has stopped residing at a previously recorded address, provide a stop date for the previous address's Dates of Occupancy.

Once recorded on GIS_ADDRESS, see the GIS MOP for more information on submitting address information to the University of Pittsburgh.

10.1.66 MDI Inhalation Technique Checklist (with face mask) (TECH_MDI_FACE)

Purpose: To record information related to the assessment of the participant's MDI inhalation technique using a face mask.

Who: The Pulmonary Function Technician completes the form.

When: When an MDI inhaler (with face mask) is first dispensed to a participant and as indicated on the Visit Procedure Checklists.

Form Instructions:

When the participant demonstrates the use of the MDI inhaler (with face mask), evaluate whether his or her performance on each step is wrong or correct. The participant is assigned 1 point for each correct step. Calculate the participant's score by adding the total points. Record the participant's score on the form in the designated area.

If the score is less than 6, retrain the participant and complete a new form. Be sure to complete the page numbers at the bottom of the form: 'Page _ of _'. Store all completed forms in the participant's study folder.

For use only at the clinical site – DO NOT forward to the DCC.

This form will be reviewed during AsthmaNet site visits.

10.1.67 MDI Inhalation Technique Checklist (with spacer) (TECH_MDI_SP)

Purpose: To record information related to the assessment of the participant's MDI inhalation technique using a spacer.

Who: The Pulmonary Function Technician completes the form.

When: When an MDI inhaler (with spacer) is first dispensed to a participant and as indicated on the Visit Procedure Checklists.

Form Instructions:

When the participant demonstrates the use of the MDI inhaler (with spacer), evaluate whether his or her performance on each step is wrong or correct. The participant is assigned 1 point for each correct step. Calculate the participant's score by adding the total points. Record the participant's score on the form in the designated area.

If the score is less than 12, retrain the participant and complete a new form. Be sure to complete the page numbers at the bottom of the form: 'Page _ of _'. Store all completed forms in the participant's study folder.

For use only at the clinical site – DO NOT forward to the DCC.

This form will be reviewed during AsthmaNet site visits.

10.1.68 MEMS®6 Monitor Log (MEMS_LOG)

Purpose: To track the MEMS®6 monitors used in AsthmaNet studies.

Who: An AsthmaNet coordinator completes the log.

When: The log is updated every time a MEMS®6 monitor is dispensed or returned.

Form Instructions:

In the Balance column of the first row of the log, record the total number of MEMS®6 monitors available for distribution at your site. When completing each subsequent row, subtract one from the Balance column. If a returned MEMS®6 monitor is put back into the pool of monitors for distribution to future participants, add one to the Balance column in the next available row. A previously distributed MEMS®6 monitor can be distributed to another participant if the validity date of the monitor is greater than the date the participant would be enrolled in the study, the monitor's battery voltage is $\geq$ 2.90 volts and the monitor's used memory is $\leq$ 90%. The validity date can be determined by selecting the "Read Monitor Info" in the PowerView software.

A row must be completed in the MEMS®6 Monitor Log, every time a monitor is distributed to a participant in an AsthmaNet study. When a MEMS®6 monitor is dispensed, record the serial number, validity date, participant ID, the date dispended, and the dispenser's initials on the log.

When a monitor is returned, record the date returned, collector's initials, and whether the MEMS®6 Monitor failed quality control testing. When a monitor fails quality control testing, indicate this on the MEMS®6 Monitor Log. Send the failed MEMS®6 Monitor along with a copy of the corresponding MEMS®6 Quality Control form (MEMSQC) to the DCC.

To organize multiple pages of the MEMS_LOG, complete and update the 'Page _ of _' at the bottom of each page.

This log will be reviewed during AsthmaNet site visits.

10.1.69 Pediatric Participant Contact Information (CONTACT_PED)

Purpose: To record pertinent identification information for all pediatric participants so that the AsthmaNet coordinator will know how and when to easily contact the participant.

Who: The participant or participant's parent/legal guardian completes the form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

This form ***must*** be completed at the first study visit. At subsequent study visits, update this form as indicated on the Visit Procedure Checklists.

For use only at the clinical site – DO NOT forward this form to the DCC.

This form will be reviewed during AsthmaNet site visits.

10.1.70 Spirotel® Device Log (SPIROTEL_DEVICE)

Purpose: To track the spirotel® devices used in AsthmaNet studies.

Who: An AsthmaNet coordinator completes the log.

When: The log is updated every time a spirotel® device is dispensed or returned.

Form Instructions:

A row must be completed in the Spirotel® Device Log, every time a device is distributed to a participant in an AsthmaNet study. When a spirotel® is dispensed, record the serial number, participant ID, the date dispended, and the dispenser's initials on the log.

When a device is returned, record the date returned, collector's initials, and whether the spirotel® device failed quality control testing. When a spirotel® fails quality control testing, indicate this on the Spirotel® Device Log. Send the failed spirotel® to Respitech Medical, Inc. Record the Date Shipped to Respitech and any Comments on the log. Please refer to Appendix 6 of the AsthmaNet General MOP for details related to packaging and shipping the device to Respitech.

To organize multiple pages of the SPIROTEL_DEVICE log, complete and update the 'Page _ of _' at the bottom of each page.

This log will be reviewed during AsthmaNet site visits.

10.1.71 Spirotel® Performance Checklist (SPIROTEL_PERF)

Purpose: This form is a record of the participant's ability to use the spirotel® device for recording daily diary information and/or scheduled peak flow values.

Who: An AsthmaNet coordinator or technician certified in spirotel® procedures.

When: When spirotel® device is first dispensed to a participant and as indicated on the Visit Procedure Checklists.

Form Instructions:

When the participant demonstrates the use of the spirotel® device, evaluate whether his or her performance on each step is wrong or correct. The participant is assigned 1 point for each correct step. Calculate the participant's score by adding the total points. Record the participant's score on the form in the designated area.

If the score is less than 13, retrain the participant and complete a new form. Be sure to complete the page numbers at the bottom of the form: 'Page _ of _'. Store all completed forms in the participant's study folder.

See Appendix 6 of the AsthmaNet General MOP for detailed instructions on using the spirotel® device.

For use only at the Clinical Center – DO NOT forward to the DCC.
This form will be reviewed during AsthmaNet site visits.

10.1.72 Spirotel® Turbine Log (SPIROTEL_TURBINE)

Purpose: To track the spirotel® turbines used in AsthmaNet studies.

Who: An AsthmaNet coordinator completes the log.

When: The log is updated every time a spirotel® turbine is dispensed or returned.

Form Instructions:

A row must be completed in the Spirotel® Turbine Log, every time a turbine is distributed to a participant in an AsthmaNet study. When a spirotel® is dispensed, record the serial number (4-digit number etched into the turbine), participant ID, the date dispended, and the dispenser's initials on the log.

When a turbine is returned, record the date returned, collector's initials, and whether the spirotel® turbine failed quality control testing. When a turbine fails quality control testing, indicate this on the Spirotel® Turbine Log. After all steps have been taken to ensure that the turbine will not pass quality control testing (see Appendix 6 of the AsthmaNet General MOP), discard the turbine and contact Respitech Medical, Inc. to receive a replacement turbine. Record in the Comments section the date the turbine was discarded.

To organize multiple pages of the SPIROTEL_TURBINE log, complete and update the 'Page _ of _' at the bottom of each page.

This log will be reviewed during AsthmaNet site visits.

10.1.73 Sputum Induction Worksheet (SPUTUM_INDUCTION_WKS)

Purpose: To record information related to the participant's sputum induction procedure.

Who: The Sputum Induction Technician completes the form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

For use only at the clinical sites. DO NOT forward this form to the DCC.

10.1.74 Sputum Processing Worksheet (SPUTUM_PROCESS)

Purpose: To record detailed information related to processing of the sample.

Who: The AsthmaNet sputum slide reader completes the form.

When: Refer to Visit Procedure Checklists.

Form Instructions:

One worksheet should be completed for each processed sample and sent to the AsthmaNet sputum slide reader when related slides are sent for reading.

For use only by the AsthmaNet sputum slide readers. DO NOT forward this form to the DCC.

ADVERSE EVENTS

4. ADVERSE EVENT

4.1. Reporting Procedures for AsthmaNet

This section outlines the identification, handling, and reporting of adverse events (AEs). Adverse events experienced by study participants must be documented appropriately in order to:

Provide the accurate reporting of all adverse events, both serious and non-serious (CFR 312.64(b). These reports will be submitted to the DSMB who will determine if one or more of the treatment groups place individuals at undue risk by participating in the study.

Permit the use of adverse events as outcome variables to allow comparisons of participant safety between treatment groups.

4.2. Definitions

4.2.1. Laboratory Adverse Event

A laboratory adverse event is any clinically important worsening in a laboratory variable that occurs during the course of the study, whether or not considered to be drug-related.

4.2.2. Clinical Adverse Event

A clinical adverse event is any unintended worsening in the structure or function of the body, whether or not it is considered to be drug-related or study-related. This includes any side effect, injury, sensitivity reaction, or any other illness or condition occurring while a participant is in the study. Worsening of variables monitored by an ECG would be considered a clinical adverse event.

4.2.3. Serious Adverse Event

A serious adverse event (SAE) is any experience that suggests a significant hazard, contraindication, side effect, or precaution. With respect to human clinical experience, a serious adverse event includes any experience that is fatal or life threatening, is permanently disabling, requires or prolongs an existing hospitalization, or is a congenital anomaly, cancer, or overdose.

Note that any hospitalization, even for elective surgery, constitutes a serious adverse event and should be documented as such. This includes a hospitalization for an asthma exacerbation. If the elective surgery required hospitalization afterwards, then it should be considered a serious adverse event. If the elective surgery took place in an ambulatory surgery area and the participant went home the same day, then it would not be considered a serious adverse event.

Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse drug experience when, based upon appropriate medical judgment, they may jeopardize the participant and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an ER or at home, blood dyscrasias or convulsions that do not result in hospitalization, or the development of drug dependency or abuse.

4.2.4. Unanticipated Problem

An unanticipated problem (UP) is any incident, experience, or outcome that meets all of the following criteria: 1) unexpected; 2) related or possibly related to participation in the research; and 3) suggests that the research places subjects or others at a greater risk of harm than was previously known or recognized. An unanticipated problem may not necessarily be an adverse event, which is the case when the problem does not cause actual harm to participant(s). For example, if a laptop computer with sensitive, identifiable study data is stolen, this theft places the participants at greater risk of psychological or social harm; this is an unanticipated problem that is not an adverse event.

4.2.5. Unexpected Adverse Event

An unexpected adverse event is any adverse event that is not consistent with the currently approved research protocol, investigator brochure, or informed consent form, or one that is not part of the normal disease progression.

4.3. Adverse Event Reported to the Clinic Coordinator

Study personnel may learn of the occurrence of an adverse event in a variety of ways:

> Study visit: The participant (or his/her parent/guardian) reports the adverse event at a scheduled study visit. Participants are instructed to note any medical problems and non-study medications which are reviewed at each visit in order to aid in the identification and reporting of recent medical

problems. In addition, at each study visit, participants are asked about the occurrence of any medical problems since the last visit.
Telephone contact: The participant reports the adverse event during a telephone contact.
Unscheduled reporting: The participant or treating physician calls or visits the clinic to report an adverse event.

In each case, the incident must be brought to the attention of the clinic coordinator so that appropriate documentation can be completed.

4.3.1. Was there a Laboratory Adverse Event?

Laboratory tests are done if required by a protocol at a given visit or if a participant exhibits related symptoms. If the results of any of these tests are abnormal, the participant is experiencing a laboratory adverse event and the Clinical Adverse Events form (AECLIN) should be completed. The definition of abnormal for relevant tests is determined by the particular protocol. Abnormal may be defined as being out of range as a percent of normal (e.g., >125% of normal, where normal may be a participant's baseline value). Normal ranges for tests from each clinical lab will be maintained at the DCC along with copies of the lab certifications from the College of American Pathologists.

Participants may exhibit symptoms that call for additional tests that have not been specified by the protocol. Results that are not within the normal range, as specified by the clinical lab, will also be reported as laboratory adverse events.

4.3.2. Was there a Clinical Adverse Event?

If there was a clinical adverse event, then the Clinical Adverse Events form (AECLIN) should be completed. This form documents all clinical adverse events experienced by a participant for the duration of a study. The DCC will perform interim reporting to the DSMB of adverse events for all studies.

Only conditions that first appear or become worse after study entry will be recorded. It is essential, therefore, that pre-existing medical conditions be accurately identified, characterized, and documented at the time of trial entry to prevent a medical event from being interpreted as an adverse event, when it is simply a reoccurrence of an existing medical problem. For example, a migraine attack may occur during the course of the study in a participant with a long-standing history of such headaches. Such an attack should be recorded as an adverse experience only if the event is different than before (e.g., of worse severity, duration, or frequency). If the pre-existing condition requires a medication change, where the new medication is equivalent to the old medication (i.e. a

change from one antihistamine to another), it does not require reporting as an adverse event.

Any unfavorable sign, symptom, disease, injury or syndrome that occurs during the study period should be recorded. This includes: any intercurrent illness, lab abnormality, symptoms significant enough to warrant therapy (including over-the-counter medications), any symptom significant to the participant, or any worsening of baseline conditions. Minor traumas such as bumps, bruises, hangnails, etc. that are part of normal childhood should not be recorded, unless they are clinically significant or significantly increased from baseline (i.e. sudden, diffuse bruising that can not be explained).

Participants who experience minor illnesses while in the study (intercurrent illnesses) may continue study participation. Examples of minor intercurrent illnesses include acute rhinitis, sinusitis, urinary tract infections, and gastroenteritis. Medications allowed for treatment of these conditions are described in the study-specific protocol and are in accordance with the judgment of the responsible physician. Illnesses constitute adverse events and require documentation ***only*** if they are appearing for the first time or if they represent a worsening of a prior condition. Adverse events are identified by the clinic coordinators in collaboration with the Clinical Center Investigators.

4.3.3. Was the Event Serious?

If the adverse event is deemed to be serious, appropriate procedures must be followed. This applies to significant asthma exacerbations as well as laboratory and clinical adverse events. The definition of a serious adverse event is described in the MOP and specific procedures for reporting are outlined. Investigators at the clinical centers will be responsible for assessing severity of adverse events and prescribing treatment.

4.3.4. Adverse Event Follow-Up

Adverse events are followed until the condition is resolved or stabilized. The medical judgment of the investigators must be used to determine what events must be followed after study termination. Events that are thought to be related to the study drug should be followed to resolution or stability of the event.

Adverse events due to either illnesses or injury may be grounds for withdrawal if the condition is considered to be significant by the investigator or if the participant is no longer able to effectively participate in the study.

4.3.5. Enter data and Submit Forms to DCC

The Clinical Centers are responsible for the timely documentation of adverse events and the submission of documentation to the DCC. A Serious Adverse Event Reporting (SERIOUS) form should be completed and faxed to the DCC at (717) 531-3922 within 72 hours of notification of a serious adverse event. Adverse Event forms should receive priority entry to maintain up-to-date safety information. It is the responsibility of the DCC to confirm that each adverse event is sufficiently documented.

Descriptions of adverse events should be clear and concise and accompanied by an ICD9 code. Note that codes should indicate the underlying condition causing an adverse event; procedure codes should not be submitted. Diseases or syndromes should be documented, not the individual symptoms (i.e. URI is documented, not the individual symptoms associated with the URI). A reference ICD9 code list (ICD9) which contains a list of common adverse events can be used for ease of reference.

For AsthmaNet purposes, reported ICD-9 codes should describe the underlying condition causing an adverse event; procedure codes should not be submitted. For example, if a participant undergoes a hysterectomy for treatment of uterine fibroids and related dysmenorrhea, codes for dysmenorrhea and uterine fibroids should be reported on the AECLIN form; no code for the hysterectomy procedure is necessary.

When assigning an ICD-9 code to an adverse event, the AsthmaNet Adverse Events ICD-9 Code Excel spreadsheet should be consulted first. This spreadsheet contains a comprehensive list of ICD-9 codes for common symptoms and conditions. It serves as the only acceptable reference for assigning ICD-9 codes for participants in any AsthmaNet protocols. As new conditions arise, the spreadsheet will be supplemented with additional codes, as needed. The spreadsheet is located on the AsthmaNet secure website in folder Application: ICD9 Codes. Alternatively, there is a search tool available during data entry of the AECLIN form.

It is essential that the following adverse event information be documented: date of onset, date stopped, type (intermittent, ongoing), maximum intensity (mild, moderate, severe), seriousness, likelihood of relationship of the adverse experience to study drugs, associated change in the drug dosage, outcome and treatment required. An explanation of all the data collected and copies of the forms are provided in the protocol-specific MOP.

The primary characteristics used to classify adverse events are:

1. the maximum intensity of the event, and;
2. the likelihood of its relationship to the study drug.

4.4. Maximum Intensity of the Event

Adverse events will be graded according to maximum intensity on a 3-point scale:

Maximum intensity	Event characteristics
Mild	No interruption in normal activities, study medications, or procedures. Symptoms noticeable but easily tolerated.
Moderate	Some interruption of normal activities (e.g., loss of school day or parent's work day due to illness or doctor's visit) or brief interruption of study medications or procedures.
Severe	Significant interruption of activities and unlikely to be able to effectively continue participation in the study; an incapacitating event.

The term "severe" is a measure of intensity. A severe reaction is not necessarily serious. For example, complete alopecia (hair loss) may be considered severe, but not serious. Conversely, a serious reaction may not necessarily be severe, e.g., a stroke that results in only a limited disability may be considered mild, but it would be a serious adverse event.

While **cancer and overdose** are not included in the ICH E2A definition of "serious" which has been adopted by worldwide regulators, the AsthmaNet will record these events and report them to the DSMB.

4.5. Relationship to Study Drug

The causal relationship between an adverse event and a protocol-prescribed medication will be assessed and categorized:

Relationship to study drug	Event characteristics
None - not related	Event for which there is another explanation, i.e., gunshot wound.

Unlikely - remote	Event relationship to drug is doubtful, but it cannot be completely ruled out.
Possible	Event may have been caused by clinical state or other therapy.
Probable	Condition recedes when the study drug is withdrawn and cannot be explained by participant's clinical state.

4.6. Reporting Adverse Events

Routine adverse event reporting is an important component of the interim and final analyses presented to the DSMB. Adverse event reports will include the frequency, severity and likelihood of relationship to study drug for documented events for each treatment group. Investigators must submit a written summary of the DSMB periodic review to their IRB (per the 7/1/99 NIH policy entitled, "Guidance on Reporting Adverse Events to Institutional Review Boards for NIH-Supported Multicenter Clinical Trials").

4.7. Reporting Serious Adverse Events and Unanticipated Problems

Studies involving human subjects research must include procedures for identifying, monitoring, and reporting adverse events and unanticipated problems. For clinical trials and studies with greater than minimal risk, these procedures should be described in the study's Institutional Review Board-approved data and safety monitoring plan which is sent to the NHLBI.

4.7.1 Expedited Reporting

Expedited reporting to the NHLBI Program Official or Project Officer is required for unanticipated problems or unexpected serious adverse events that may be related to the study protocol as follows:

Any event or problem that is:

1. Unexpected

AND

2. Possibly, probably, or definitely related to study participation

AND one of the following:

3a. Is fatal, life-treatening or serious (SAE + UP) – **Report within 7 calendar days**

OR

3b. Suggests greater risk of harm to study participant(s) than was previously known or recognized (UP) – **Report within 30 calendar days**

4.7.2 Review of Serious Adverse Event Report with M.D. at Clinical Center

1. *Complete Serious Adverse Event Reporting form (SERIOUS).* Fax all completed forms to the DCC within 72 hours of initial report to Clinical Center. The completed forms and supporting documentation includes the associated Clinical Adverse Event (AECLIN) form, the Concomitant Medication (CMED) form and the appropriate protocol-specific Change in Medication (PX_CHANGE_MEDS) form (if applicable). Any Emergency Department records, clinical notes, and other clinical documentation should be included as well, with all identifying information blacked out and replaced with participant's study ID number and initials.
2. In addition, the PI should send a final resolution report to the DCC, with relevant documents attached (including ER report, discharge summary, relevant clinical notes, pathology reports, ECG reports, laboratory reports, etc.). Participant name and other clear identifiers should **NOT** appear on these records; only the participant ID and initials should be used.
3. The P.I. or Co-Investigator should also provide the DCC with a brief summary on the disposition of a participant who experienced a serious adverse event. These follow-up plans should include the participant's status in the study, if they will be continuing on study medication, if they will be dropped from the study, when the next visit is scheduled and what communication occurred with the treating physician and participant's parent.

4.7.3 Review of Serious Adverse Event Report by PI or Co-PI at DCC

Does the event require immediate reporting? The PI or Co-PI at the DCC will review all documentation. Based on the seriousness of the event and the likelihood of its relationship to the study drug, urgency of reporting will be determined. Members of the AsthmaNet Steering Committee will be consulted as needed. If AsthmaNet holds an investigator IND and the SAE is thought to be related to the study drug, a report will be filed with the FDA in accordance with FDA guidelines (21 CFR 312.32) detailed in item 4.7.4.

- DCC reports to DSMB, NIH and AsthmaNet Steering Committee; pharmaceutical supplier and FDA (when appropriate; 4.7.4). These individuals will be informed of the event, within 24 hours of receipt at the DCC and assessment of urgency.
- DCC and PI's at Clinical Centers report to Institutional Review Boards. The DCC and PI's at the Clinical Centers are responsible for informing their local Institutional Review Boards.
- DSMB members must review the SAE and complete a comment ballot within one week of receipt. The comment ballot allows the DSMB members to make comments, request a conference call to discuss the SAE, or request other action. The comment ballots are sent directly to the AsthmaNet project scientist at NIH.
- A report recognizing the reporting of the SAE to the IRB at the clinical centers should be forwarded to the DCC and NHLBI. This will ensure that appropriate local reporting has been accomplished.

4.7.4 Reporting of Serious Adverse Events by DCC PI or Co-PI – FDA

If an SAE occurs in a protocol under FDA Investigational New Drug (IND) oversight, follow reporting requirements under 21 CFR 312.32.

Written IND Safety Reports:

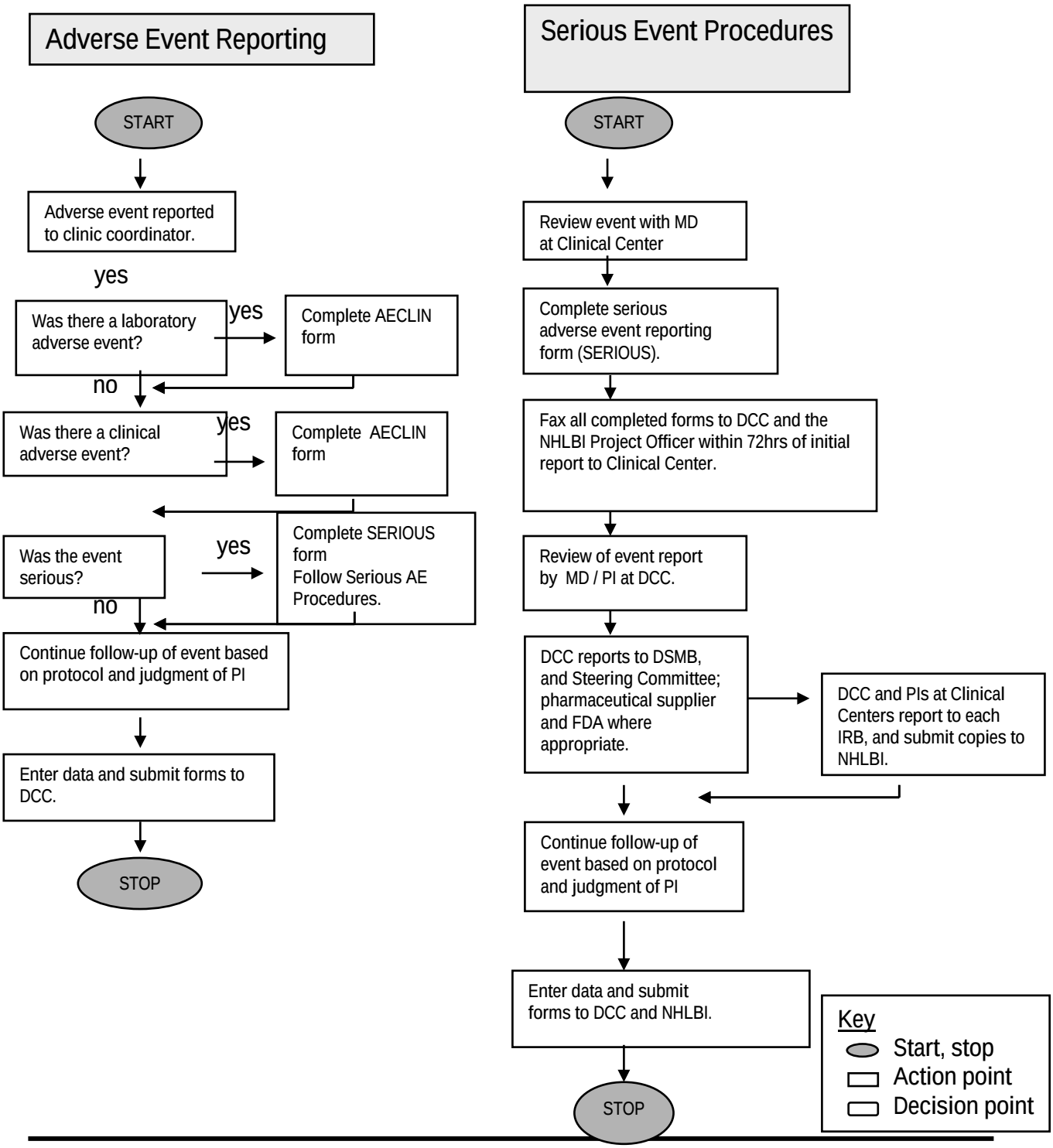
- The DCC PI or Co-PI will submit a written IND Safety Report (i.e., completed FDA Form 3500A) to the responsible new drug review division of the FDA for any observed or volunteered adverse event that is determined to be a *serious and unexpected, suspected adverse reaction*. Each IND Safety Report will be prominently labeled, "IND Safety Report", and a copy will be provided to all participating investigators (if applicable) and sub-investigators.
- Written IND Safety Reports will be submitted to the FDA as soon as possible and, in no event, later than 15 calendar days following the DCC PI or Co-PI's receipt of the respective adverse event information and determination that it meets the respective criteria for reporting.
- For each written IND Safety Report, the DCC PI or Co-PI will identify all previously submitted IND Safety Reports that addressed a similar suspected adverse reaction experience and will provide an analysis of the significance of newly reported, suspected adverse reaction in light of the previous, similar report(s) or any other relevant information.

- Relevant follow-up information to an IND Safety Report will be submitted to the applicable review division of the FDA as soon as the information is available and will be identified as such (i.e., “Follow-up IND Safety Report”).
- If the results of the DCC PI or Co-PI’s follow-up investigation show that an adverse event that was initially determined to not require a written IND Safety Report does, in fact, meet the requirements for reporting; the DCC PI or Co-PI will submit a written IND Safety Report as soon as possible, but in no event later than 15 calendar days, after the determination was made.

Telephoned IND Safety Reports – Fatal or Life-threatening Suspected Adverse Reactions:

- In addition to the subsequent submission of a written IND Safety Report (i.e., completed FDA Form 3500A), the DCC PI or Co-PI will notify the responsible review division of the FDA by telephone or facsimile transmission of any *unexpected, fatal or life-threatening suspected adverse reaction.*
- The telephone or facsimile transmission of applicable IND Safety Reports will be made as soon as possible but in no event later than 7 calendar days after the DCC PI or Co-PI’s receipt of the respective adverse event information and determination that it meets the respective criteria for reporting.

Flow Chart for Handling of Adverse Events



4.8. Rescue algorithm for asthma research participants

In order to identify and possibly prevent serious adverse events, the following guidelines must be followed by Clinical Center coordinators unless they conflict with institutional policies. Institutional policies override the instructions in this section.

4.8.1. Prevention of Exacerbations

1. Never leave a participant unattended.
2. Do not perform procedures with the potential for worsening asthma (e.g., methacholine testing, skin testing, sputum induction) without ready access to a physician.
3. Do not perform procedures with the potential for worsening asthma (e.g., methacholine testing, skin testing, sputum induction) during times of unstable asthma.
4. Perform appropriate clinical assessments and vital signs including peak flows should asthma worsening occur. Document this information in the participant's clinic notes.

4.8.2. Treatment of Exacerbations

1. If a participant is in impending or actual respiratory or cardiac arrest, activate Code _____, call 911, or STAT call AsthmaNet MD or designate:
   _____
   _____
   _____

   Evaluate for CPR, administer 6L/min O_2, and consider epinephrine (0.01 ml/kg, max 0.3 ml IM) in outer surface of upper arm.
2. If a participant is in severe respiratory distress based on one or more of the following symptoms:
   - Cyanotic (blue nail beds and lips)
   - Inability to complete full sentences
   - Accessory muscle use

- O_2 saturation < 90%
- Respiratory rate > 30/minute
- Heart rate > 130/min (>160/min for participants < 18 years)
- Diaphoretic (sweating)
- Asthma score (see page 16 for determination) $\geq$ 5
- Confused
- PF below 25% predicted
- FEV_1 below 25% predicted

Immediately call the AsthmaNet MD or designate to the participant's room.

_____
_____
_____

Assess participant and obtain vital signs (B/P, HR, RR, and oxygen saturation) and administer:

- Oxygen at 4L/min to maintain O_2 saturations > 90%
- Albuterol (4-6 puffs MDI or nebulized albuterol solution (0.5 ml of 0.5% multidose solution and 2.0 ml saline or unit dose of 0.083% albuterol)

and if not responding

- Epinephrine (0.01 ml/kg, max 0.3 ml IM) OR SQ.

3. If the participant is not severe enough to declare an emergency, administer albuterol by MDI 2-4 puffs or, then perform PEF 15 minutes later and evaluate asthma score (see page 16), then contact AsthmaNet MD:

_____
_____
_____

4. If the participant's PEF is less than 25% predicted (40% for participants < 18 years) or asthma score is ≥ 4 (see page 16 for determination), nebulized albuterol solution (0.5 ml of 0.5% multi-dose solution and 2.0 ml saline or unit dose of 0.083% albuterol). If needed, repeat nebulized treatment at the same dose. MD will completely assess the participant's clinical status.
5. If the participant's PEF is equal to or greater than 60% predicted or the asthma score is ≤ 1 (See page 16 for determination), the participant should be instructed to

use the "PRN beta-agonist MDI" for home treatment according to their established protocol guidelines.

6. If the participant's FEV_1 is greater than 25% predicted (40% for participants < 18 years) but less than 60% predicted or the asthma score is 2 but less than 4 (see page 16 for determination) repeat albuterol 2-4 puffs or nebulized albuterol solution every 20 minutes up to an hour. Continue to assess clinical status and pulmonary function and follow NAEPP guidelines for acute asthma treatment.
7. By physician discretion add prednisone 80 mg po or Methylprednisolone 60 mg IV. Follow the prednisone course per AsthmaNet schedule. (For participants > 18 years: By physician discretion add prelone (15 mg/ml) or prednisone at a dose of 2 mg/kg (maximum 60 mg or 20 ml) p.o. if determined necessary. Follow the prelone course (2 mg/kg per day for 2 days, 1 mg/kg per day for 2 days))
8. If clinical status does not improve or PEF or FEV_1 remains below 50% predicted despite aggressive therapy consider hospitalization or transfer to ER.
9. If appropriate, contact the participant's primary care physician to inform him/her of the exacerbation.
10. Follow-up in 1 week to ensure stability of asthma.

Asthma Score

Sum the scores for the individual parameters to determine the total score. If the score is greater than or equal to 5, the participant is in severe respiratory distress.

Asthma Score	0	1	2
	On Room Air	On Room Air	On 40% Oxygen
O_2 saturation or Cyanosis	≧ 93% No	< 93% Yes	< 93% Yes
Breath sounds	Equal	Unequal	Absent
Wheezing	None	Moderate	Marked
Accessory muscles	None	Moderate	Marked
Consciousness	Normal	Agitated or depressed	Coma

4.9. Rescue Algorithm for Systemic Allergic Reactions to Skin Testing in Research Participants

4.10. Activation of CODE BLUE

The following guidelines need to be followed by Clinical Center coordinators unless they conflict with institutional policies.

To call CODE BLUE, dial _____, listen for tone and an operator will come on to assist you.

Comments:

_____

_____

4.11. Emergency Equipment Locations

Emergency Equipment	Clinic Location (Room #, etc.)
Crash Cart	
EKG Machine	
Pulse Oximeter	
Bag and Mask (O_2 Setup)	
Suction Setup	
Nebulizer Treatment Setup	
IV Equipment (Catheters, Fluids, etc.)	
1:1,000 Epinephrine	

spirotel®
MANUAL OF OPERATIONS
Peak Flow and E-Diary
Medical International Research, Inc. (MIR)

6.0 spirotel®

Peak Flow Meter and E-Diary
Medical International Research, Inc. (MIR)

6.1 Description of spirotel®

The spirotel® is a peak flow meter and electronic diary (e-diary) combined into one device. The spirotel® is manufactured by Medical International Research, Inc. (MIR) and meets ATS standards (ATS-ERS 2005 Update) for accuracy and reproducibility. Long term calibration accuracy and reading reliability are maintained with the use of a Pulmonary Waveform Generator that is an integral part of MIR's production and quality check. The memory storage will allow a participant to record data for a period of weeks between study visits.

The spirotel® device consists of the main unit and a turbine (if used for peak flow measurements). Each unit has a unique serial number located on the silver plate on the back of the device. Each turbine has a 4-digit number from 1000-9999 etched into the plastic portion of the turbine. Make sure the turbine is securely locked in place before distributing the device to the participant.

The spirotel® can be programmed to:

- Present protocol-specific daily diary questions within pre-defined time windows and save responses
- Prompt the participant to complete three peak flow maneuvers and save the highest peak flow completed during the scheduled assessments
- Alert the participant to take study medications during AM and PM scheduled assessments
- Alert the participant to complete specific forms based on diary responses during scheduled assessments
- Alert the participants to possible treatment failure based on protocol-specific criteria
- Allow the participant to complete an unscheduled peak flow maneuver

The software needed to complete the process from configuring a spirotel® to uploading the spirotel® data to a central database includes:

- **Spirotel AsthmaNet Suite** software from MIR – to configure a device, perform quality control testing, and download spirotel® data to the MedGraphics' spirometry PC
- **DB Tools** from MedGraphics – to convert downloaded spirotel® data into the Breeze Suite database and to export spirotel® data to a folder for uploading to the MedGraphics' central database
- **Breeze Suite** software from MedGraphics – to view spirotel® data and generate participant reports

- **Files to Go** – a product to securely transfer files over the Internet from the export folder on the MedGraphics' PC to the MedGraphics' Breeze Suite central database

6.2 Operating Environment

The spirotel® should not be used near inflammable liquids or inflammable gases such as oxygen or nitrogen or detergents. Do not use the device in direct air currents (e.g., wind), sources of heat or cold, direct sun rays or other sources of light or energy, dust, sand or any other chemical substances. High frequency emissions may interfere with the correct operations of the spirotel®. For this reason, the user should be no closer than 10 feet within range of high-frequency appliances such as a TV, radio, portable phone, etc. or other electronic units operating at the same time in the same room. The spirotel® may give inaccurate readings in the presence of strong electromagnetic sources such as electrosurgical equipment or computed tomography (CT) equipment.

Do not expose the turbine to a direct jet of water or air. Do not immerse the turbine in hot water or any other hot solution. Do not allow dust or foreign bodies to enter the turbine to avoid incorrect functioning and possible damage. The presence of any impurities such as hairs, sputum, thread, etc. within the body of the turbine may slow down or "brake" the propeller and thus seriously compromise the accuracy of the measurements.

6.3 Types of spirotel® Devices

Two types of spirotel® devices will be distributed to the performance sites:

- Protocol-specific demonstration (demo) devices.
    - These devices will be used to train the participants on how to complete daily scheduled assessments for a specific protocol as well as complete unscheduled peak flow maneuvers, if applicable to the protocol. The participants will use these devices to complete a formal spirotel® performance assessment using the protocol-specific Spirotel® Performance Checklist. The participant must pass the performance check to remain eligible for a study.
    - The demo devices will have one or more options to practice an AM scheduled session, a PM scheduled session, a daily session, and/or an unscheduled peak flow depending on the protocol.
    - These devices also will be used to take peak flow readings during the sputum induction procedure. Refer to Section IV B in the Sputum Manual, Appendix 7 of the AsthmaNet General MOP.
    - All demo devices will be configured at the DCC and labeled appropriately prior to sending them to the performance sites.
- Protocol-specific participant devices
    - The most up-to-date protocol-specific firmware will be loaded onto these devices at the DCC prior to shipment to the performance sites.

- Spirotel® certified staff at the performance sites can update the version of a specific protocol (when necessary) or load a different protocol firmware onto a device with assistance from the DCC.

6.4 Turning the spirotel® On and Off

- To turn on a spirotel® I device, hold down the power/enter button  on the device.
  - A demo device will display the protocol name of the demo, the version of the software, and the battery life indicator.
  - A protocol device will display the protocol name, the version of the software, the participant ID (if the device had been previously configured), the battery life indicator, and the amount of free memory storage.
- To turn on a spirotel® II device, press the power button on the bottom of the device.
- To turn off a spirotel®, hold the power button on the device for 2-3 seconds. If the spirotel® is idle for 3 minutes, the device will automatically shut down. At the end of a scheduled assessment session and following an unscheduled peak flow maneuver, the device will automatically shut down.

6.5 Scheduled Assessment Sessions

AM and PM scheduled assessment sessions can consist of the presentation of daily diary questions related to medication use and the severity of symptoms experienced overnight (AM assessment) and during the day (PM assessment), or over a 24-hour period.

- The text of each diary question will be abbreviated. Refer to the protocol-specific reference card and handout that are created for the coordinators and the participants for interpreting the abbreviated texts.
- To answer multiple choice questions,
  - Using the spirotel®I (INFANT), abbreviated responses will appear above two or more of the 0 through 3 buttons. The participant will press the button corresponding to the desired response. An arrow will appear next to the selected response. The participant will then press the power/enter button (OK) to save the response.
  - Using the spirotel®II (BARD, SIENA, STICS), numbered boxes will appear. After touching a box, the response text will appear above the boxes. The background of the chosen response box will turn white and a “>” link will appear in the upper right corner to move to the next question.
- To answer questions where a number is entered,
  - Using the spirotel®I (INFANT), the minimum number (default) will display in the middle of the second line. The participant will press the ‘3’ button to increase the value and the ‘0’ button to decrease the value. When the desired value is displayed, the participant will press the power/enter button to save the response.

    - Using the spirotel®II (BARD, SIENA, STICS), the participant will touch the numbered boxes. The entered digit(s) will be displayed to the participant and a ">" link will appear in the upper right corner to move to the next question. Touching the "C" link will clear one number at a time.
- After all the protocol-specific diary questions have been answered, the participant will have an opportunity to review his/her responses and make changes, if necessary. The question, 'Review Diary?' will appear. The participant will answer 'YES' to review previously entered responses for each question. The participant can choose to change each response before moving to the next saved response. The participant can continue to review and change diary data until he/she answers 'NO' to 'Review Diary?'

Scheduled assessments can include peak flow measurements.

- The participant will take the cap off of the turbine and attach the mouthpiece to the end of the turbine.
- The spirotel® will display the message, 'INHALE quickly' on the first line and 'EXHALE forcefully' on the second line. Using the instructions on the How to Use Your spirotel® Electronic Diary and Peak Flow Meter (HTSPIROTEL) form, the participant should blow out as hard and as fast as he/she can. After 6 seconds, the device will emit a long beep.
- After a brief pause, the peak flow value in liters/min (L/M) will display for 5 seconds in the middle of the second line after each blow. Some protocols may not display the value. The spirotel will show one of the following messages after the first or second peak flow for 5 seconds if the completed peak flow meets any of the criteria:
    - If the start of the forced vital capacity is not made with sufficient force and velocity, the text on the top line will be 'Next test' and the text on the bottom line will be 'start faster'.
    - If the test contains a fall (50%) and then a successive increase in the expired velocity, the text on the top line will be 'Next test' and the text on the bottom line will be 'avoid coughing.'
    - If the expiratory time is insufficient (FET < 3 seconds or the volume variation > 150 mL in the last 0.5 sec), the text on the top line will be 'Blow out air for' and the text on the bottom line will be 'a longer time'.
    - If the last expiratory flow measured is too high (> 0.2 L/s), the text on the top line will be 'Blow out ALL air' and the text on the bottom line will be 'in the lungs'
- After the third blow, the Highest PEF value (L/M) will display and an arrow will point to the participant's corresponding traffic light indicator. This indicator is based on the reference peak flow value entered during the configuration of the spirotel®. The green, yellow, and red zones will be defined for each protocol. Refer to the protocol-specific MOP for more information. Some protocols may not display the highest peak flow value.
- Only the highest peak flow value completed in the session will be saved.

Protocol-specific alerts may be programmed to appear prior to the presentation of diary questions, following the presentation of the diary questions and/or the completion of the

peak flow maneuvers. Refer to the protocol-specific MOP for more information. Some examples include:

- Reminder to take study medications following assessments, i.e., 'Take Your Meds'
- Alert that a peak flow is low and may indicate a potential treatment failure, i.e., 'Peak Flow Low/Call Clinic ASAP'
- Alert that rescue use is high and may indicate a potential treatment failure, i.e., Rescue Use High/Call Clinic ASAP'
- Reminder to complete one or more forms based on responses to the diary questions, i.e., 'Complete WURSS/Tonight'

A scheduled session can only be completed if the participant turns on the spirotel® within the protocol specific pre-defined time window and the corresponding session has not already been completed. The question, 'Sched Session?' or 'Scheduled Session?' will appear. The participant should answer 'YES' to begin a scheduled session or 'NO' to complete an unscheduled peak flow (for protocols using peak flow measurements) (see Section 6.6 below).

- Refer to the protocol specific MOP for corresponding session times windows
- A participant has 20 minutes to complete a session after answering the first question. If the participant turns off the device (or if the device is idle for 3 minutes and automatically shuts down) and turns it back on within 20 minutes of answering the first question, the scheduled assessment session will pick up where it left off. If the participant does not complete the entire scheduled assessment period within the 20-minute time frame, only the data entered will be saved. No alerts will appear to the participant.
- If the protocol includes peak flow measurements, the device will prompt the participant to complete a peak flow maneuver if:
    - the participant turns on the spirotel® outside of the defined scheduled assessment windows.
    - the participant turns on the spirotel® within a scheduled assessment session window and has already completed the scheduled session.
    - the participant turns on the spirotel® to complete a scheduled assessment that he/she already started, but did not turn the device on within 20 minutes of completing the first session action (such as answering the first diary question).

The spirotel® device will automatically turn off after completing the AM or PM scheduled assessment session.

6.6 Unscheduled Peak Flow Session

If peak flows are performed as part of a scheduled session, an unscheduled peak flow maneuver can be completed at any time the participant is experiencing discomfort or would like to determine his/her current peak flow value.

- If the participant turns on the device and the question, 'Sched Session?' or 'Scheduled Session?' appears, the participant will answer 'NO.'

- The spirotel® will prompt the participant to 'INHALE quickly' and 'EXHALE forcefully.' Using the instructions on the How to Use Your spirotel® Electronic Diary and Peak Flow Meter (HTSPIROTEL) form, the participant should blow out as hard and as fast as he/she can. After 6 seconds, the device will emit a long beep. The blow finishes automatically. The peak flow value in liters/min (L/M) will display after each blow. A traffic light indicator will not be displayed. The spirotel® will automatically shut off within 5 seconds.
- If the participant turns the spirotel® back on and completes a second blow within 20 minutes of the first blow, the highest of the two blows with display with a traffic light indicator based on the baseline peak reference value entered during configuration.
- If the participant completes a third blow within 20 minutes of the first blow, the highest peak flow of the three will display.
- If the participant completes a fourth blow within 20 minutes of the first blow, this will count as the first blow of a new session.
- Only the highest peak flow will be saved for each unscheduled peak flow session completed.
- Only peak flow data from the first 10 unscheduled sessions performed in a day will be saved. The participant can perform as many as needed.

6.7 Dispensing spirotel® Devices

A spirotel® can be configured for any AsthmaNet protocol currently in the data collection phase. Each spirotel® at a site will be configured for a specific protocol. The site can load another protocol's firmware onto the device with assistance from the DCC. Please ensure that the spirotel® II is fully charged before dispensing it to a participant. You can charge the device by connecting it to any computer using the USB cable included with each device. The participants can choose to charge the spirotel®II at home using any charger with a micro USB end. After the device is configured for a specific participant and the spirotel®/turbine combination passes quality control testing (if the protocol is performing peak flows), record information on the following logs:

- Spirotel® Device Log (SPIROTEL_DEVICE)
    - Spirotel® Serial Number - This is the last 6 digits of the line labeled 'SN' on the plate located on the back of the device.
    - Participant ID
    - Date Dispensed
    - Dispenser's Initials

AsthmaNet SPIROTEL® Device Log

SPIROTEL® Serial Number	Participant ID	Date Dispensed	Dispenser's Initials	Date Returned	Collector's Initials	QC Failed Y=Yes N=No	If Yes, Date Shipped to Respitech	Comments

- Spirotel® Turbine Log (SPIROTEL_TURBINE)
  - Turbine Serial Number – This 4-digit number ranging from 1000 – 9999 is etched into the plastic portion of the turbine.
  - Participant ID
  - Date Dispensed
  - Dispenser's Initials

AsthmaNet SPIROTEL® Turbine Log

Turbine Serial Number	Participant ID	Date Dispensed	Dispenser's Initials	Date Returned	Collector's Initials	QC Failed Y=Yes N=No	If Yes, Date Respitech Contacted For Replacement	Comments

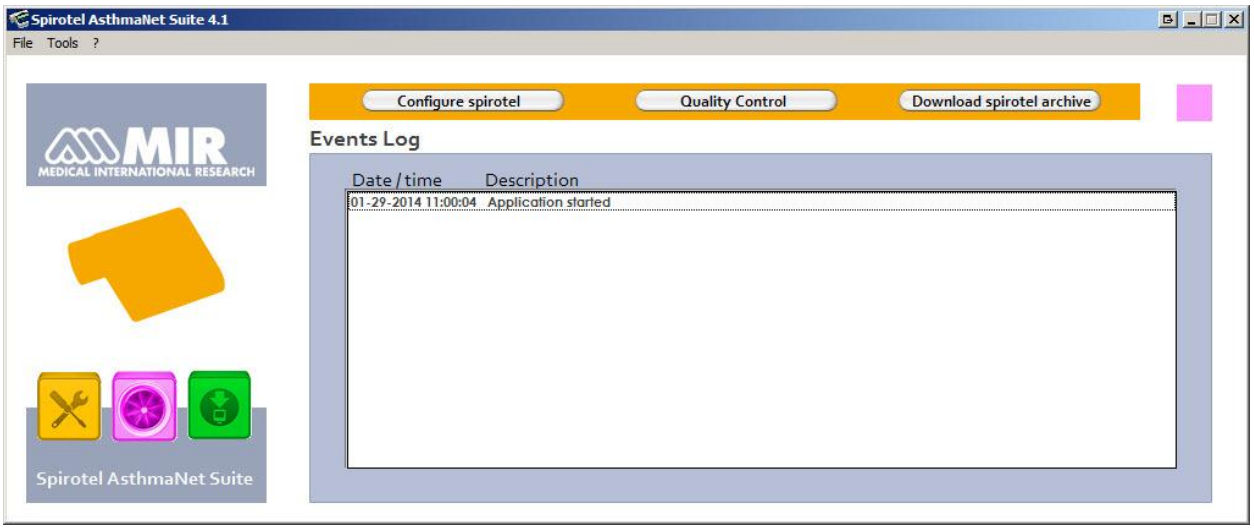
The 'Date Returned' and the 'Collector's Initials' should be recorded when the spirotel® and turbine are returned and available for distribution to another participant. The remaining columns on these logs should be completed following the Quality Control procedure described in Section 6.9.

If the protocol does not perform peak flows as part of the scheduled session, the spirotel® will not be distributed to the participant with a turbine. Remove the turbine (if the spirotel® currently has one) and place the caps provided by the DCC over the openings where the turbine would be located.

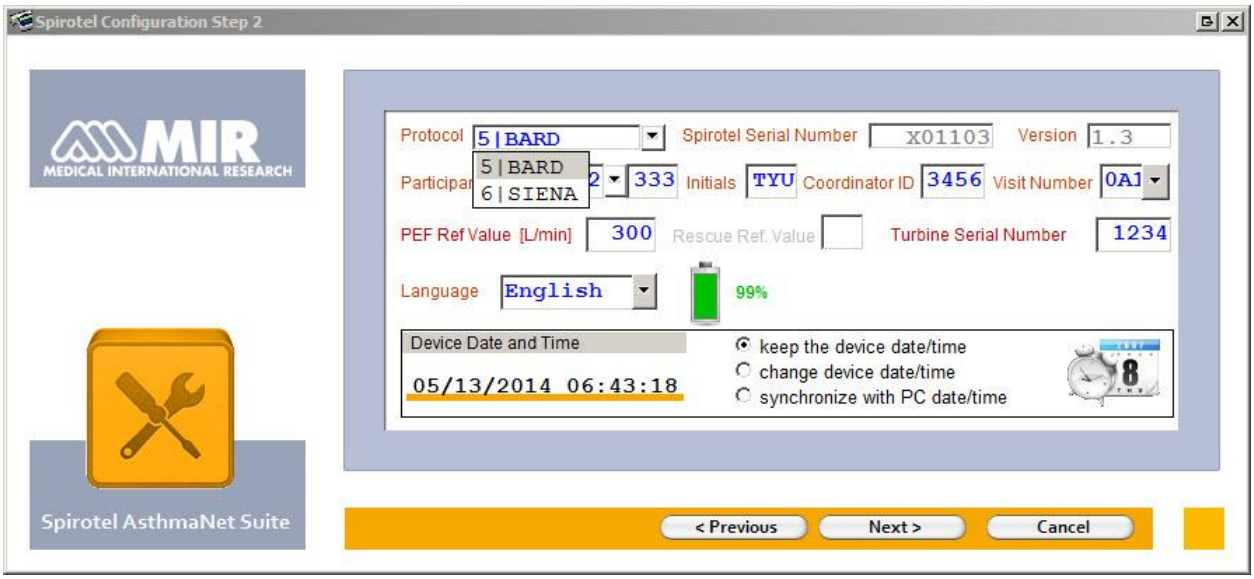
6.8 Configuring a spirotel® for Initial Distribution to a Participant

1. Double-click on the Spirotel AsthmaNet Suite icon located on the desktop of the MedGraphics' spirometry PC.

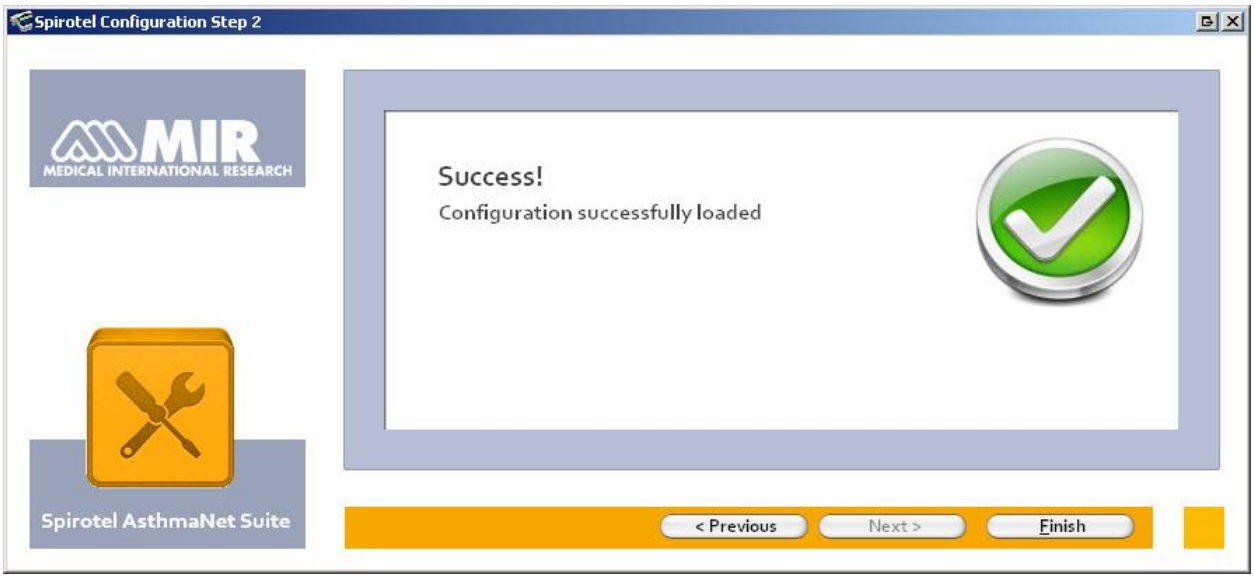
2. Click on the 'Configure spirotel' button on the Spirotel AsthmaNet Suite home page.



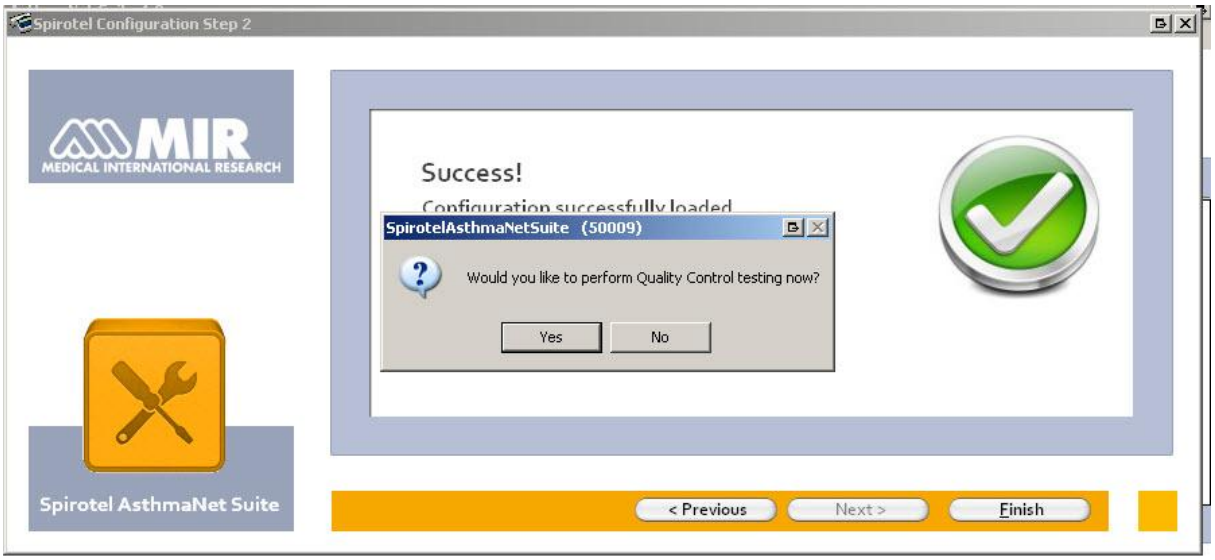
3. Connect the spirotel® to the appropriate USB cable for either the spirotel®I or spirotel®II device (converter cable) and the converter cable to the USB port of the MedGraphics' PC and click on the 'Next' button. Warnings will display if the spirotel® is not connected to the converter cable or the converter cable is not connected to the USB port. Make sure the device is turned off before proceeding.
4. The Spirotel Configuration Step 2 screen will display. If this is the first time this spirotel® has been configured, the spirotel® serial number, protocol name (for INFANT only), and version will be the only fields that pre-populate. If the spirotel® was configured previously, all the fields will pre-populate based on data entered for the last participant it was configured for.



5. Enter the following required information:
    - Protocol number for BARD or SIENA; INFANT and STICS will automatically pre-populate.
    - Participant ID: This consists of 3 parts: (1) protocol number (automatically pre-filled); (2) the site number chosen from a drop-down list specific to the selected protocol; and (3) the ID number assigned by the site.
    - Participant Initials: Must include 3 characters
    - Coordinator ID: This is the 4-digit identification number belonging to the person who is configuring the participant's device.
    - Visit Number: The return visit number should be entered. For example, if the spirotel® is initially given to the participant at Visit 2, the return visit number should be specified as 3. This value should be updated at each return visit.
    - Peak Flow Reference Value (L/min): This is the participant's baseline peak flow value. Not all protocols will be recording peak flow measurements. Please refer to the protocol-specific MOP for instructions on how this value is determined.
    - Rescue Reference Value: This is the participant's baseline rescue use value in puffs/day. Not all protocols will be recording rescue use. Please refer to the protocol-specific MOP for instructions on how this value is determined.
    - Turbine Serial Number: This is a 4-digit number etched into the turbine. The acceptable range is 1000-9999. For protocols not recording peak flow measurements, spirotel devices will be distributed without turbines.
    - Language: Select the Language that will appear on the spirotel® display. Language defaults to English. If the protocol allows for Spanish speaking participants, select the appropriate language for the participant.
6. The percent of battery life remaining will display.
7. The Device Date and Time will display. The coordinator can choose to:
    - Keep the current device date/time
    - Change the device date/time: This option can be used if a participant is traveling to another time zone. The participant should come to the clinic before traveling to have the spirotel® date and time changed to match the participant's destination.
    - Synchronize with PC date/time: This should be done when configuring a device for the first time. Verify the PC date and time are accurate.
8. Click the 'Next' button to load these data into the spirotel® and complete the configuration process. Warnings will display if any fields have been left blank or if any of the entered information violates programmed ranges and specifications.



9. Click the 'Finish' button.
10. The question, 'Would you like to perform Quality Control testing now?' will only appear for protocols requiring peak flow measurements.



11. Selecting 'Yes' will take the user to the Quality Control Test procedure. See Section 6.9 below.
12. Selecting 'No' will take the user back to the Spirotel AsthmaNet Suite home page.

6.9 Performing spirotel® Quality Control Testing – Only Performed for Protocols Requiring Peak Flow Measurements

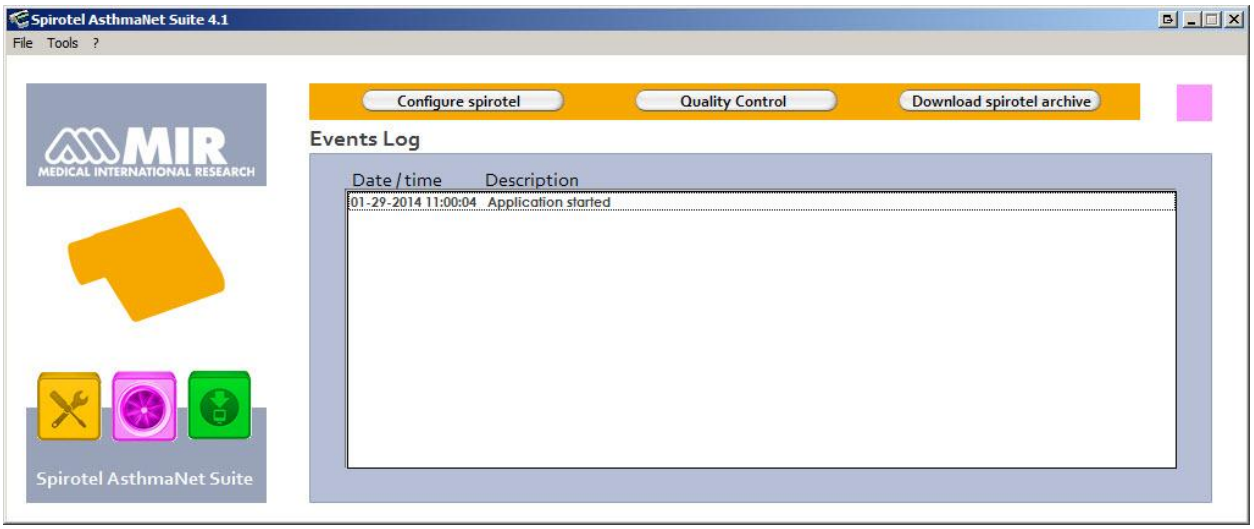
Quality Control Testing ensures that the turbine and spirotel® device combination are working properly according to ATS standards. Quality Control Testing will only be

performed in protocols that require peak flows as part of the scheduled AM and/or PM sessions. Quality Control Testing should be completed in the following instances:

- When assigning and distributing a device to a participant for the first time
- At each participant's study visit **after spirotel® data have been downloaded**
- After a turbine that has failed a previous Quality Control Test has been cleaned
- Once a month for a demo device

The Quality Control Test will verify that the average expiration value is less than or equal to ± 5.5% correction factor from the standard. If the expiration correction value [Q1040 on the Spirotel® Quality Control (SPIROTELQC) form] is <= ± 5.5%, the turbine/device combination will pass quality control testing. This will ensure that the device exceeds ATS standards.

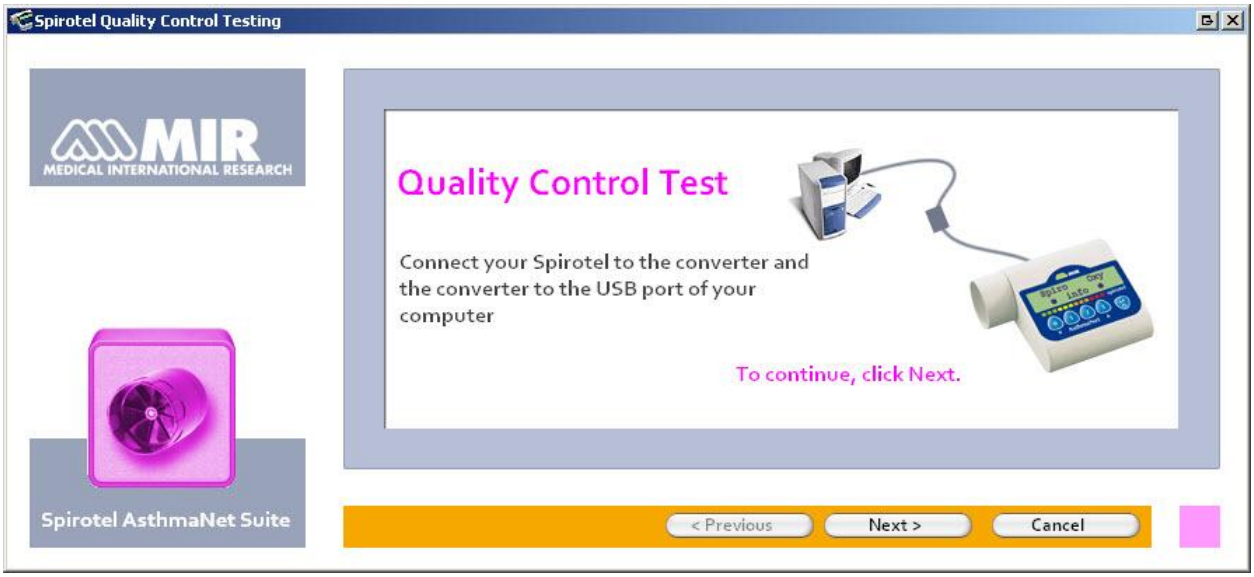
To perform Quality Control testing, click the 'Quality Control' button on the Spirotel AsthmaNet Suite home page or select 'Yes' to the question 'Would you like to perform Quality Control testing now?' following a configuration.



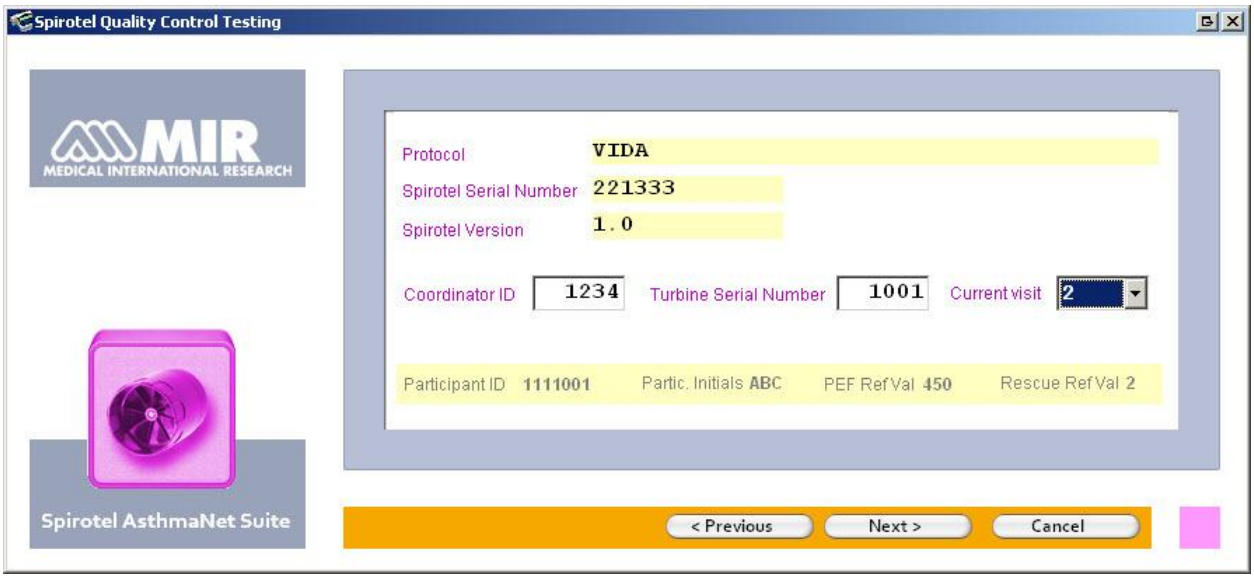
To perform Quality Control testing on a configured device

1. Connect the spirotel® to the appropriate converter cable and the converter cable to the USB port of the MedGraphics' spirometry PC. Warnings will display when initiating the quality control testing if the spirotel® is not connected to the converter cable or the converter cable is not connected to the USB port.
2. Connect the calibration adapter to the end of the 3-liter syringe supplied by MedGraphics.
3. Remove the turbine cap and attach the spirotel® to other end of the calibration adapter.

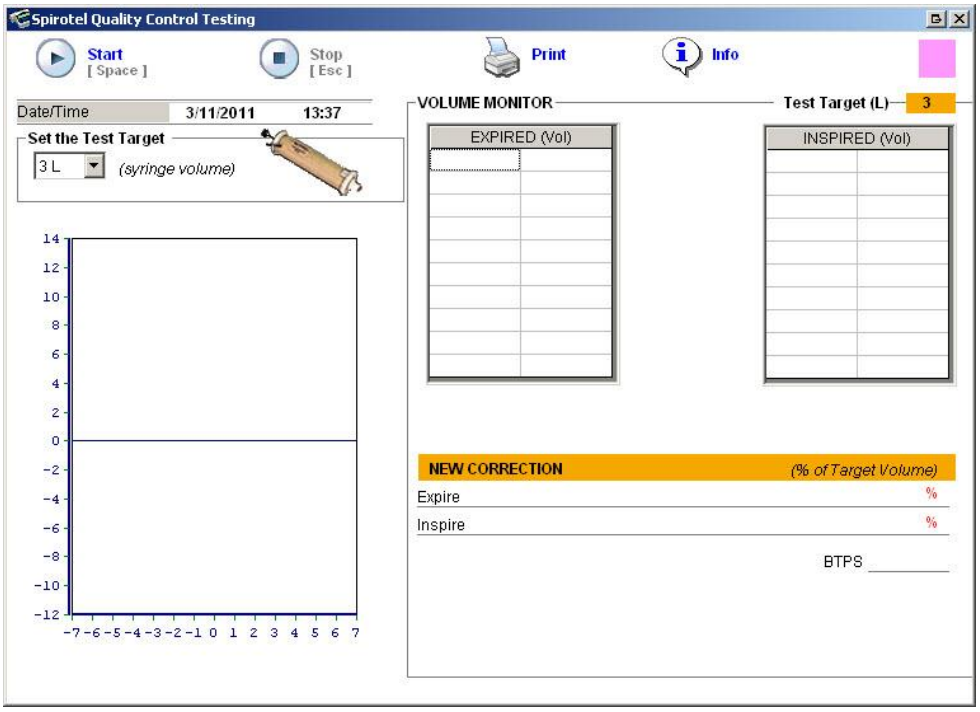
4. Pull the 3-liter piston fully out before beginning the test.
5. Click the 'Next' button on the Spirotel Quality Control Testing page.



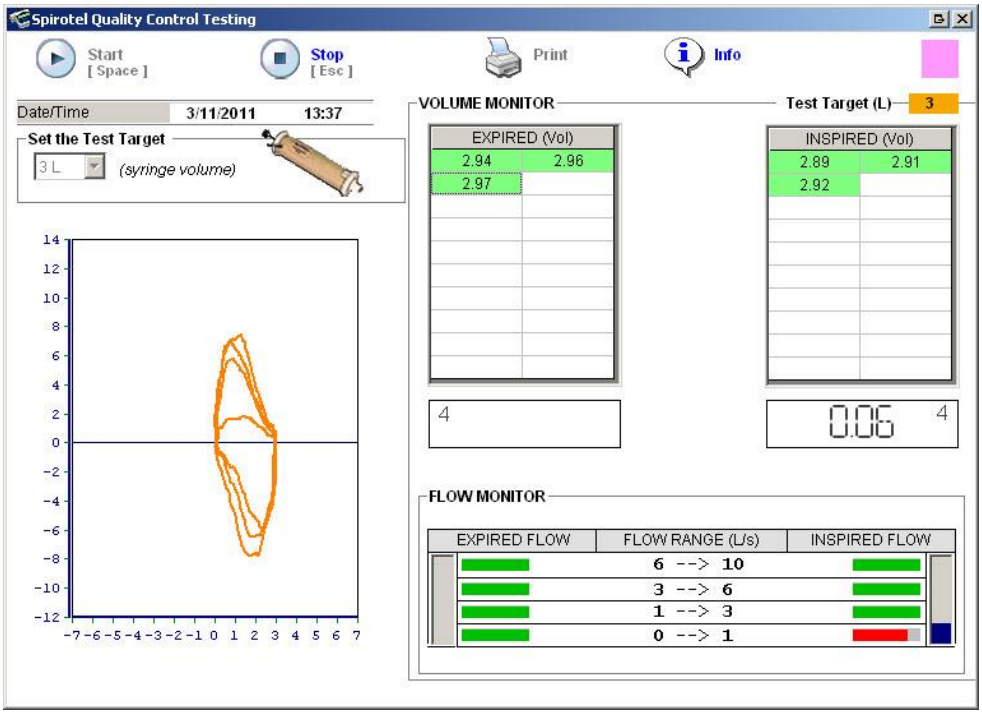
6. The following fields will pre-populate from the configuration entry: Protocol Name, Spirotel® Serial Number, Spirotel® Version, Coordinator ID, Turbine Serial Number, Participant ID, Participant Initials, Peak Flow Reference Value and Rescue Reference Value.



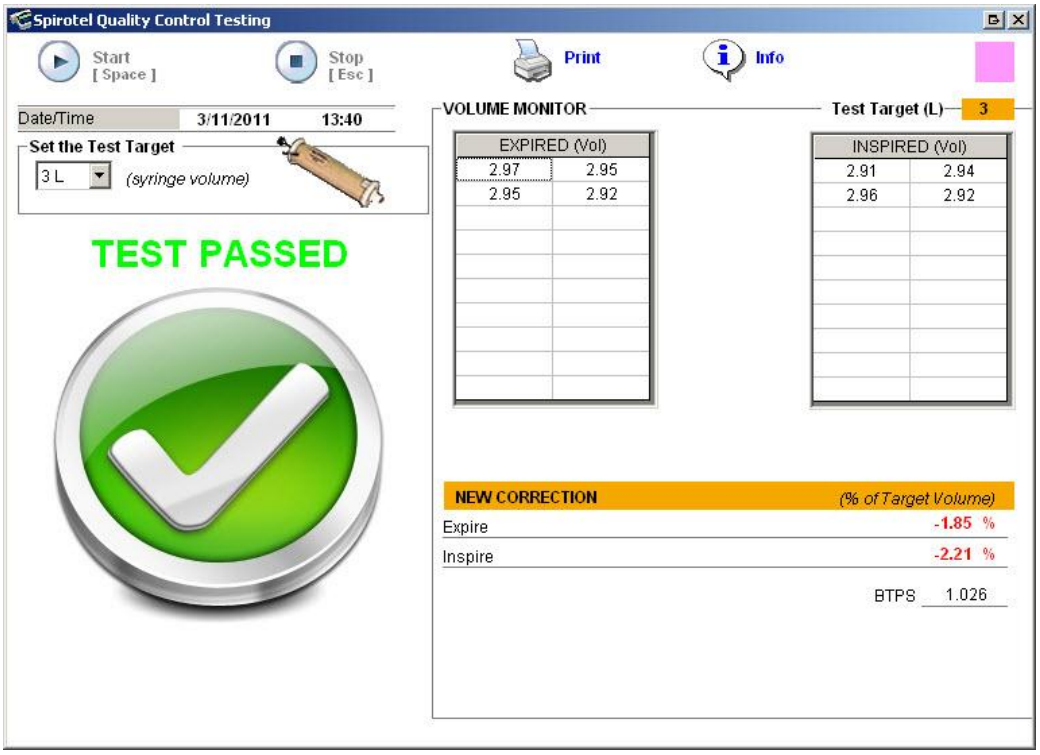
7. The Coordinator ID and Turbine Serial Number can be updated, if appropriate.
8. Enter the **current** visit. This visit number will print out on the Spirotel® QC report (SPIROTELQC).
9. Click on the 'Next' button to continue.
10. Verify that the syringe volume is set to 3L.
11. Click on the 'Start' button in the upper left corner.



12. Make several complete expirations and inspirations (piston fully out to piston fully in) at different flow rates so that a green indicator bar appears for each expired flow rate and inspired flow rate. When all the flow rates are green, extend the piston fully in and out one more time for the test result to appear.



13. The result of the test will appear on the left side of the screen.



14. The spirotel® quality control test report will automatically display.

SPIROTEL®
QUALITY CONTROL

Part. ID: 1111001
Part. Initials: ABC
Visit: 2
Visit Date: 03/11/2011
Coordinator ID: 1234

Spirometer Calibration report

1. Test Date	(1000)	03/11/2011 MM DD YYYY	
2. Test Time *(based on 24-hour clock)*	(1010)	1340	
Device			
3. spirotel® Serial Number	(1020)	221333	
4. Turbine Serial Number	(1030)	1001	
Calibration Test Results			
5. Expiration Correction	(1040)	-1.85	%
6. Expiration	(1050)	2.97	L
	(1060)	2.95	L
	(1070)	2.95	L
	(1080)	2.92	L
7. Did the spirotel® pass?	(1090)	☒ 1 Yes	☐ 0 No

→ If the spirotel did not pass Quality Control Testing, refer to Appendix 6 of the AsthmaNet General MOP for instructions on how to proceed.

→ Only the report for the spirotel® and turbine that passed Quality Control Testing and was sent home with the participant should be data entered.

2/1/2011 version 1.0 Page 1 of 1

15. Print the Spirotel® Quality Control (SPIROTELQC) form for inclusion into the visit packet of forms that will be forwarded to the DCC.
16. A pdf version of the report will be saved automatically in the directory, C:\MIR\SpirotelAsthmanet\ QC, in a folder with the device's corresponding serial number and named using the format "spirotel serial number_year_month_day_time." The date and time represents the date and time the test was performed.
17. If the test failed, print the Spirotel® Quality Control (SPIROTELQC) report, file it in the participant's study folder for the current visit. Do not enter the failed report into the AsthmaNet application and do not send a failed report to the DCC.
18. Close the Quality Control testing window by clicking the 'X' button in the upper right corner.
19. Clean the failed turbine following the instructions in Section 6.10 below.

Procedures to follow if a spirotel® fails quality control testing

1. Remove the current turbine from the spirotel®.
2. Select another turbine from your site's stock and insert the turbine into the device
3. Perform another quality control test.
4. If the spirotel® passed the test, print the spirotel® quality control report (SPIROTELQC) and file it in the participant's study visit packet for entry and transmission to the DCC.
5. If the spirotel® fails the second quality control test, assign a new spirotel® device to the participant.
6. Perform a third quality control test on the new spirotel®/turbine combination.
7. Continue steps 1 through 6 until a successful quality control test is performed.

6.10 Turbines Failing Quality Control Testing

1. If a turbine fails quality control testing, remove the turbine from the spirotel® and clean/disinfect the turbine using an approved cold sterilization process. MIR recommends using Control III solution or Dupont's Perasafe solution as the cleaning agents. Soak the turbine in the solution for 10 minutes. After removing the turbine from the solution, the turbine should air dry for 10 minutes.
2. Insert the clean and dry turbine into a demo spirotel® or another spirotel®.
3. Perform a quality control test.
4. If the quality control test passes, the turbine can be placed in the stock for reuse.
5. If the quality control test fails, place the turbine in another spirotel and perform another quality control test. If the quality control test fails again, record 'Y' in the QC failed column of the Spirotel® Turbine Log (SPIROTEL_TURBINE) and contact the DCC for a replacement turbine.
6. Return the failed turbine to the DCC for replacement.

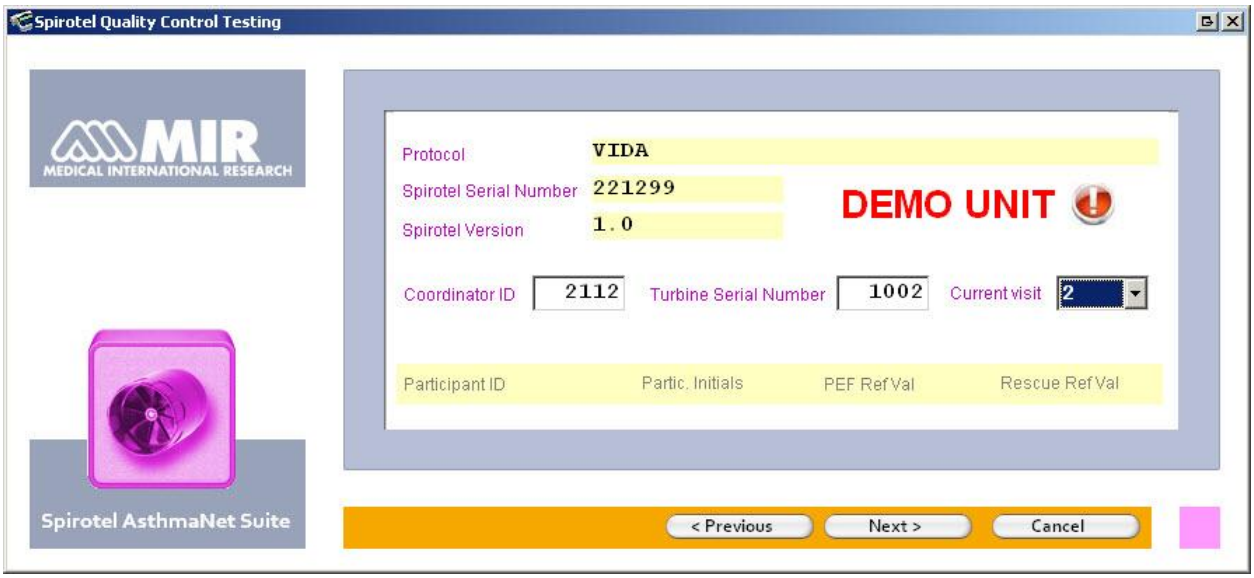
6.11 Replacing/fixing a Malfunctioning spirotel®

If two turbines fail quality control testing using the same spirotel®, it is possible that the spirotel® device is malfunctioning. In addition, participants might report that they were having problems with the spirotel® after it was distributed to them. Follow the steps below if you suspect a malfunctioning device or broken turbine, or if a device is damaged at the site or in the participant's possession.

1. Use the device at your site and try to replicate the problem.
2. Contact either the primary data manager or the manager of the data management unit if you have a malfunctioning device.
3. You may be asked to send the device to the DCC for further evaluation or replacement. Please send the device to:
   Department of Public Health Sciences
   Attention: Primary Data Manager
   Penn State College of Medicine
   The Milton S. Hershey Medical Center
   90 Hope Drive, Suite 2200
   P.O. Box 855
   Hershey, PA 17033-0855
4. Complete the Equipment Return Form and send it with the malfunctioning equipment.

6.12 To Perform Quality Control Testing on a Demo Device with a Turbine

1. Turn on the demo spirotel® and select a protocol, either BARD, SIENA, or STICS.
2. Connect the demo spirotel® to the appropriate converter cable and the converter cable to the USB port of the MedGraphics' spirometry PC. Warnings will display when initiating the quality control testing if the spirotel® is not connected to the adapter cable or the adapter cable is not connected to the USB port.
3. Connect the calibration adapter to the end of the 3-liter syringe supplied by MedGraphics
4. Remove the turbine cap and attach the spirotel® to the other end of the calibration adapter
5. Pull the 3-liter piston fully out before beginning the test
6. Click the 'Next' button on the Spirotel® Quality Control Testing page
7. The following fields will pre-populate: Protocol Name, Spirotel® Serial Number, and Spirotel® Version.



8. Enter the Coordinator ID performing the quality control testing and the turbine serial number.
9. Select any Current Visit from the available dropdown list. This value will not print out on the Spirotel® Quality Control (SPIROTELQC) report.
10. Click on the 'Next' button to continue.
11. Verify that the syringe volume is set to 3L.
12. Click on the 'Start' button in the upper left corner.
13. Make several complete expirations and inspirations (piston fully out to piston fully in) at different rates so that a green indicator bar appears for each expired flow rate and inspired flow rate. When all the flow rates are green, extend the piston fully in and out one more time for the test result to appear.
14. The result of the test will appear on the left side of the screen.
15. The spirotel® quality control test report will automatically display.

	SPIROTEL® **QUALITY CONTROL**	Part. ID: Part. Initials: Visit: Visit Date: Coordinator ID: 2222

Print and file the report in the spirotel demo device QC folder. Do not forward to the DCC.
Spirometer Calibration Report

1. Test Date	(1000)	03/04/2011 MM DD YYYY	
2. Test Time *(based on 24-hour clock)*	(1010)	1104	
Device			
3. spirotel® Serial Number	(1020)	221478	
4. Turbine Serial Number	(1030)	1234	
Calibration Test Results			
5. Expiration Correction	(1040)	0.70	%
6. Expiration	(1050)	3.03	L
	(1060)	3.01	L
	(1070)	3.05	L
	(1080)	3.00	L
7. Did the spirotel® pass?	(1090)	☒ 1 Yes ☐ 0 No	

→ If the spirotel did not pass Quality Control Testing, refer to Appendix 6 of the AsthmaNet General MOP for instructions on how to proceed.

→ Only the report for the spirotel® and turbine that passed Quality Control Testing and was sent home with the participant should be data entered.

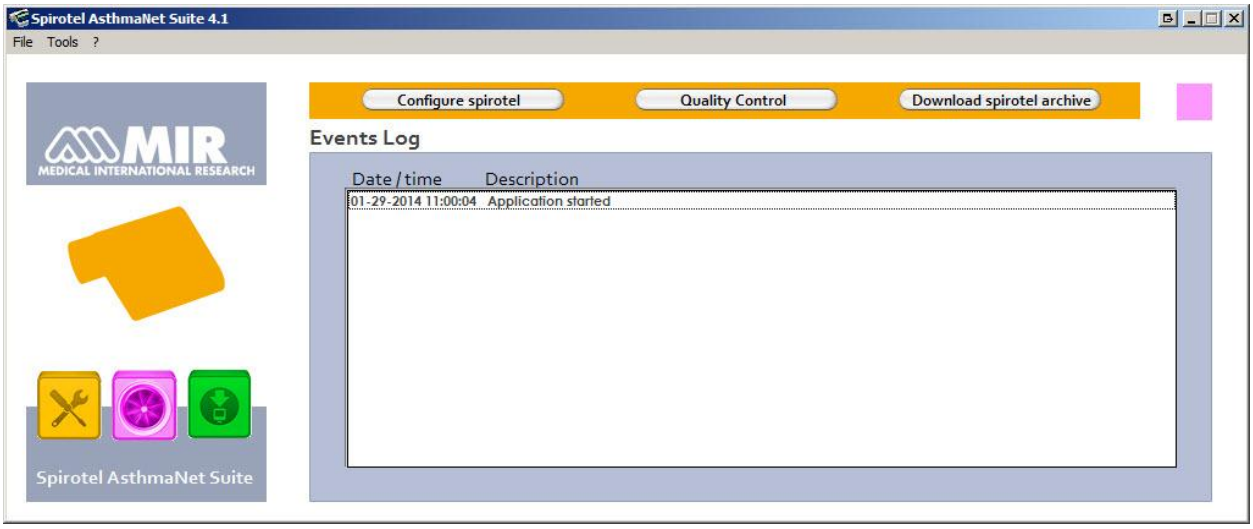
2/1/2011 version 1.0 Page 1 of 1 *SPIROTELQC*

16. Print the Spirotel® Quality Control (SPIROTELQC) report and file the form in a demo device QC folder. Do not forward the report to the DCC. These reports will be reviewed during site visits.
17. A pdf version of the report will be saved automatically in the directory, C:\MIR\SpirotelAsthmanet\ QC, in a folder with the device's corresponding serial number and named using the format "spirotel® serial number_year_month_day_time." The date and time represents the date and time the test was performed.
18. If the test fails, replace the current turbine with another turbine and perform the quality control testing again.
19. Close the Quality Control testing window by clicking the 'X' button in the upper right corner.

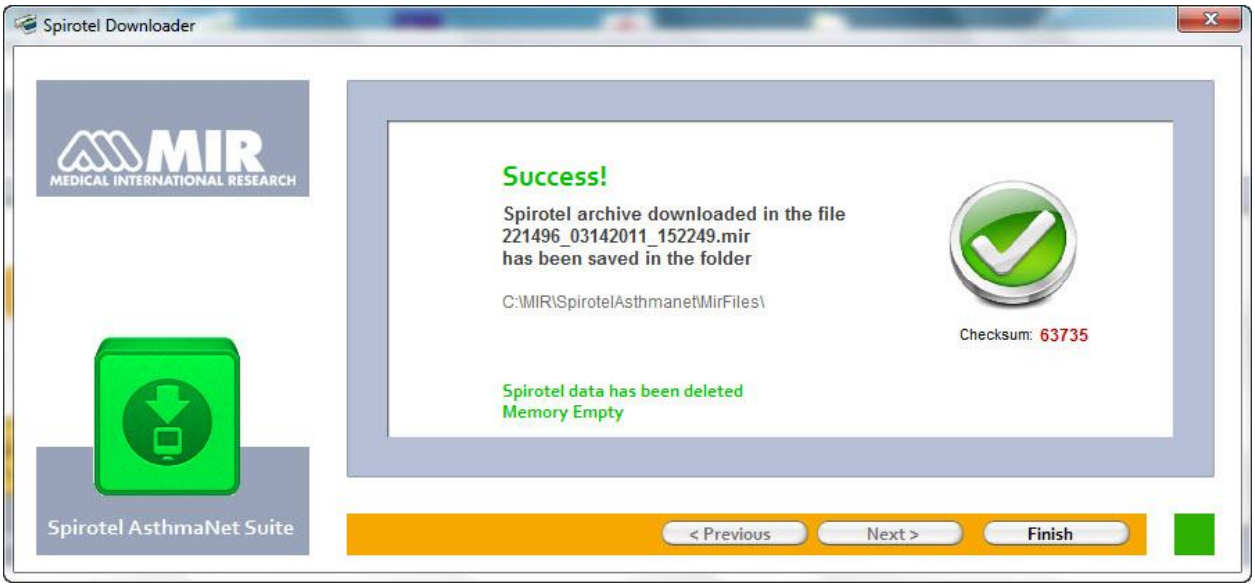
6.13 Downloading spirotel® Data to the MedGraphics' PC

Every time a participant returns to the performance site with a spirotel®, the data should be downloaded from the device to the MedGraphics' PC and converted to the Breeze Suite database in order to view the data and print the appropriate visit reports to assess compliance and/or eligibility. Keep all the visit data for a specific participant on the same computer to ensure the accuracy of the Participant Compliance Report.

1. Open the Spirotel AsthmaNet Suite software on the MedGraphics PC.
2. Select the 'Download spirotel archive' option.



3. Connect the spirotel® to the appropriate converter cable and the converter cable to the PC's USB port.
4. Click 'Next'.
5. A checksum value will appear on the spirotel® display.
6. Verify that the checksum value on the spirotel® display matches the checksum value in the message from the Spirotel AsthmaNet Suite software.

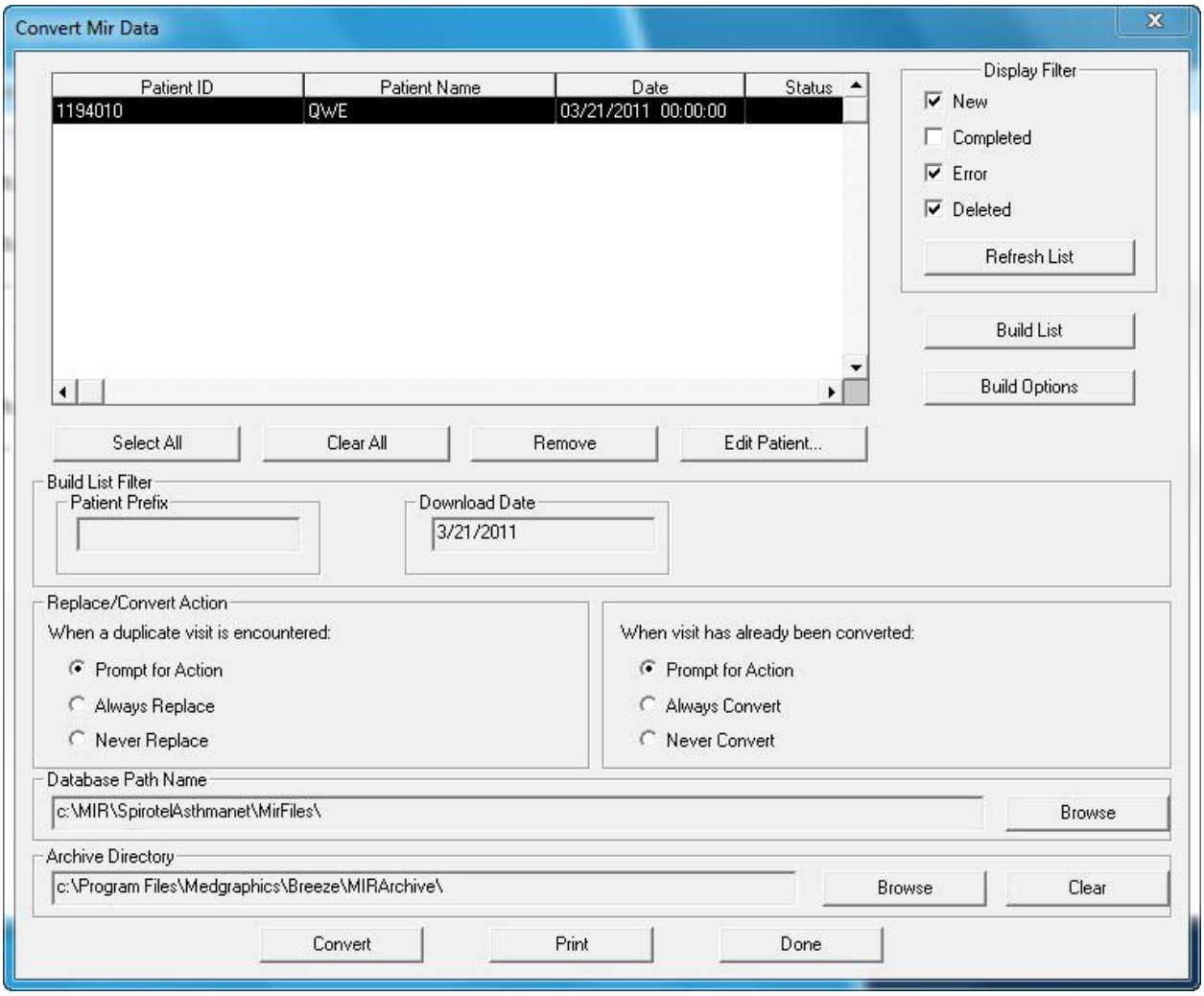


7. If the values do not match, contact the protocol primary data manager.
8. The name of the downloaded file will be formatted as spirotel serial number_month_day_year_time (including hour, minute and seconds)." The date and time represents the date and time the data were downloaded. The file will be stored in a hidden file folder.
9. Upload the spirotel® data to the site's local Breeze Suite database. See Section 6.14 below.

6.14 Converting spirotel® Data to the Site's Local Breeze Suite Database

1. Open the DBTools software on the MedGraphics' PC.

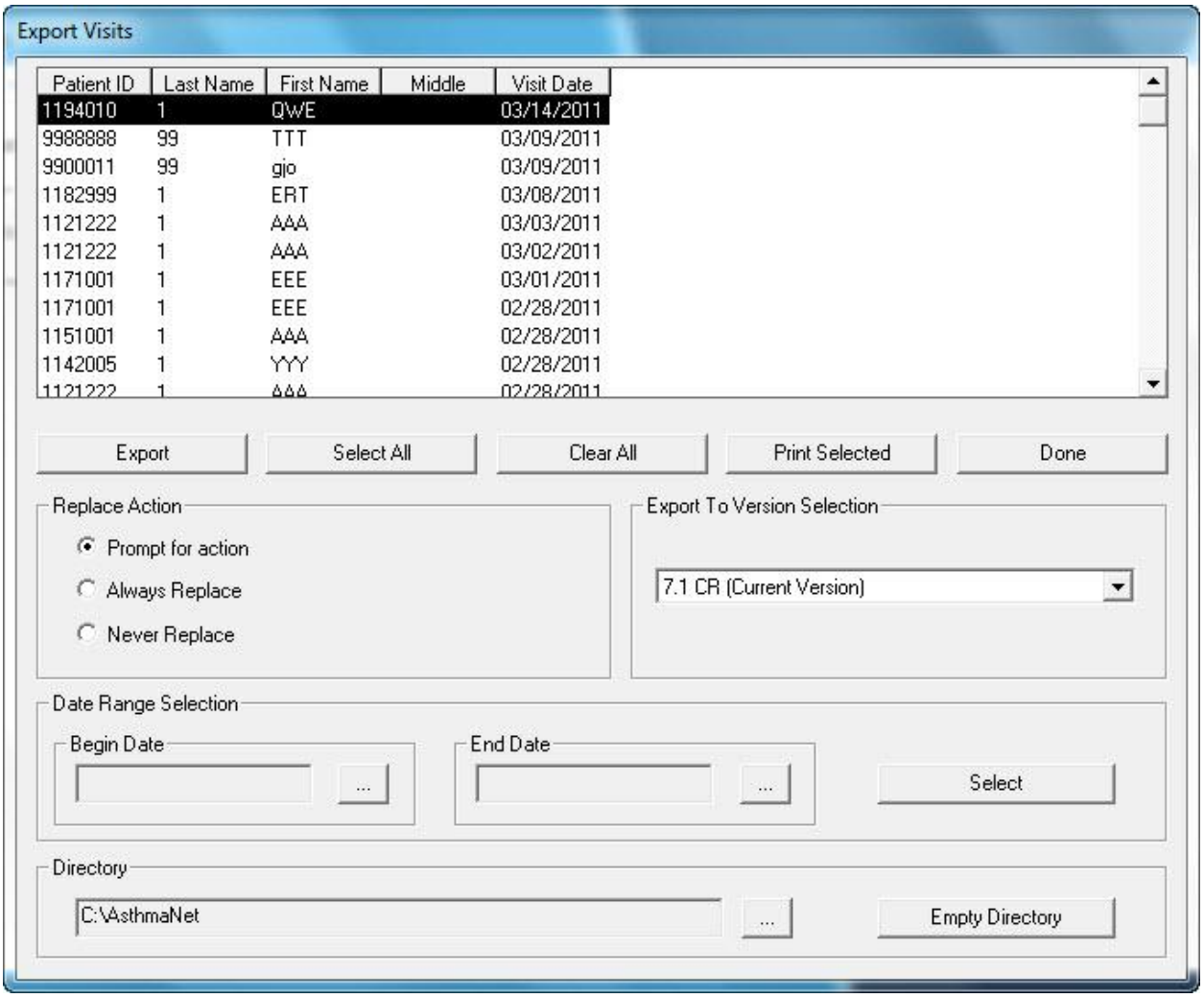
2. Leave the User Name as 'Admin' and hit the 'OK' button without entering a password
3. Select Tools → Convert Visit From→ Mir Data
4. The Data Path Name should be C:\MIR\SpirotelAsthmaNet\MirFiles. **DO NOT CHANGE THIS PATH NAME.** If the path name is changed, please contact the protocol primary data manager at the DCC.
5. Hit the 'Build List' button.
6. All Mir Files that been downloaded from the spirotel®s but have not been uploaded to the site's Breeze Suite database will be displayed. The 'Date' displayed is the date the spirotel® data were downloaded from the device.



7. Select one or more files.
8. Hit the 'Convert' button at the bottom left of the screen. 'Completed' should appear in the status column.
9. Close DBTools.
10. Upload the local spirotel® data to MedGraphics' central database. See Sections 6.15 and 6.16 below.

6.15 Uploading spirotel® Data to MedGraphics' Central Database

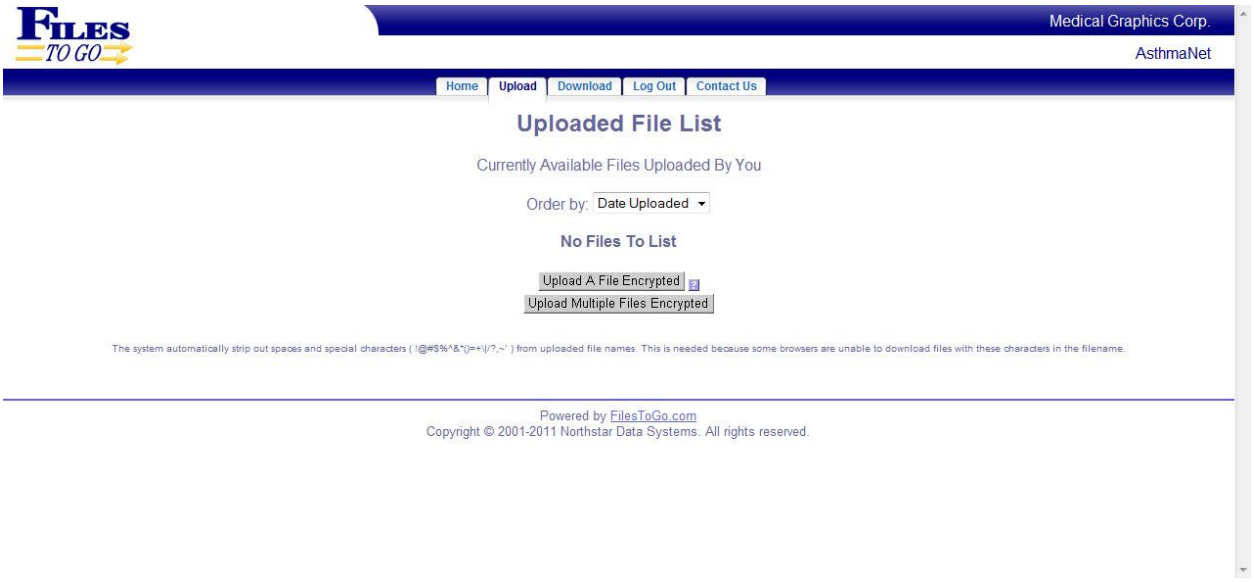
1. Open DBTools.
2. Select Tools → Export→ Patients.
3. Verify that the directory is defined as C:\AsthmaNet.
4. Select the Patient ID(s). The user can sort the list by Patient ID, Protocol Number, Participant Initials or Visit Date. The 'Visit Date' is the date the spirotel® data were downloaded from the devices.
5. Hit the 'Export' button.



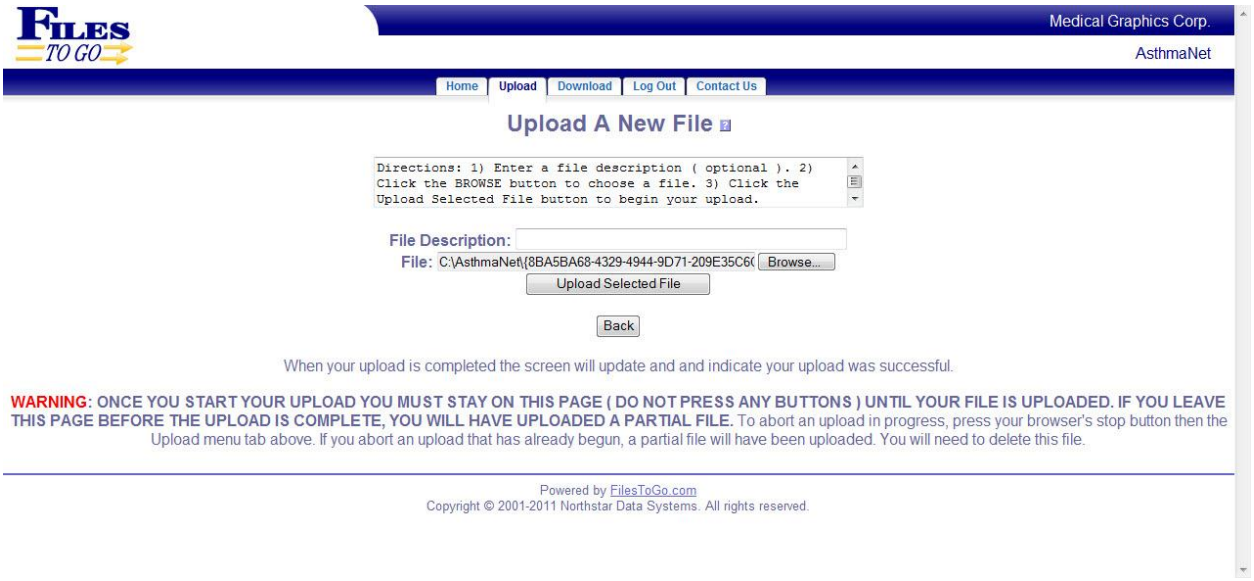
6. A message verifying a successful export will display. The files have now been forwarded to the C:\AsthmaNet folder. The names will be encrypted so that the participant ID will not be recognizable.
7. Proceed to the *Files to Go* website to transfer the files to the MedGraphics central database. See Section 6.16 below.

6.16 Transferring Data from the Site's PC to MedGraphics' Central Database

1. Open Microsoft Internet Explorer on the MedGraphics' PC.
2. The *Files to Go* website should load. If not, type in www.filestogo.com.
3. Login using 'your site's User ID and password from MedGraphics.
4. Hit the 'Upload' tab.
5. Select either 'Upload a File Encrypted' or 'Upload Multiple Files Encrypted'.



6. If 'Upload a File Encrypted' is selected,
    a. Hit the 'Browse' button
    b. Point to C:\AsthmaNet
    c. Select the file
    d. Hit the 'Open' button
    e. Upload the selected file
    f. After receiving a success message, delete the file from the C:\AsthmaNet folder.



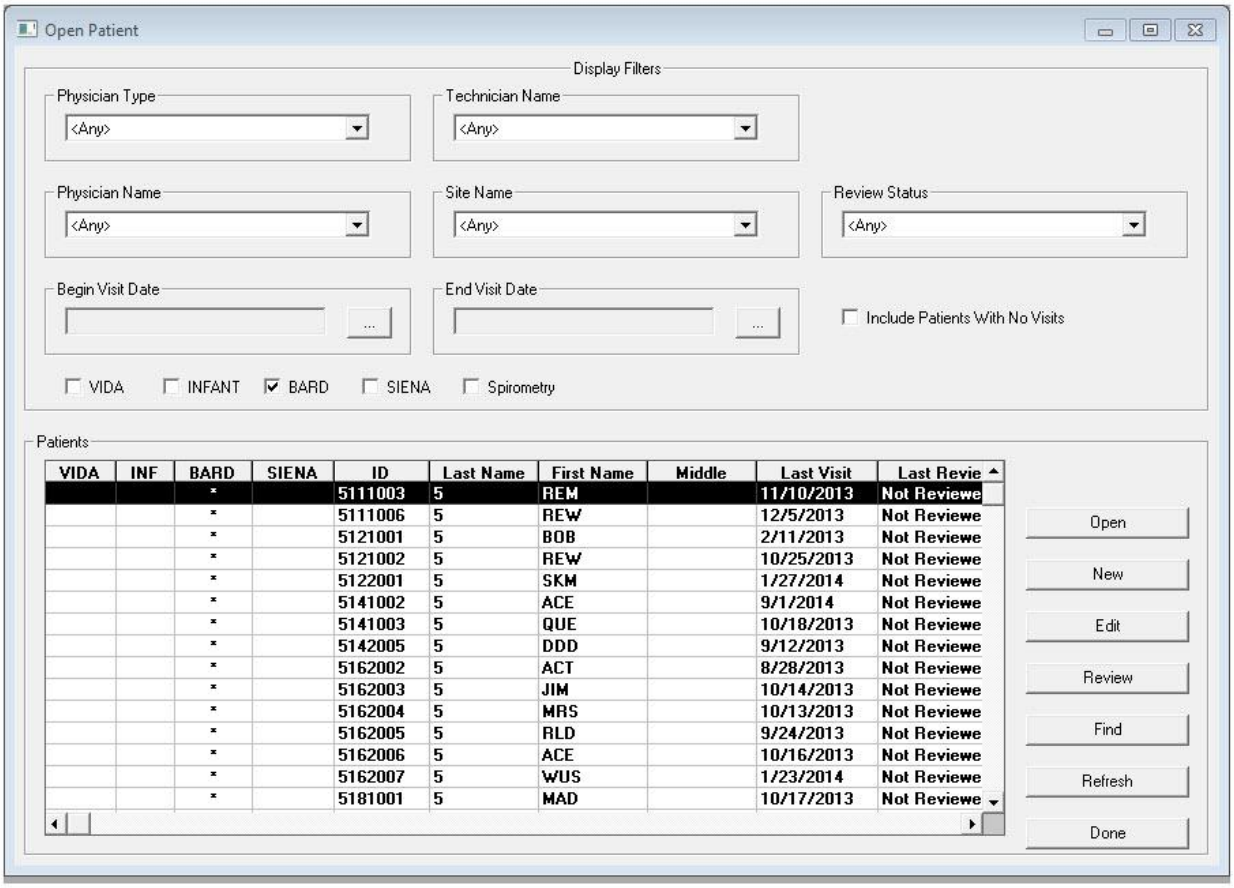
7. If "Upload Multiple Files Encrypted' is selected,
    a. Select the C:\AsthmaNet folder
    b. Drag the appropriate files to the empty pane on the right side
    c. Hit the 'Start Upload' button
    d. Hit 'Back' when uploaded successfully
    e. Delete the files from the C:\AsthmaNet folder

6.17 Viewing Participant Data and Printing Reports

After the participant's spirotel® data have been downloaded to the MedGraphics' PC (Section 6.13 above) and uploaded to the local Breeze Suite database (Section 6.14 above), the site coordinators can view the data and print the corresponding visit reports using the Breeze Suite software.

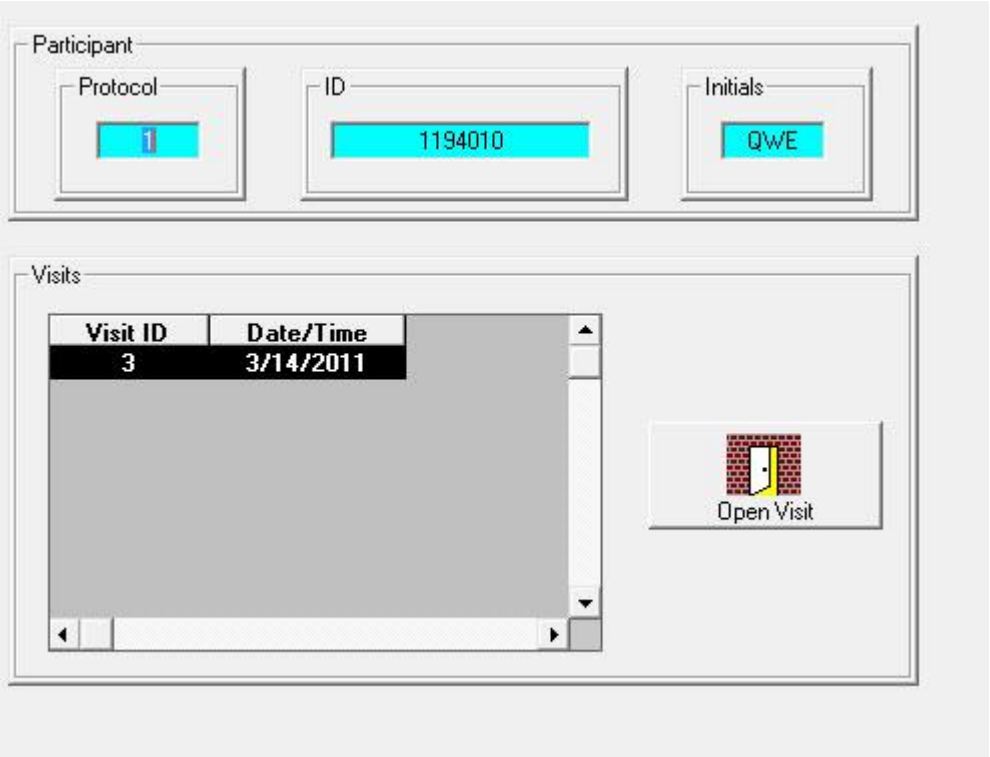
1. Open the Breeze Suite software on the MedGraphics' PC.

2. The 'Open Patient' view will display.

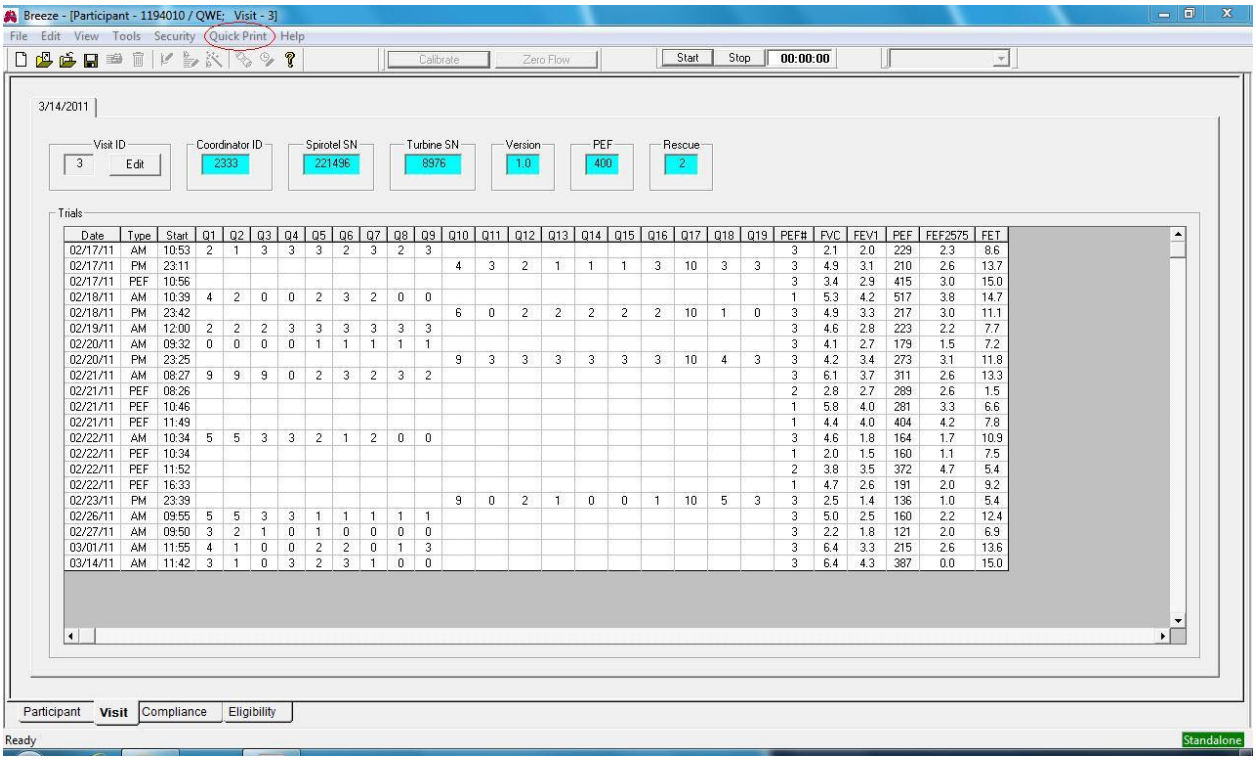


3. Select the corresponding protocol to view the list of spirotel® data saved for that list of protocol participants. Hit the "Refresh" button after selecting a different protocol.
4. The user can sort the list by choosing to sort by: Participant ID, Protocol number, Participant Initials, and Last Visit Date which is the last spirotel® download date for that participant.

5. Select the participant to review his/her spirotel® data.
6. Select the corresponding visit ID.



7. A view will display consisting of a number of tabs associated with the data for each type of participant report. Please refer to the protocol MOP for a description of the protocol-specific reports available for each visit.
    a. The Participant Visit Report will be available for each protocol visit. This report is a data dump of all the information saved in the spirotel® for one visit. The top of the report shows the device configuration data. The body of the report shows all the entered data by trial date (the date an entry was made), trial type (AM, PM or PEF), time the session started, all the diary responses identified by question number, the number of peak flow maneuvers completed, and the spirometry measurements: FVC, FEV_1, PEF, FEF25-75, and FET.
8. To print the participant reports, select the 'Quick Print' option in the toolbar from the Participant Visit screen.
9. Select the protocol-specific reports.
10. The user can choose to print 'All Reports' for the visit, the 'Participant Visit Report' or protocol-specific reports such as eligibility and compliance reports.



Date	Type	Start	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Q14	Q15	Q16	Q17	Q18	Q19	PEF#	FVC	FEV1	PEF	FEF2575	FET
02/17/11	AM	10:53	2	1	3	3	3	2	3	2	3											3	2.1	2.0	229	2.3	8.6
02/17/11	PM	23:11										4	3	2	1	1	1	3	10	3	3	3	4.9	3.1	210	2.6	13.7
02/17/11	PEF	10:56																				3	3.4	2.9	415	3.0	15.0
02/18/11	AM	10:39	4	2	0	0	2	3	2	0	0											1	5.3	4.2	517	3.8	14.7
02/18/11	PM	23:42										6	0	2	2	2	2	2	10	1	0	3	4.9	3.3	217	3.0	11.1
02/19/11	AM	12:00	2	2	2	3	3	3	3	3	3											3	4.6	2.8	223	2.2	7.7
02/20/11	AM	09:32	0	0	0	0	1	1	1	1	1											3	4.1	2.7	179	1.5	7.2
02/20/11	PM	23:25										9	3	3	3	3	3	3	10	4	3	3	4.2	3.4	273	3.1	11.8
02/21/11	AM	08:27	9	9	9	0	2	3	2	3	2											3	6.1	3.7	311	2.6	13.3
02/21/11	PEF	08:26																				2	2.8	2.7	289	2.6	1.5
02/21/11	PEF	10:46																				1	5.8	4.0	281	3.3	6.6
02/21/11	PEF	11:49																				1	4.4	4.0	404	4.2	7.8
02/22/11	AM	10:34	5	5	3	3	2	1	2	0	0											3	4.6	1.8	164	1.7	10.9
02/22/11	PEF	10:34																				1	2.0	1.5	160	1.1	7.5
02/22/11	PEF	11:52																				2	3.8	3.5	372	4.7	5.4
02/22/11	PEF	16:33																				1	4.7	2.6	191	2.0	9.2
02/23/11	PM	23:39										9	0	2	1	0	0	1	10	5	3	3	2.5	1.4	136	1.0	5.4
02/26/11	AM	09:55	5	5	3	3	1	1	1	1	1											3	5.0	2.5	160	2.2	12.4
02/27/11	AM	09:50	3	2	1	0	1	0	0	0	0											3	2.2	1.8	121	2.0	6.9
03/01/11	AM	11:55	4	1	0	0	2	2	0	1	3											3	6.4	3.3	215	2.6	13.6
03/14/11	AM	11:42	3	1	0	3	2	3	1	0	0											3	6.4	4.3	387	0.0	15.0

6.18 Making Edits to Configuration Data

The site coordinators can make edits to the spirotel® configuration data after the data have been converted into the Breeze Suite database on the PC. The site coordinators cannot make any edits to configuration data in the MedGraphics' central database. The data can be changed in two different views in the Breeze Suite software wherever data cells are highlighted in turquoise. Please be careful when making any edits to these data.

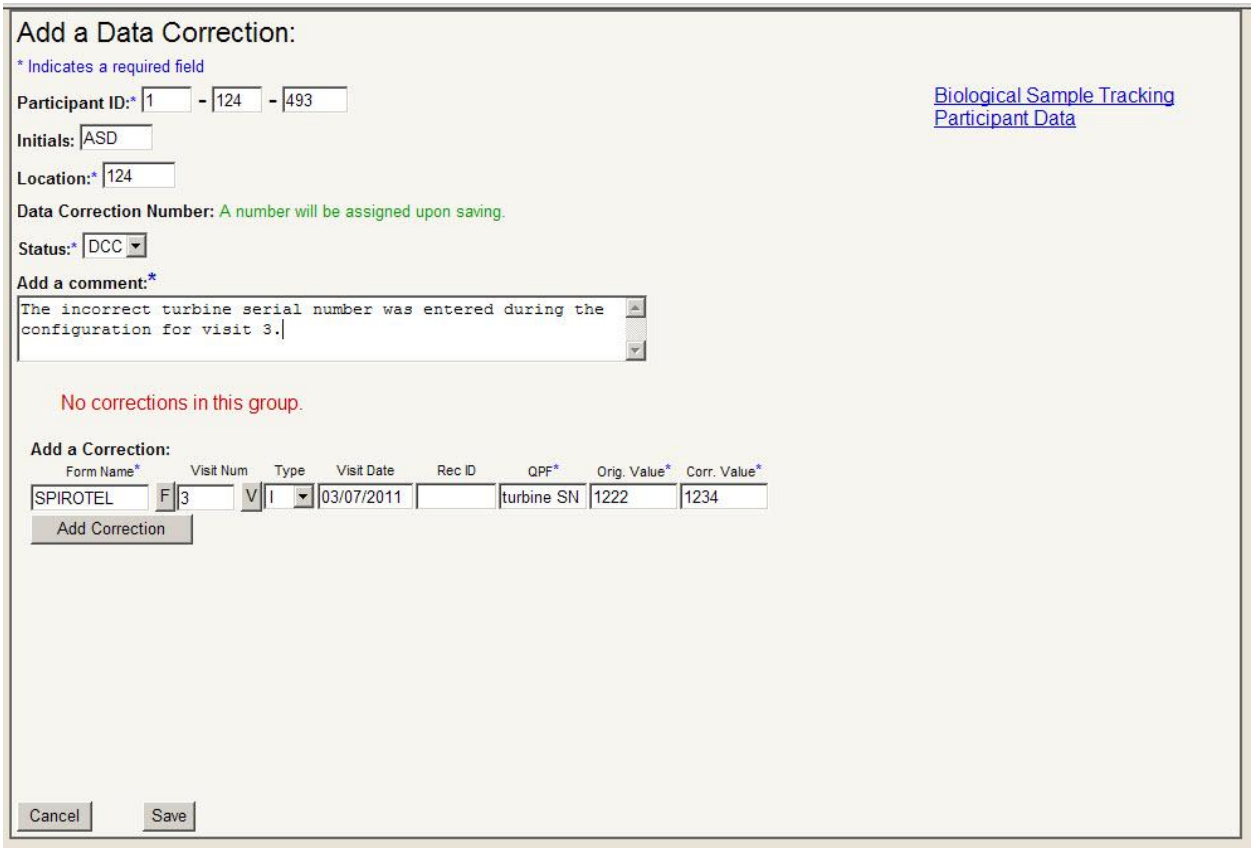
- Participant View. In this view, the user can change the Participant ID, Participant Initials, and other protocol-specific criteria.
- Visit View. In this view, the user can change the Visit ID, Coordinator ID, Turbine Serial Number, Baseline Peak Flow Reference Value (PEF) and Baseline Rescue Use Reference Value (RESCUE). The user should never change the Version number of the software. If the user needs to change the Visit ID number or Download Date (referred to as Visit Date in Breeze), hit the 'Edit' button within the Visit ID box. After this edit is made, you will need to save the visit and then reopen the visit from the Participant View to make any additional edits to the visit configuration data.

The site coordinators cannot make any changes to the spirotel® configuration data in the central database after the data have been transferred (uploaded) to MedGraphics. If the site coordinators determine that spirotel® configuration data must be changed, they should:

- Make the appropriate change to the site's local Breeze Suite database

- Use the Data Correction in the AsthmaNet Data Application to alert the DCC that a change should be made.

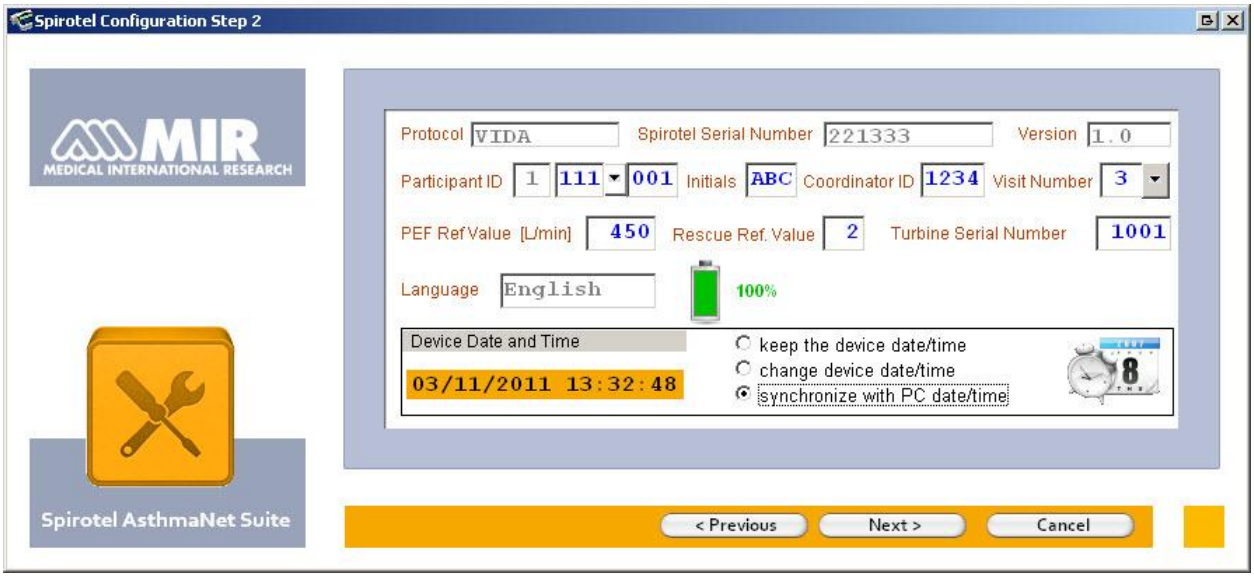
1. Open the Data Corrections module from the Application main menu or from the Protocol main menu using the AsthmaNet secure website.
2. Hit the 'Add New Correction' button.
3. Complete the following fields:
    a. Participant ID
    b. Location – will automatically populate based on participant ID
    c. Status – should default to DCC
    d. Comment – describe reason for data change
    e. Form Name – Hit the 'F' button; Hit the 'View Misc Forms' button; Select 'Spirotel' and then 'OK'
    f. Visit Number
    g. Visit Date
    h. Type – Select 'I'
    i. QPF (Primary Field) – variable name to be changed, i.e., turbine serial number
    j. Original value
    k. Corrected value
4. Hit the 'Add Correction' button.
5. The user can continue to add additional corrections prior to saving the correction. These data corrections should apply to the same participant ID and Visit Number.
6. Hit the 'Save' button when all data corrections have been listed.



6.19 Reconfiguring a spirotel®

Each time a participant returns to the performance site to complete the next scheduled protocol visit, the site coordinator should follow the steps in Section 6.13 to download the session data stored in the spirotel® to the MedGraphics' PC. If the participant is continuing in the protocol, the spirotel® should be configured for the next protocol visit. When configuring the participant's spirotel®, the configuration data entered during the last visit will pre-populate.

- Choose the next return Visit Number.
- Change the Coordinator ID, if necessary, to reflect who is currently configuring the device.
- Refer to the protocol-specific MOP for information as to when the Peak Flow Reference value and Rescue Reference value need to be changed.
- Typically, the current date and time of the device will not need to be edited.
- Change the turbine serial number if the turbine did not pass quality control testing.



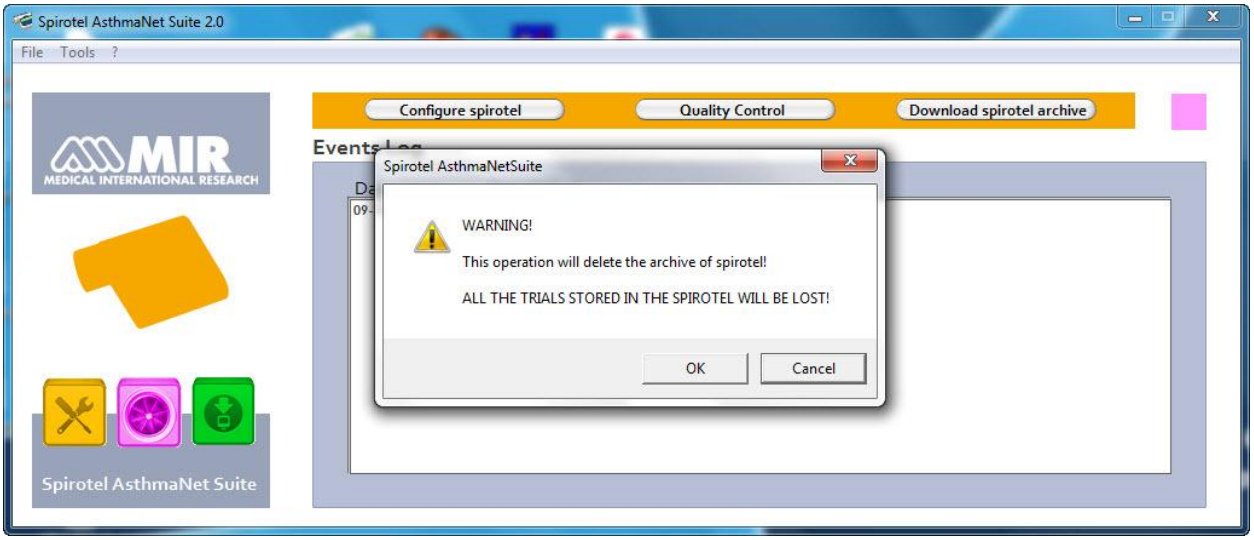
If a participant is returning to the performance site between scheduled protocol visits for evaluation for treatment failure or other protocol-specific instances, the return Visit Number **should not be changed** when configuring the device. The Coordinator ID may need to be changed based on who is reconfiguring the device. If spirotel® data are downloaded more than once with the same Visit Number, the MedGraphics' Breeze Suite database will create multiple tabs to display data associated with each download. All visit-specific participant reports that are printed will include data from all downloads containing the same visit number.

6.20 Deleting Data from a spirotel®

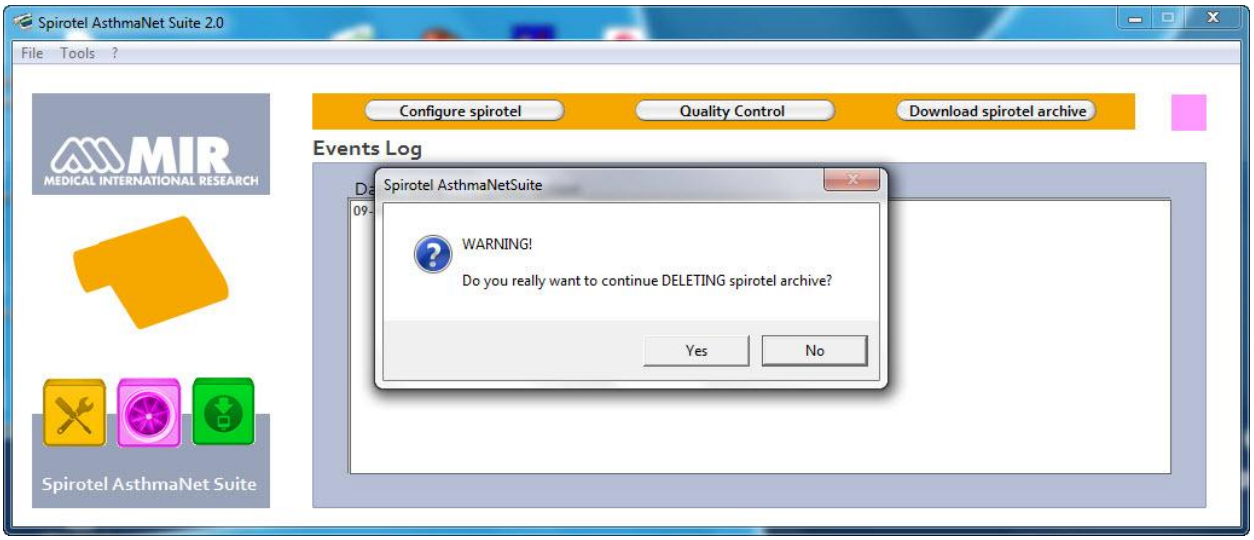
If data are collected and stored on a spirotel® device that should not be part of the Breeze Suite database, the coordinator can delete the spirotel® data from the device without downloading the data to the MedGraphics' PC.

1. Double-click on the Spirotel AsthmaNet Suite icon located on the desktop of the MedGraphics' spirometry PC.
2. Connect the spirotel® to the customized USB adapter cable (converter cable) and the converter cable to the USB port of the MedGraphic's PC and click on the 'Next' button. Warnings will display if the spirotel® is not connected to the converter cable or the converter cable is not connected to the USB port.
3. Select 'DELETE spirotel archive' from the Tools menu.

4. The first warning will appear: This operation will delete the archive of spirotel! ALL THE TRIALS STORED IN THE SPIROTEL WILL BE LOST! Hit 'OK' to continue to delete the stored data.



5. The second warning will appear: Do you really want to continue DELETING spirotel archive? Hit the 'Yes' button to continue to delete the stored data.



6. 'INSERT PASSWORD' will display. Type in the last 5 digits of the spirotel® serial number to initiate the deletion.

6.21 Handling Participant Travel to Different Time Zones

If a participant takes a trip during his/her study participation that requires sleeping for one or more nights in a new time zone, e-diary answers and peak flow measurements should be made within the specified time windows using "local" time. For example, if a participant from the Boston performance site travels to San Francisco for a five-day business meeting, then he/she should perform e-diary and peak flow procedures in the protocol time windows using local San Francisco time. This assumes that the participant will adjust his/her sleep/wake habits to Pacific Time.

To assure that the spirotel® device will accommodate the participant's measurements in the alternate time zone, and to ensure that times reflect when activities were actually performed during the participant's day, the time setting in the device must be changed by performance site personnel just prior to the participant leaving on the trip. Complete the following steps to change the spirotel® date and time prior to and following the participant's travel.

- Download the stored data from the spirotel® to the MedGraphics' PC completing steps 1 through 9 in Section 6.13.
- Configure the device using the Spirotel AsthmaNet Suite software. Do not change any of the previously entered configuration data.
- Select the radio button, 'change device date/time'.
- Set the time (and change the date, if necessary).

6.22 Calibrating the 3-Liter Syringe

The calibration of the 3-L syringe used to perform quality control testing of the spirotel® devices must be up-to-date at all times. Please note that there are stickers attached to the underneath of the calibration syringe. One sticker has the manufacturer's information: A-M Systems with the company's address. The second sticker has the calibration date printed on it and the recalibration due date. The third sticker contains the serial number, product number, and manufacture date.

When the syringes become due for calibration, contact A-M Systems for an RMA number and provide the company with the serial number(s) of the calibration syringe(s) you will be forwarding to them. There is a calibration fee. You will also need to purchase an additional syringe through A-M's special program so the performance site will always have a backup unit. A-M will ship the new syringe. Box up the syringe that is due for servicing and send it into A-M Systems.

Please indicate that the performance site is part of the AsthmaNet.

Contact Person:

Trish Winkelman
trish@a-msystems.com
1-800-426-1306

Shipping Address (For Packages)

A-M Systems
131 Business Park Loop
Sequim, WA 98382-8338

6.23 Changing the Lithium Battery in the spirotel® I

The expected life of the lithium battery in the INFANT devices is approximately 6 months. When the spirotel® I is turned on, the battery strength will be displayed on a scale of 1 to 4 (using battery icons). If the battery is completely discharged, the warning message 'LOW BATTERY/Call coordinator' will display. If the battery strength is low, consider changing the battery prior to distributing the spirotel® to a participant whose returning visit may be several weeks in the future. Change the battery if the device does not turn on. When inserting the new battery, pay close attention to the polarity +/- shown inside the battery cover.

The original battery in the spirotel is a Sanyo #CR123A 3-volt lithium. However, you can order the same part number for batteries manufactured by Rayovac, Panasonic, etc. If a performance site does not have a source to purchase the batteries, Respitech stocks the Rayovac #CR123A. See Section 6.24 below.

6.24 Additional Supplies

The following supplies can be purchased from Respitech Medical, Inc., 250 Ranck Avenue, Lancaster, PA 17602, 1-800-399-0250:

- Mouthpieces – 100 per box
- Lithium batteries
- Converter cables
- Adapters for 3-liter syringe

6.25 Spirotel® Certification for Peak Flow and E-Diary Protocols

Individuals must be certified in using the spirotel® device before they can configure a device for distribution to an AsthmaNet participant, perform quality control testing on a device, process spirotel® data from downloading the data from the device to eventually uploading the data to the MedGraphics' central database. The following steps must be completed to become certified:

1. Review the Spirotel® Manual, Appendix 6 of the AsthmaNet General MOP.
2. Review the *How to Use Your spirotel® Electronic Diary and Peak Flow Meter* (HTSPIROTEL) handout.
3. Dispense a spirotel® for your own use. Complete the *Spirotel® Device Log* (SPIROTEL_DEVICE) and the *Spirotel® Turbine Log* (SPIROTEL_TURBINE). The device and turbine logs used for certification should be kept separately from the logs used for the AsthmaNet protocols.
4. Configure a BARD/SIENA/STICS device with the protocol you will be primarily working on using the Spirotel® AsthmaNet Suite software. Create a participant ID ending with '499' for the first certification at your site. Continue to create new participant IDs by counting down from 499. For example, the second participant ID should end with '498.' The user must enter his/her 4-digit coordinator ID during configuration.
5. Perform Quality Control Testing and print out the *Spirotel® Quality Control* (SPIROTELQC) form.
6. Take the spirotel® home and perform AM and PM scheduled sessions along with a few unscheduled peak flows until you have completed 5 scheduled AM and 5 scheduled PM sessions. Refer to the protocol specific coordinator reference card (P#_SPIROTEL_CREF) for session windows and full question text. Download the data to the MedGraphics' PC using the Spirotel® AsthmaNet Suite software.

7. Convert the spirotel® file to the MedGraphics' Breeze Suite Database using DBTools.
8. Open the participant's spirotel® visit data in the MedGraphics' Breeze Suite database and print out the corresponding Participant Report.
9. Complete the Spirotel® Certification exam posted on the AsthmaNet web site at Home: Certification: spirotel®.
10. Scan the completed exam, SPIROTELQC form, and the Participant Report.
11. E-mail the scanned images to AsthmaNet-Certification@phs.psu.edu. In the subject line of the e-mail, type 'spirotel certification, site number, and coordinator id number.'
12. Delete the participant visit from the MedGraphics' Breeze Suite database.
13. Clean the turbine for future use.

The DCC will inform you when you have been certified. When configuring a spirotel device for participant use in a specific protocol, a coordinator must have spirotel certification as well as certification in that protocol.

6.26 Spirotel® Certification for E-Diary Only Protocols

Individuals must be certified in using the spirotel® device before they can configure a device for distribution to an AsthmaNet participant, process spirotel® data from downloading the data from the device to eventually uploading the data to the MedGraphics' central database. The following steps must be completed to become certified:

1. Review the Spirotel® Manual, Appendix 6 of the AsthmaNet General MOP.
2. Review the How to Use Your spirotel® Electronic Diary and Peak Flow Meter handout.
3. Dispense a spirotel® for your own use. Complete the *Spirotel® Device Log* (SPIROTEL_DEVICE). The device log used for certification should be kept separately from the log used for the AsthmaNet protocols.
4. Configure the protocol-specific device using the Spirotel® AsthmaNet Suite software. Create a participant ID ending with '999' for the first certification at your site. Continue to create new participant IDs by counting down from 999. For example, the second participant ID should end with '998.' The user must enter his/her 4-digit coordinator ID during configuration.

5. Take the spirotel® home for 5 days and complete the daily diary session each day.
6. After 5 days, download the data to the MedGraphics' PC using the Spirotel® AsthmaNet Suite software.
7. Convert the spirotel® file to the MedGraphics' Breeze Suite Database using DBTools.
8. Open the participant's spirotel® visit data in the MedGraphic's Breeze Suite database and print out the corresponding Participant Report.
9. Complete the E-diary only Spirotel® Certification exam posted on the AsthmaNet web site.
10. Scan the completed exam and the Participant Report.
11. E-mail the scanned images to AsthmaNet-Certification@phs.psu.edu. In the subject line of the e-mail, type 'spirotel certification, site number, and coordinator id number.'
12. Delete the participant visit from the MedGraphics' Breeze Suite database.

The DCC will inform you when you have been certified. When configuring a spirotel device for participant use in a specific protocol, a coordinator must have spirotel certification as well as certification in that protocol.

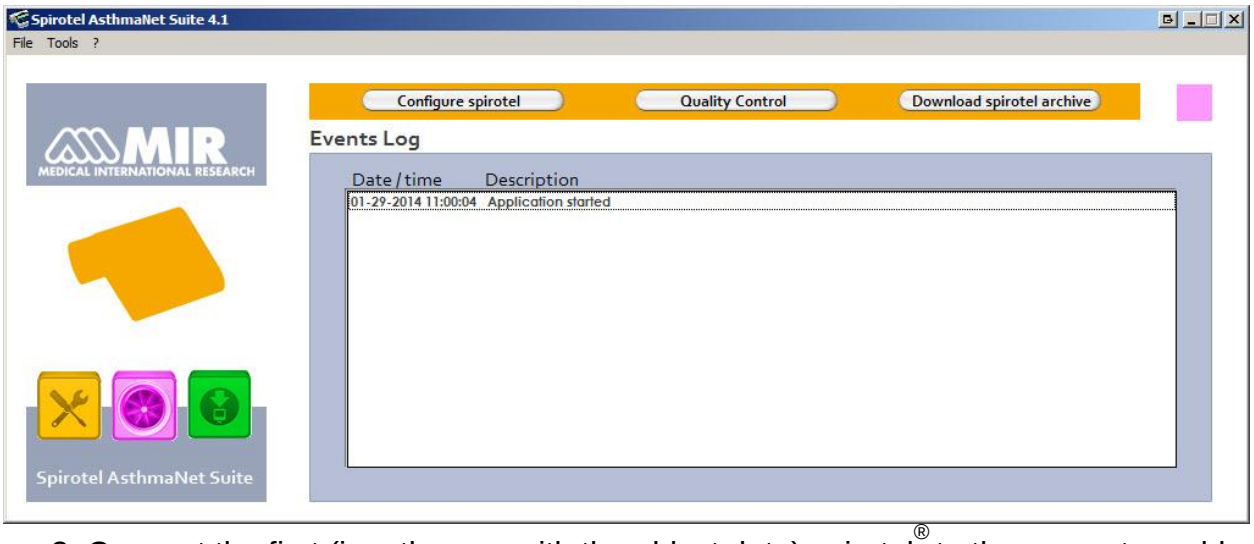
6.27 Troubleshooting

6.27.1 How to download two spirotel® devices at the same visit

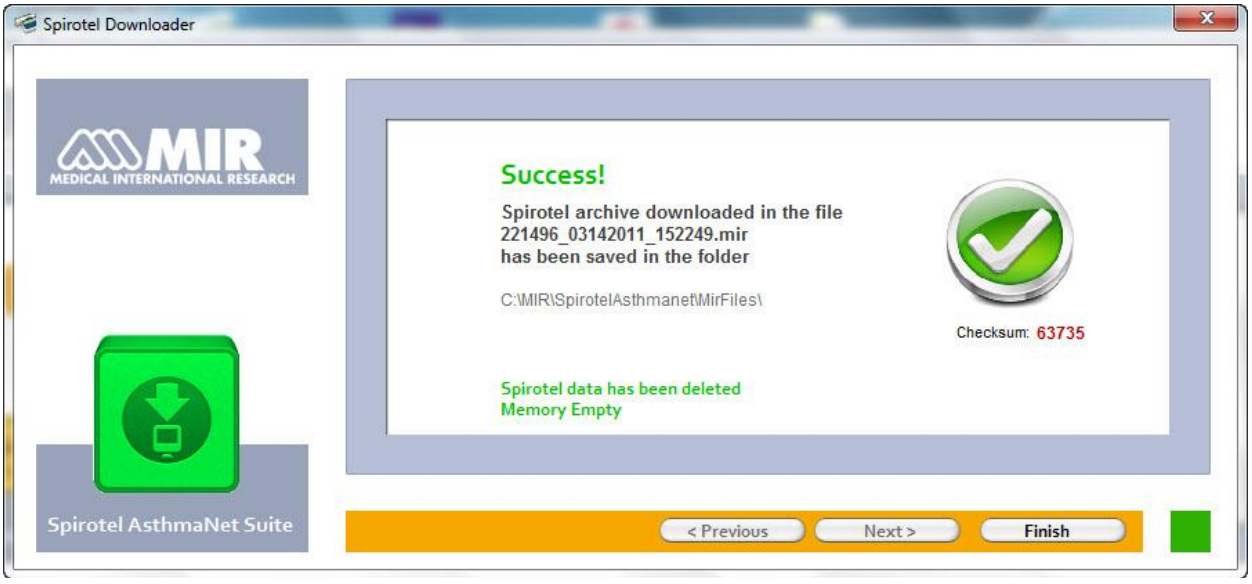
This issue happens when a participant brings more than one spirotel device to a visit to be downloaded on the same day. **This section should be reviewed prior to downloading either device.**

Download 1st spirotel® to the MedGraphics' PC

1. Open the Spirotel AsthmaNet Suite software on the MedGraphics PC.
2. Select the 'Download spirotel archive' option.



3. Connect the first (i.e., the one with the oldest data) spirotel® to the converter cable and the converter cable to the PC's USB port.
4. Click 'Next'.
5. A checksum value will appear on the spirotel® display.
6. Verify that the checksum value on the spirotel® display matches the checksum value in the message from the Spirotel AsthmaNet Suite software.

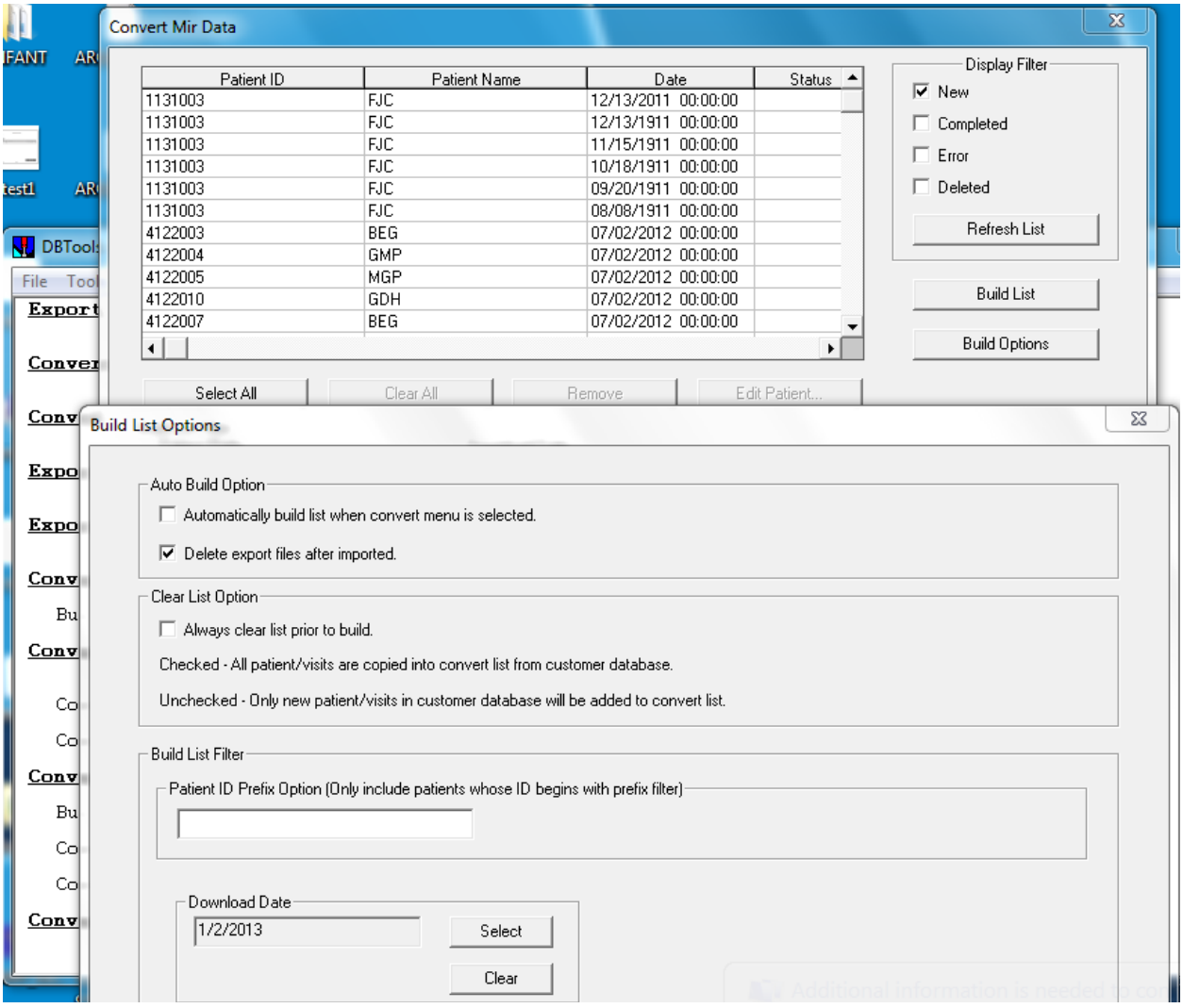


7. If the values do not match, contact the protocol primary data manager.
8. The name of the downloaded file will be formatted as spirotel serial number_month_day_year_time (including hour, minute and seconds)." The date and time represents the date and time the data were downloaded. The file will be stored in a hidden file folder.

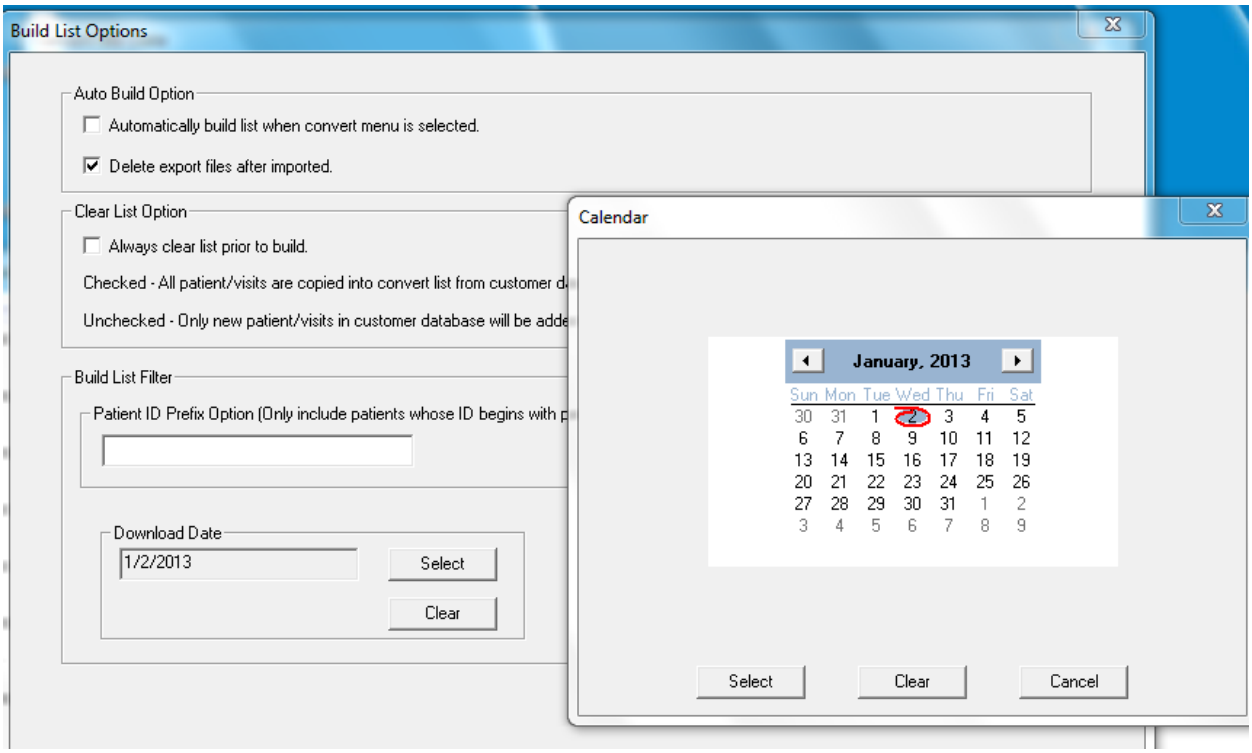
Convert Data from 1st spirotel® to the Site's Local Breeze Suite Database

NOTE: DO NOT SELECT 'BUILD LIST' BUTTON UNTIL STEP 9.

1. Open the DBTools software on the MedGraphics' PC
2. Leave the User Name as 'Admin' and hit the 'OK' button without entering a password
3. Select Tools → Convert Visit From→ Mir Data
4. The Data Path Name should be C:\MIR\SpirotelAsthmaNet\MirFiles. **DO NOT CHANGE THIS PATH NAME.** If the path name is changed, please contact the protocol primary data manager at the DCC.
5. Select the Build Options button
6. Under the heading Build List Filter and subheading Download Date, select the Select button



7. Select the day ***prior to the current date*** on the calendar and select the Select button



8. Select the OK button
9. Hit the 'Build List' button.
10. A list of all MIR files with a download date of the selected calendar day should be populated.
11. Select the file for the Participant
12. Hit the 'Convert' button at the bottom left of the screen.
13. Close DBTools.

Download 2nd spirotel® to the MedGraphics' PC

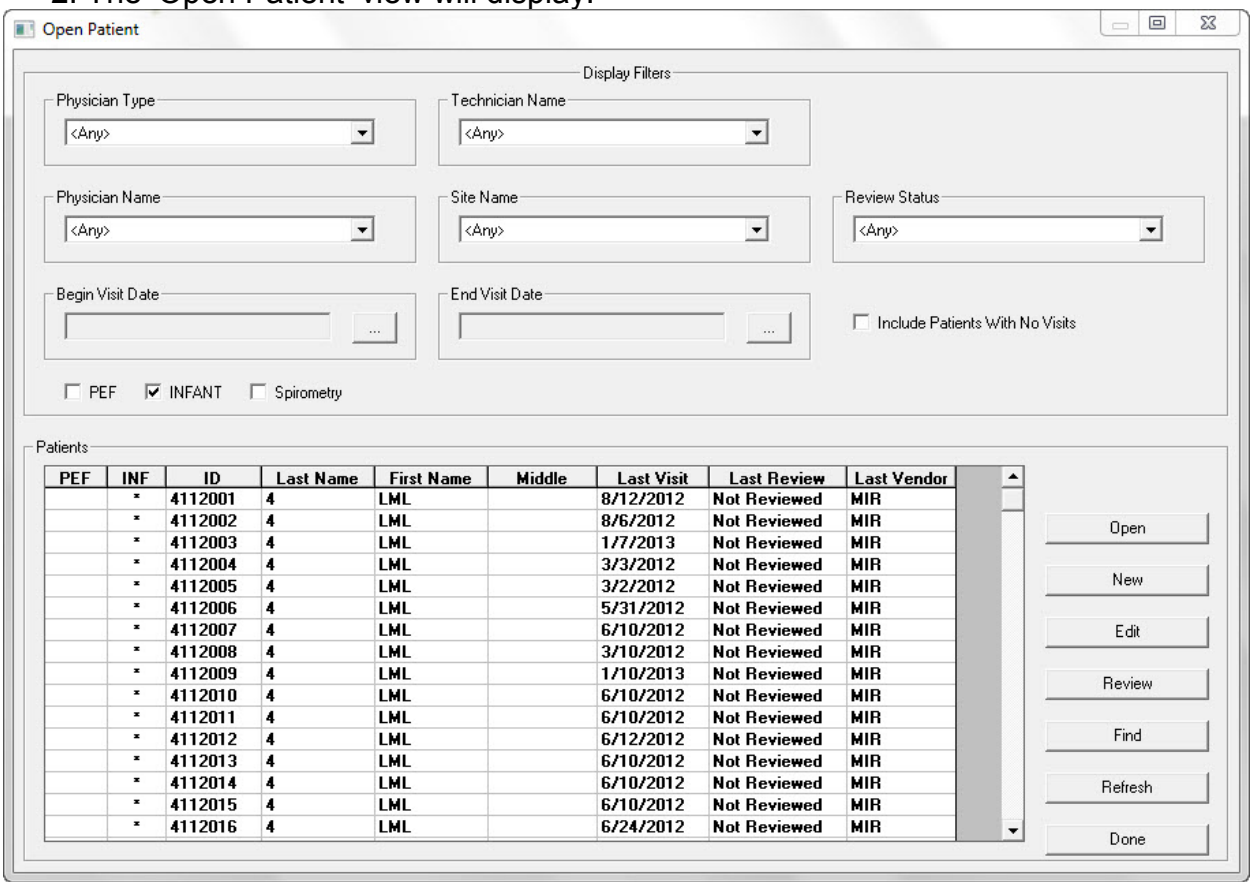
1. Open the Spirotel AsthmaNet Suite software on the MedGraphics PC.
2. Select the 'Download spirotel archive' option.
3. Connect the spirotel® to the converter cable and the converter cable to the PC's USB port.
4. Click 'Next'.
5. A checksum value will appear on the spirotel® display.
6. Verify that the checksum value on the spirotel® display matches the checksum value in the message from the Spirotel AsthmaNet Suite software.
7. If the values do not match, contact the protocol primary data manager.
8. The name of the downloaded file will be formatted as spirotel serial number_month_day_year_time (including hour, minute and seconds)." The date and time represents the date and time the data were downloaded. The file will be stored in a hidden file folder.

Convert Data from 2nd spirotel® to the Site's Local Breeze Suite Database

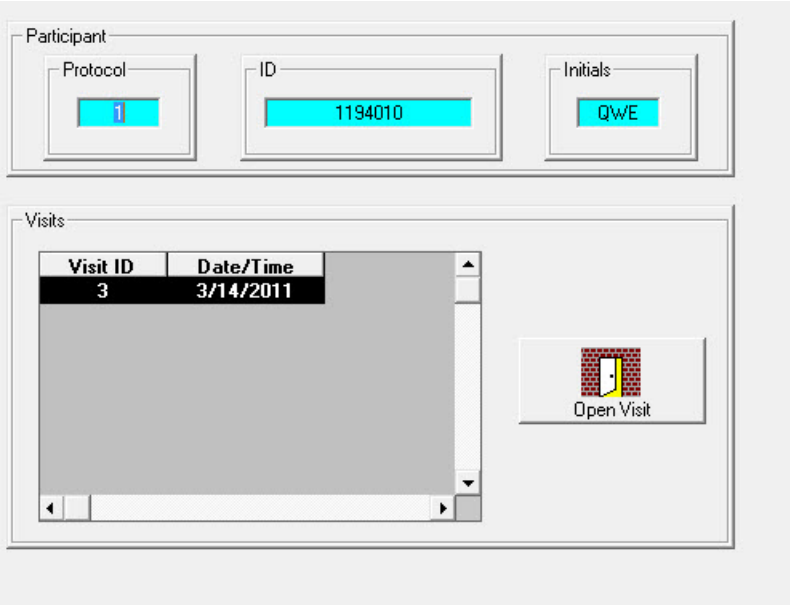
1. Open DBTools.
2. Leave the User Name as 'Admin' and hit the 'OK' button without entering a password
3. Select Tools → Convert Visit From → Mir Data
4. The Data Path Name should be C:\MIR\SpirotelAsthmaNet\MirFiles. **DO NOT CHANGE THIS PATH NAME.** If the path name is changed, please contact the protocol primary data manager at the DCC.
5. Hit the 'Build List' button.
6. A list of all MIR files with a download date of the current calendar day (day of current visit) should be populated.
7. Select the file for the Participant
8. Hit the 'Convert' button at the bottom left of the screen.
9. Close DBTools.

Viewing Participant Data and Printing Reports

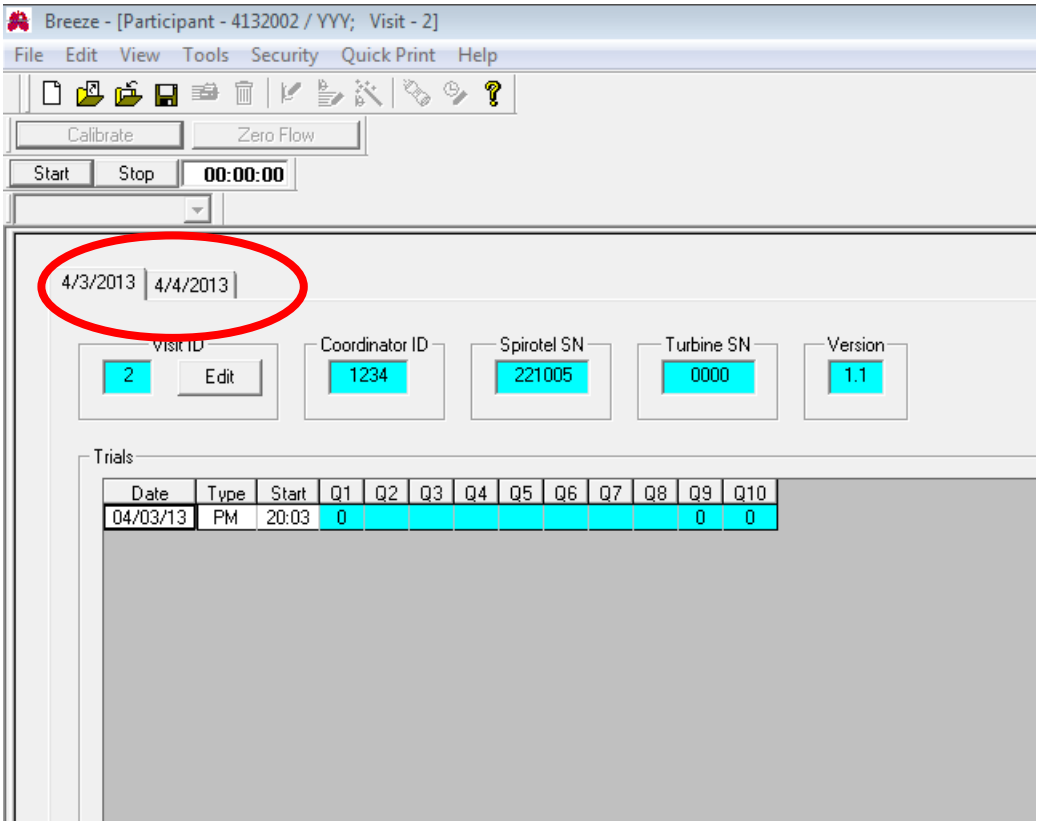
1. Open the Breeze Suite software on the MedGraphics' PC.
2. The 'Open Patient' view will display.



3. Select the appropriate protocol.
4. Select the participant to review his/her spirotel® data.
5. Select the corresponding visit ID.



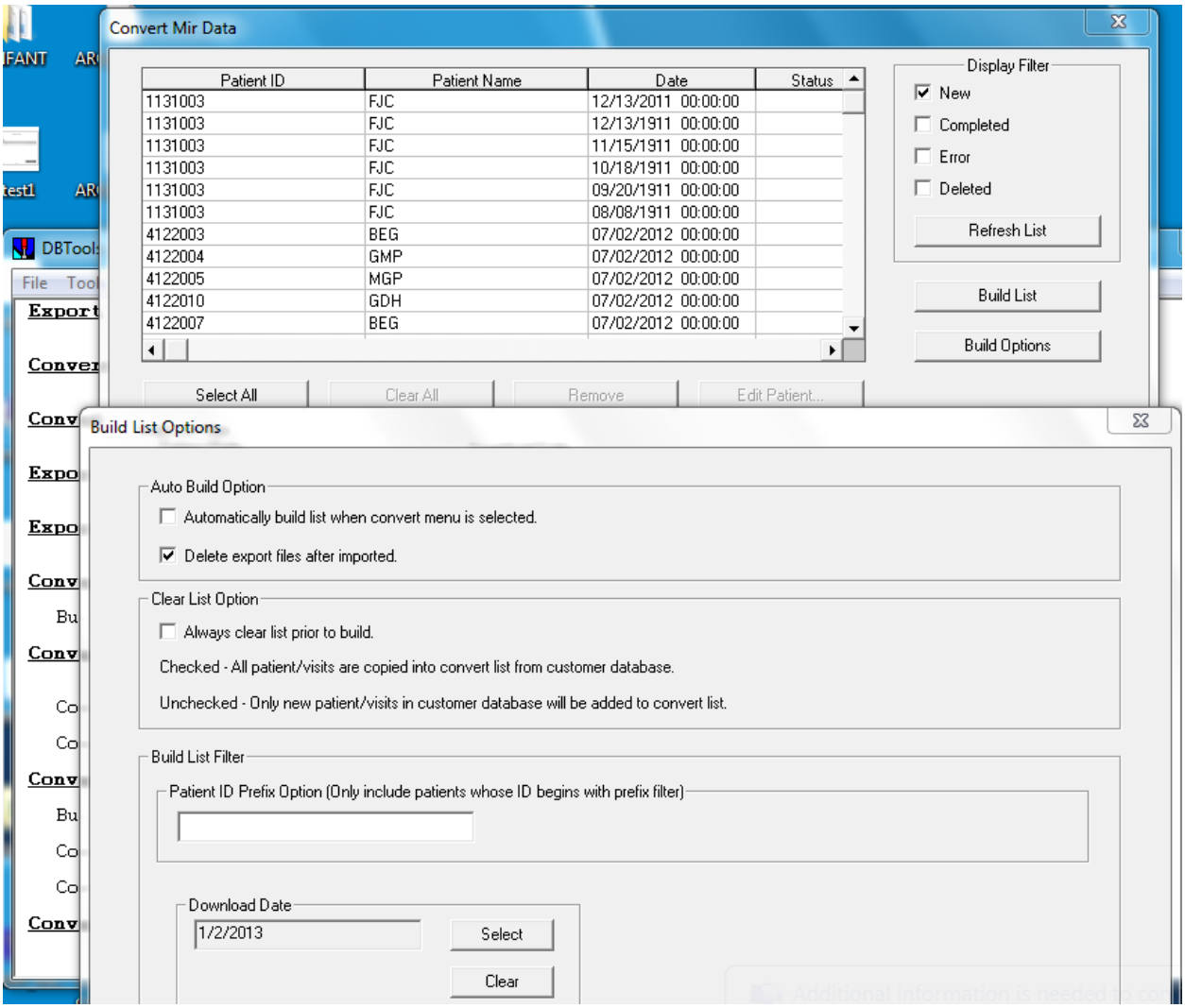
When you open the visit you will see two tabs representing the two download dates. Any reports that are generated will combine the data from both downloads.



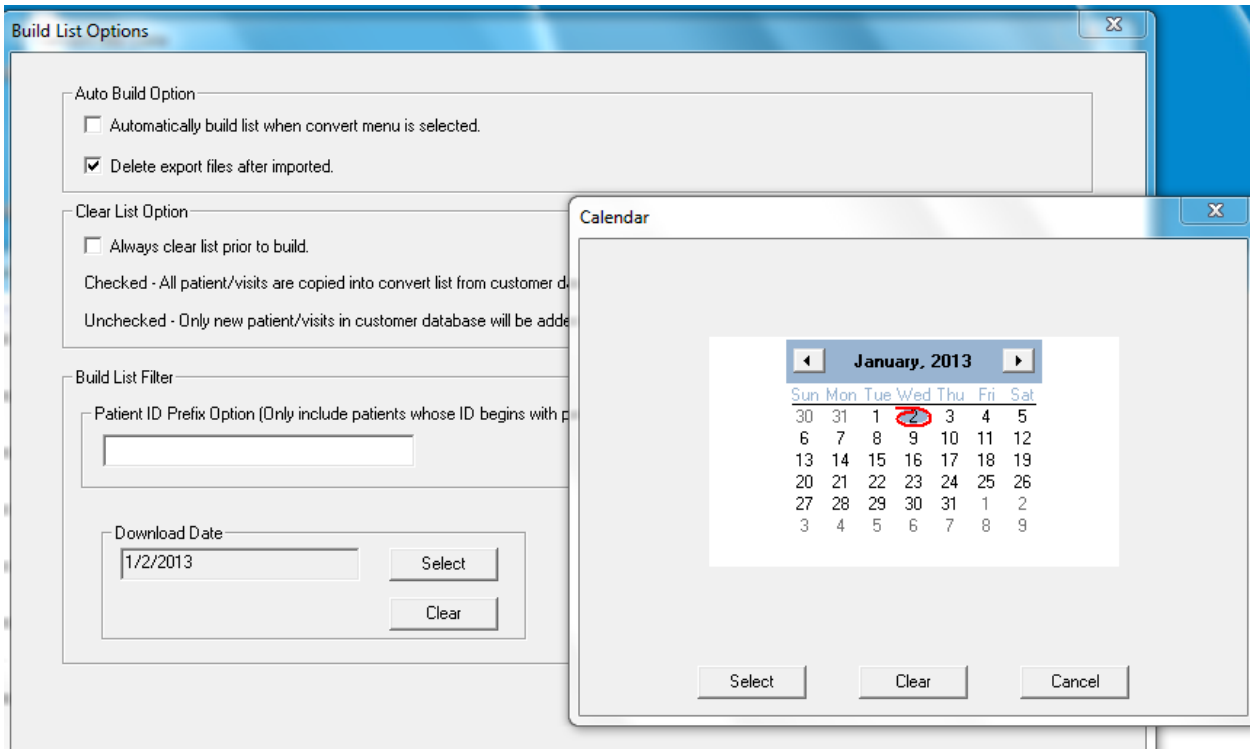
6.27.2 Changing the spirotel® Download Date in DBTools

1. Open the DBTools software on the MedGraphics' PC
2. Leave the User Name as 'Admin' and hit the 'OK' button without entering a password

3. Select Tools → Convert Visit From→ Mir Data
4. The Data Path Name should be C:\MIR\SpirotelAsthmaNet\MirFiles. **DO NOT CHANGE THIS PATH NAME.** If the path name is changed, please contact the protocol primary data manager at the DCC.
5. Select the Build Options button
6. Under the heading Build List Filter and subheading Download Date, select the Select button



7. Select the appropriate day on the calendar and select the Select button



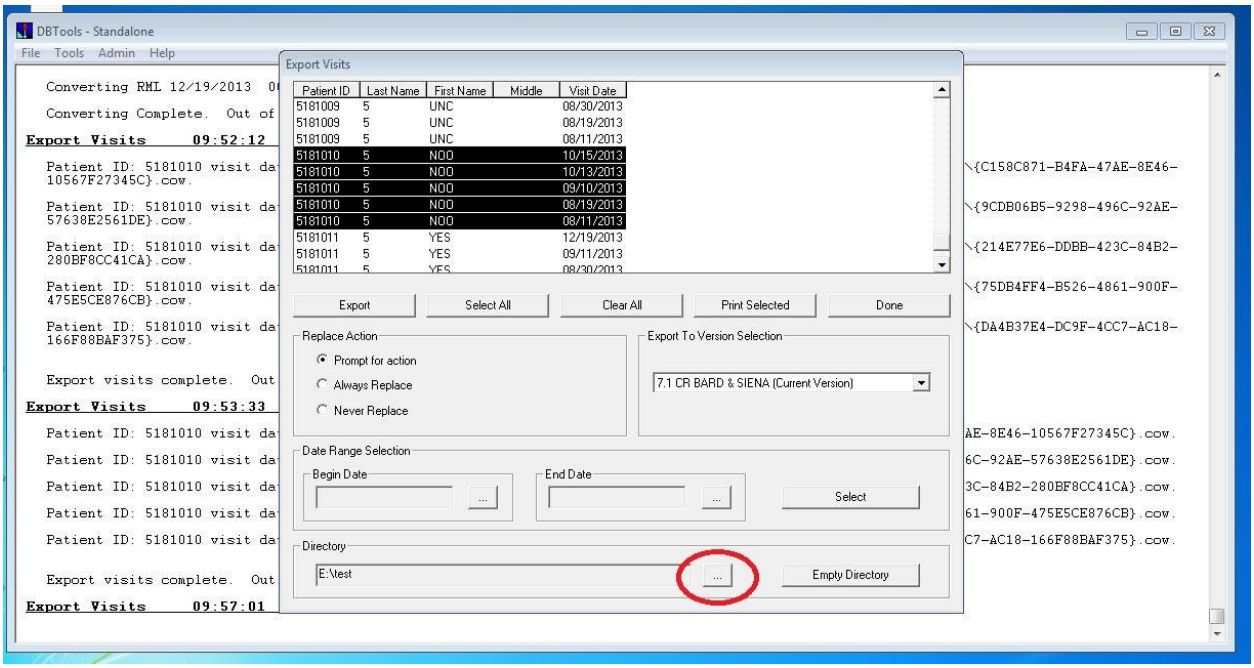
8. Select the OK button
9. Hit the ‘Build List’ button.
10. A list of all MIR files with a download date of the selected calendar day should be populated.
11. Select the file for the Participant
12. Hit the ‘Convert’ button at the bottom left of the screen.
13. Continue with steps to upload data to Medgraphics.

6.27.3 How to transfer spirotel® data to a different site for a transfer participant

Exporting spirotel® Data Using DTBOOLS
(Instructions for site in which participant is leaving)

1. Open the DBTools software on the MedGraphics' PC.
2. Leave the User Name as 'Admin' and hit the 'OK' button without entering a password
3. Select Tools → Export→ Patients
4. Specify the Export Directory (see Image 1). Can use the Desktop or a flashdrive.
5. Select Patient ID column heading to sort by Patient ID
6. Highlight the rows to be exported and select Export
7. ".COW" files will be exported to the location specified in step 4.

Image 1:



6.27.4 Importing spirotel® Data Using DTBOOLS
(Instructions for site in which participant is transferring)

1. Open the DBTools software on the MedGraphics' PC.
2. Leave the User Name as 'Admin' and hit the 'OK' button without entering a password
3. Connect the flashdrive containing the .COW files to the laptop
4. Select Tools → Import→ Patients
5. Specify the Import Directory as the location of the flashdrive in step 3 (see Image 2).

6. Select the Patient IDs or click Select All.
7. Select Import/Restore.
8. Spirotel data will be available when Breeze is opened.

Image 2: