4 STUDY FORMS AND INSTRUCTIONS

This section provides information about two types of forms: data collection forms and administrative forms. Data collection forms are used to collect data from or about the participant. These forms are entered into the AsthmaNet database and submitted to the DCC. Administrative forms facilitate the processing of the participant and the visit flow by the performance sites and the DCC. Administrative forms are not entered into the AsthmaNet database and they are not submitted to the DCC in most cases.

These instructions are divided into two parts—instructions for data collection forms followed by instructions for administrative forms. The instructions for both parts are in alphabetical order based on the full form name found in the header of the form. Forms with a 'P6' prefix are specific to the SIENA protocol.

For each form, the following information is provided: the purpose of the form, who completes the form, when the form should be completed, and form instructions. Most forms have a comments section (Q6000) at the bottom of the form. The coordinator can record additional comments or information related to the form in this section. This information is entered into the AsthmaNet database management system. If you are unable to find the specific information needed to complete a form, please contact the SIENA Primary or Secondary Data Manager at (717) 531-3663.

This section also includes SIENA-specific guidance for interacting with the spirotel II device and MedGraphics software.

4.1 SIENA Data Collection Forms

Packet data forms are found in visit-specific packets, and they are submitted to the DCC as packets. Individual data forms (single forms) are submitted on an as-needed basis. Concurrent forms (AECLIN, CMED) are completed at each study visit and can be updated throughout the SIENA study. All concurrent forms should be submitted when the participant concludes his or her participation in the SIENA study. Some forms (e.g., SIENA Scheduled Medications (P6_MED)) can be submitted as part of a visit packet or as a single form, depending on the specific circumstances. The schematic of the SIENA visit structure is posted as a sub-item to this section on the website.

4.1.1 Acute Asthma Assessment Questionnaire (AAAQ)

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

Who: The participant completes this form.

When: Visits 3, 90-92, 90A-92A, 90B-92B, 90C-92C, 90D-92D

Form Instructions:

To introduce the questionnaire to the participant and to establish a baseline, the Acute Asthma Assessment Questionnaire (AAAQ) will be administered at the initial randomization study visit (Visit 3).

An AAAQ will be included in the Asthma Exacerbation Kit to be completed at home by the participant on the day he/she starts prednisone for an asthma exacerbation (or in-clinic if Day 0 occurs at an FEV_1 re-assessment visit). Additional AAAQ forms will be completed at the in-clinic asthma exacerbation visit (90A, 91A, or 92A), and the subsequent asthma exacerbation phone contacts (90B-92B, 90C-92C, 90D-92D).

When preparing an Asthma Exacerbation Kit or refill packet, pre-fill the participant's ID, initials and visit ID prior to distributing the forms to the participant. When the participant returns forms completed at home, review the forms prior to the participant leaving the clinic to ensure that the participant completed the forms correctly. **The coordinator should complete the visit date based on the source documentation date. If the source documentation is not present or not decipherable with the participant's assistance, the form should not be entered.** The Coordinator ID on the forms should be completed by the coordinator collecting and reviewing the form.

Participant completed forms should always be reviewed by the coordinator upon completion/receipt. 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.

See the Acute Asthma Assessment Questionnaire and Asthma Exacerbation Kit discussions in Section 2 for further details.

4.1.2 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 the form.

When: Visits 3, 5, 7, 9, 90-92, 90B-92B, 90C-92C, 90D-92D

Form instructions:

To introduce the questionnaire to the participant and to establish a baseline, the Asthma-Specific Work Productivity and Activity Impairment Questionnaire (WPAI_ASTHMA) will be administered to participants at the initial randomization study visit (Visit 3).

A WPAI_ASTHMA form will be included in the Asthma Exacerbation Kit to be completed at home by the participant on the day he/she starts prednisone for an asthma exacerbation (or in-clinic if Day 0 occurs at an FEV_1 re-assessment visit). Additional WPAI_ASTHMA forms will be completed during the subsequent asthma exacerbation phone contacts (90B-92D).

When preparing an Asthma Exacerbation Kit or refill packet, pre-fill the participant's ID, initials and visit ID prior to distributing the forms to the participant. When the participant returns forms completed at home, review the forms prior to the participant leaving the clinic to ensure that the participant completed the forms correctly. **The coordinator should complete the visit date based on the source documentation date. If the source documentation is not present or not decipherable with the participant's assistance, the form should not be entered.** The Coordinator ID on the forms should be completed by the coordinator collecting and reviewing the forms.

In addition to forms completed at Visits 3, 5, 7 and 9, for participants completing the significant asthma exacerbation packets (90-92, 90B-92B, 90C-92C, 90D-92D), upon obtaining the completed-at-home WPAI_ASTHMA form at the next clinic visit, the coordinator should transcribe the participant's answer to Q4, Q8 and Q9 in the 'Coordinator Completed' box next to each question (Q1030, Q1070, Q1080, respectively).

Participant completed forms should always be reviewed by the coordinator upon completion/receipt. 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.

See the Work Productivity and Activity Impairment Questionnaire and Asthma Exacerbation Kit discussions in Section 2 for further details.

4.1.3 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: Visits 0A, 0B, 1-9

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:

Clinical adverse events that started in between visits but were reported by the participant at the following regular visit should be recorded on the current visit's AECLIN form. For example, events started in between Visit 3 and Visit 4 and reported at Visit 4 would get recorded on the Visit 4 AECLIN form.

If the participant contacts the clinic coordinator between visits, record the new event(s) on the AECLIN form completed at the last regular visit. This new event should be updated in the Participant Data module within the data management application. The same applies for events reported at the significant asthma exacerbation visits – the new event(s) should be recorded on the AECLIN form completed at the last regular visit. The new event(s) should be updated in the Participant Data module within the data management application.

For more information on recording Clinical Adverse Events (AECLIN), see Section 10 of the AsthmaNet General MOP.

4.1.4 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: Visits 0A, 0B, 1-9

Note: This form should be completed if the participant 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:

Concurrent medications that were started in between visits but were reported by the participant at the following regular visit should be recorded on the current visit's CMED form. For example, medications started in between Visit 3 and Visit 4 and reported at Visit 4 would get recorded on the Visit 4 CMED form.

If the participant contacts the clinic coordinator between visits, record the new medication(s) on the CMED form completed at the last regular visit. This new medication should be updated in the Participant Data module within the data management application. The same applies for medications reported at the significant asthma exacerbation visits – the new medication(s) should be recorded on the CMED form completed at the last regular visit. The new medication(s) should be updated in the Participant Data module within the data management application.

For participants completing the Supervised Washout visits for SIENA, their medication and use should be recorded on the Concomitant Medications for Asthma/Allergy and Adverse Events (CMED) form. For example, if a participant signs the informed consent on the day he/she completes Visit 0A, the medication would not be recorded on the CMED form until date of Visit 0B (or Visit 1). If a participant signs the informed consent prior to the date of Visit 0A completion, the medication can be recorded on the Visit 0A CMED form. In both cases, the start date of the medication should be the informed consent date.

If the participant is taking allergy shots or has received any vaccines, these should be noted on the CMED_NON form and not recorded on the CMED form.

For more information on recording Concomitant Medications for Asthma/Allergy and Adverse Events (CMED), see Section 10 of the AsthmaNet General MOP.

4.1.5 Adult Methacholine Challenge Testing Checklist (METHACHK_ADULT) and Pediatric Methacholine Challenge Testing Checklist (METHACHK_PED)

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

Who: A Pulmonary Function Technician completes the form.

When: Visit 1 (Single form – Only for those completing continuation visit)

Form Instructions:

For participants age 12-17, the pediatric version of the checklist (METHACHK_PED) should be completed. For participants age 18+, the adult version of the checklist (METHACHK_ADULT) should be completed.

Question 1050. Refer to the Concomitant Medications for Asthma/Allergy and Adverse Events (CMED) form, the SIENA Significant Asthma Exacerbation (P6_SIGEX) form and the SIENA Asthma Monitoring Log (P6_ASTHMA_LOG) for records regarding systemic corticosteroid use for the treatment of an asthma exacerbation in the last 4 weeks.

For more information on the Adult Methacholine Challenge Testing Checklist (METHACHK_ADULT) or Pediatric Methacholine Challenge Testing Checklist (METHACHK_PED), see Section 10 of the AsthmaNet General MOP. For additional instructions for the SIENA protocol, see the Methacholine Challenge discussion in Section 2 of this MOP.

4.1.6 Genetics Analysis Blood Draw (GABLOOD)

Purpose: To record information related to a participant's genetic analysis blood draw.

Who: An AsthmaNet coordinator completes the form.

When: Visit 2 or at a later visit, if necessary

Form Instructions:

The Genetic Analysis Blood Draw form (GABLOOD) should be completed for most participants at the time of Visit 2 when the blood draw is first attempted. If the blood draw is successful, this form is entered at Visit 2 as a packet form.

If the genetics blood draw is not done at Visit 2, but is instead deferred to a later visit in the SIENA study, the Visit 2 packet Genetics Analysis Blood Draw (GABLOOD) form should be marked missing. The Genetics Analysis Blood Draw (GABLOOD) form should be completed and entered as a single form for the visit at which the blood draw takes place.

If the participant terminates early from the study and never completes a blood draw at a subsequent visit, submit a data correction to have the Visit 2 Genetics Analysis Blood Draw (GABLOOD) form set to present. Q1000 and Q1010 should be completed, indicating that a blood sample was not obtained. When the data correction is submitted through the AsthmaNet application, complete the form and send a copy of the Genetics Analysis Blood Draw (GABLOOD) form for Visit 2 to the DCC for first and second entry. A subsequent blood draw could also be missing because the participant is deemed ineligible or consent is withdrawn.

If the blood draw is attempted at Visit 2 but is unsuccessful, and the participant is unwilling to have another draw attempted at a future visit, then the Genetics Analysis Blood Draw (GABLOOD) form should be completed and data entered as part of the Visit 2 packet. In that case, Q1000 and Q1010 should be completed, indicating that a blood sample was not obtained, and the participant should provide source documentation.

See the Genetics Blood Draw discussion in Section 2 for more details on the genetics analysis blood draw and Appendix 4 of the AsthmaNet General MOP for more details on the Genetics Analysis Blood Draw (GABLOOD) form.

4.1.7 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: Visits 0A, 0B, 1-9, 90A-92A

Form Instructions:

Question 1020. Open-label mometasone, and blinded Respimat® and Twisthaler®/MDI given out as part of the study should be considered "study drug" when answering this question. Rescue prednisone is not considered a "study drug".

For more information on the Serious Adverse Event Reporting Form (SERIOUS), see Section 10 of the AsthmaNet General MOP.

For further details on the reporting of adverse events in the SEINA trial, see the Adverse Events discussion in Section 2 of this MOP.

4.1.8 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: Visits 0A, 0B, 1-9, 90A-92A

Form Instructions:

If the Spirometry Testing (SPIRO) form is completed between visits at an FEV_1 re-assessment visit, specify the number of the last visit completed and the current visit date in the upper right-hand corner. This form should be entered as a single form.

If methacholine challenge is completed at a Visit 1 Continuation visit, the single Spirometry Testing Report (SPIRO_RPT) should be marked 'No' in the database. The single 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 at Visit 1 or 2A, 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 at Visit 2, 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.

For more information on the Spirometry Testing (SPIRO) form, see Section 10 of the AsthmaNet General MOP.

4.1.9 SIENA Baseline PEF and Rescue Use Values (P6_BASELINE)

Purpose: The participant's baseline peak flow (PEF) and baseline rescue use values are recorded on this form.

Who: An AsthmaNet coordinator completes the form. At Visits 0B, 1 (for Supervised Washout participants) and 2, the P6_BASELINE form will generate as a report from the MedGraphics system that will be used as the data collection form.

When: Visits 0A, 0B, 1-2

Note: This form should **NOT** be completed at Visit 2 for participants who completed Supervised Washout visits.

Form Instructions:

Question 1000. Record the participant's baseline peak flow (PEF) value in Q1000 according to the following rubric:

Visit	Scenario	Baseline Peak Flow (PEF) Value
0A; 1	Visit 1 only if did not complete Supervised Washout visits	From prebronchodilator (baseline) spirometry at Visit 0A/initial Visit 1, converted to L/M
0B	Completed Supervised Washout visits	Average of the AM PEFs collected the 14 days prior to Visit in the spirotel® device – will be present on the SIENA Spirotel® Baseline Report generated from MedGraphics system
1	Completed Supervised Washout visits	
2	Did not complete Supervised Washout visits	

Note: If participant completed Continuation or Split Visit 1, and did not complete Supervised Washout visits, baseline PEF should be calculated using FEF Max value from baseline Spirometry testing at the initial Visit 1 (visit when reversibility testing was performed).

Question 1010. Record the participant's baseline rescue use value in Q1010 according to the following rubric:

Visit	Baseline Rescue Value
0A; 1 for non-Supervised Washout	Self-reported average daily use of albuterol during the 14 days prior to Visit
0B, 1 for Supervised Washout, 2	Average daily use of albuterol during the 14 days prior to Visit in the spirotel® device – will be present on the SIENA Spirotel® Baseline Report generated from MedGraphics system

4.1.10 SIENA Change in Study Medications (P6_CHANGE_MEDS)

Purpose: Changes in study medications after a participant experiences a significant asthma exacerbation, another adverse event, via physician discretion, or for another reason are recorded on this form.

Who: An AsthmaNet coordinator completes this form.

When: Visits 3-9, 90A-92A

Note: This form must be completed each time a change in study medications occurs. If the study medications are altered because of an adverse event, one copy of the form should be completed when the study medications are discontinued; a second copy of the form should be completed when the study medications are resumed.

Form Instructions:

Question 1000. Indicate the reason for the change in study medications.

Question 1010. Record the adverse event number from the Clinical Adverse Events (AECLIN) form that corresponds to the event prompting a change in study medications. Note that the corresponding adverse event should have Q1090 = 2 on the AECLIN form since it did alter study dose. If the participant's study medication regimen is altered for a reason other than an adverse event, a related adverse event number should not be recorded in Q1010.

Questions 1020 and 1030. Record how a participant's scheduled medications are altered in Q1020 ('Current status of participant's medications'). Q1030 ('Date change took effect') should be the first day the participant discontinued or resumed his/her study medications.

At subsequent SIENA study visits, the study medication status should be reviewed. When another change to the study medication regimen is made, another copy of the form should be completed. The P6_CHANGE_MEDS form is a repeating form, which means that multiple records can be entered within a single form entry (like the WURSS_21 form, for example). To capture the P6_CHANGE_MEDS forms for a complete event (i.e., medications are discontinued due to an event for a period of time and then resumed following cessation of the same event), all applicable P6_CHANGE_MEDS forms (records) should be entered under the same visit ID and visit date. Q1030 will capture the pertinent date of the changes. The

P6_CHANGE_MEDS forms should not be sent to the DCC until both records (discontinuation and resumption of study medication) are complete.

Prompts to complete P6_CHANGE_MEDS form for stop and start of blinded medication due to significant asthma exacerbation are included on applicable visit checklists.

Each unique event indicating a change in study medications on the Clinical Adverse Events (AECLIN) form (Q1090 is answered ‘2’) should have a corresponding SIENA Change in Study Medications (P6_CHANGE_MEDS) form completed.

If a change to study medications occurs between visits, the SIENA Change in Study Medications (P6_CHANGE_MEDS) form should be entered as a single form with the visit number of the last visit completed.

4.1.11 SIENA Compliance Checklist (P6_COMPLY)

Purpose: The participant's compliance with diary and peak flow, dosing from the Respimat® inhaler, and dosing from the Twisthaler®/MDI inhaler are recorded on this form.

Who: An AsthmaNet coordinator completes this form.

When: Visits 0B, 1-9

Note: This form should **NOT** be completed at Visit 1 for participants who did not complete Supervised Washout visits.

Form Instructions:

The information for Q1000-1020 is obtained from the participant's Spirotel Participant Compliance Report (P6_COMPLY_RPT) at Visits 0B, 1-9.

Questions 1000-1020. The values will be transcribed directly from the report; the field annotations and text from the SIENA Compliance Checklist (P6_COMPLY) are used to display the results.

The information for Q1030-Q1060 is obtained from the participant's scheduled Respimat(s)® at Visits 2-9.

If participant had a Visit 2A, Q1000-Q1020 will capture all of the spirotel data from Visit 2 to Visit 3.

Question 1030. Scheduled puffs are 2 puffs per day starting the morning after Visit 1. A SIENA Scheduled Puffs Calculator is available on the website to help determine this value (under Home: Protocols: SIENA).

If participant had a Visit 2A, Q1030 will capture the number of scheduled puffs since 2A.

Question 1040. Count the number of remaining puffs on all returned Respimats®. During the run-in, participants will be given one Respimat® at each visit. Starting at Visit 3, participants will be given two Respimats® at each visit.

If more than 1 Respimat® was required between visits, record the remaining puffs on Respimat® 1 + remaining puffs on Respimat® 2 for Q1040. This will occur when the time between visits is greater than 30 days.

Question 1050. Calculate the number of puffs taken by subtracting the number of remaining puffs (Q1040) from 60 times the number of used Respimats® and record the value in Q1050.

*If two Respimats® were required between visits, Q1050 will be calculated by subtracting the remaining puffs (Q1040) from 120.

Question 1060. Calculate the percent compliance by dividing the number of puffs taken (Q1050) by the number of scheduled puffs (Q1030) and multiplying by 100. Round to the nearest tenth of a percent and record the value in Q1060.

The information for Q1070-Q1100 is obtained from the participant's scheduled Twisthaler(s)® or MDI(s) at Visits 4-9.

Question 1070. For participants on Twisthaler®, scheduled puffs is 2 puffs two times a day starting the evening of Visit 3.

For participants on MDI, scheduled puffs is 1 puff two times a day starting the evening of Visit 3.

A SIENA Scheduled Puffs Calculator is available on the website to help determine this value (under Home: Protocols: SIENA).

If participant had a Visit 2A, Q1070 will capture the number of scheduled puffs since 2A.

Question 1080. Count the number of remaining puffs on all returned Twisthalers®/MDIs. The participant will be given 3 Twisthaler® inhalers or 1 MDI inhaler at each visit starting at Visit 3. Record the remaining puffs on the MDI device or on Twisthaler® 1 + Twisthaler® 2 + Twisthaler® 3 for Q1080.

Question 1090. Calculate the number of puffs taken by subtracting the number of remaining puffs (Q1080) from 60 times the number of used Twisthalers®/MDIs and record the value in Q1090.

For participants randomized to the Twisthaler, 3 Twisthaler® inhalers will be dispensed starting at Visit 3, so Q1080 will usually be subtracted from 180. If more than 3 inhalers are returned due to a visit extension, Q1080 will be subtracted from (# inhalers x 60).

For participants randomized to MDI, one MDI inhaler will be dispensed starting at Visit 3, so Q1080 will usually be subtracted from 120. If more than 1 inhaler is returned due to a visit extension, Q1080 will be subtracted form (# inhalers x 120).

Question 1100. Calculate the percent compliance by dividing the number of puffs taken (Q1090) by the number of scheduled puffs (Q1070) and multiplying by 100. Round to the nearest tenth of a percent and record the value in Q1100.

Question 6000. If a participant is recounseled on how to improve low compliance, please provide a comment documenting this in Q6000. Recounseling should be provided each time the participant has low spirotel or medication compliance (< 75%).

See the Dosing Compliance discussion in Section 2 for more details on the compliance calculations.

4.1.12 SIENA Coordinator Study Treatment Questionnaire (P6_CTXQX)

Purpose: This form helps to determine whether the blind on the scheduled medications was effective from the coordinator's perspective.

Who: The AsthmaNet coordinator who was primarily responsible for the participant's SIENA visits completes the form.

When: Visits 3-9, 90A-92A

Form Instructions:

The SIENA Coordinator Study Treatment Questionnaire (P6_CTXQX) form should be completed at Visits 5, 7, and 9 or on the day of a randomized participant's last visit if he or she terminates prior to Visit 9.

If a randomized participant terminates:

- **during** a post-randomization visit, the SIENA Coordinator Study Treatment Questionnaire (P6_CTXQX) form should be completed at the end of a treatment period and entered as a packet form at Visits 5, 7, and 9. It should be entered as a single form if completed at Visits 4, 6, or 8.

- **between** visits, the coordinator should complete the SIENA Coordinator Study Treatment Questionnaire (P6_CTXQX) form and enter it as a single form with the number of the last visit completed in the upper right-hand corner. For instance, a participant could be terminated from the SIENA study following Visit 4 due to loss to follow up. In this case, the SIENA Coordinator Study Treatment Questionnaire (P6_CTXQX) should be entered as a single form with the last visit number completed in the upper right-hand corner of the form, or Visit 4.

The visit date recorded on the form should be the date the form is completed. If the coordinator who was primarily responsible for the participant's SIENA study visits is not present during a visit when this form is to be completed, it should be completed upon his or her return and dated appropriately.

Question 1000. Q1000 should be answered with the option that most closely represents the coordinator's feelings about which type of Twisthaler®/MDI the participant received during the treatment period.

Question 1020D. Any comments with respect to any other observations the coordinator may have made that helped him or her make a choice in Q1 should be recorded in Q1020D and entered into the AsthmaNet database (up to 250 characters).

Question 1030. Q1030 should be answered with the option that most closely represents the coordinator's feelings about which type of Respimat® the participant received during the treatment period.

Question 1050D. Any comments with respect to any other observations the coordinator may have made that helped him or her make a choice in Q4 should be recorded in Q1050D and entered into the AsthmaNet database (up to 250 characters).

To verify that the information collected on this form is correct, the coordinator who completed the form should initial and date the form in the shaded source documentation box provided (Q1060-1070) at the bottom of the page.

4.1.13 SIENA Device Technique MDI (Without Spacer) (P6_TECH_MDI_NOSP)

Purpose: This form tracks a participant's ability and attempts to correctly use the MDI device.

Who: An AsthmaNet coordinator completes this form.

When: Visit 1

Form Instructions:

Question 1000. All participants should complete a pre-education (Q1000 = 0) P6_TECH_MDI_NOSP form. If the participant's pre-education score is perfect (11 out of 11), post-education P6_TECH_MDI_NOSP forms do NOT need to be completed.

If the participant's pre-education score is less than 11, provide coaching/corrections as needed and complete up to one additional P6_TECH_MDI_NOSP form.

Questions 1020-1120. Observe the participant's use of MDI device and select whether technique is wrong or correct for each item.

Question 13. This field is not entered into the database. To calculate score, assign 1 point to each correct step and sum across Q2-Q12 (at V1) or Q2-Q11 (at V3, 5, 7, 9).

Once a score of 11 (V1) or 10 (V3, 5, 7, 9) is achieved, no further P6_TECH_MDI_NOSP forms need to be completed at the visit.

At Visit 1, if the participant cannot achieve a score of 11 out of a total of 2 forms (including the pre-education assessment), he/she is ineligible. At Visit 3, if the participant cannot achieve a score of 10 out of a total of 2 forms (including the pre-education assessment), he/she is ineligible.

4.1.14 SIENA Device Technique Respimat® (P6_TECH_RESP)

Purpose: This form tracks a participant's ability and attempts to correctly use the Respimat® device.

Who: An AsthmaNet coordinator completes this form.

When: Visits 1, 3, 5, 7, 9

Form Instructions:

Question 1000. If the participant has used a Respimat® device before, complete a pre-education (Q1000 = 0) P6_TECH_RESP form.

If the participant has never used a Respimat® device before or pre-education score is not perfect (13 out of 13), post-education P6_TECH_RESP forms should be completed.

If the participant's score is less than 13, provide coaching/corrections as needed and complete P6_TECH_RESP forms until a perfect score is achieved.

Questions 1020-1140. Observe the participant's use of the Respimat® device and select whether technique is wrong or correct for each item.

Question 15. This field is not entered into the database. To calculate score, assign 1 point to each correct step and sum across Q2-Q14.

Once a score of 13 is achieved, no further P6_TECH_RESP forms need to be completed at the visit.

4.1.15 SIENA Device Technique Twisthaler® (P6_TECH_TWIST)

Purpose: This form tracks a participant's ability and attempts to correctly use the Twisthaler® device.

Who: An AsthmaNet coordinator completes this form.

When: Visits 1, 3, 5, 7, 9

Form Instructions:

Question 1000. If the participant has used a Twisthaler® device before, complete a pre-education (Q1000 = 0) P6_TECH_TWIST form.

If the participant has never used a Twisthaler® device before or pre-education score is not perfect (13 out of 13), post-education P6_TECH_TWIST forms should be completed.

If the participant's score is less than 13, provide coaching/corrections as needed and complete P6_TECH_TWIST forms until a perfect score is achieved.

Questions 1020-1140. Observe the participant's use of Twisthaler® device and select whether technique is wrong or correct for each item.

Question 15. This field is not entered into the database. To calculate score, assign 1 point to each correct step and sum across Q2-Q14.

Once a score of 13 is achieved, no further P6_TECH_TWIST forms need to be completed at the visit.

4.1.16 SIENA Eligibility Checklist 0A (P6_ELIG0A)

Purpose: This form consists of interview questions that assist in determining if a participant is eligible for the Supervised Washout visits in the SIENA study.

Who: An AsthmaNet coordinator completes the form.

When: Visit 0A

Form Instructions:

For detailed information regarding eligibility criteria, see the Eligibility Criteria discussion in Section 2.

Question 1000. Do not ask the participant this question.

Data can **only** be collected if the participant has signed an informed consent form for the SIENA study. See the Informed Consent discussion in Section 2 for further details.

Question 1010. The signature date should be the date the participant signed the consent document. If the consent was signed prior to Visit 0A, the consent should be reviewed by the participant on the day Visit 0A takes place. The date the consent form was signed should **not** be updated.

Question 1020. Do not ask the participant this question.

If the participant is between ages 12 and 17, data can **only** be collected if the participant has signed and dated the assent form or given verbal assent for the SIENA study. See the Informed Consent discussion in Section 2 for further details.

If IRB approval for protocol version 4.1 has NOT yet been obtained:
Question 1030. If the participant has used an inhaled corticosteroid in the past 6 weeks, he/she is eligible for the Supervised washout visits. Complete the P6_ELIG0A form and Visit 0A.

If the participant has not used an inhaled corticosteroid in the past 6 weeks, he/she should proceed with Visit 1 procedures. The P6_ELIG0A form should **not** be completed nor sent to the DCC. The participant is ineligible for the Supervised washout visits.

If IRB approval for protocol version 4.1 has been obtained:
Question 1043. If the participant has used an inhaled corticosteroid or combination inhaled corticosteroid/LABA in the past 3 weeks, he/she is eligible for the Supervised washout visits. Complete the P6_ELIG0A form and Visit 0A.

If the participant has not used an inhaled corticosteroid or combination inhaled corticosteroid/LABA in the past 3 weeks, complete Q1045.

Question 1045. If the participant has used a leukotriene modifier in the past 3 weeks, he/she is eligible for the Supervised washout visits. Skip to Q8, complete the P6_ELIG0A form and Visit 0A.

If the participant has not used a leukotriene modifier in the past 3 weeks, he/she should proceed with the Visit 1 procedures. The P6_ELIG0A form should **not** be completed nor sent to the DCC. The participant is ineligible for the Supervised washout visits.

Question 1050. Record the number of days per week, on average, the participant has used inhaled corticosteroid over the past three months. For example, if the participant responds that he/she used inhaled corticosteroid therapy an average of three days a week over the past three months, record 3 for Q1050.

If the participant responds that he/she used inhaled corticosteroid therapy an average of 10 times a month over the past 3 months, record 3 for Q1050 (10 times a month/4 weeks in a month = 2.5 days a week which rounds to 3). If unsure of the number of days per week, estimate to the nearest number of days.

Question 1070. If Q1060 is answered No, complete Q1070 by referring to the SIENA ICS Equivalency Reference Card (P6_ICS_EQUIV). If the participant has used greater than the equivalent of 80-240 mcg of inhaled beclomethasone daily, he/she is ineligible for the SIENA study.

If IRB approval for protocol version 4.1 has been obtained:
Question 1073. Record the number of days per week, on average, the participant has used combination inhaled corticosteroid/LABA therapy. For example, if the participant responds that he/she used combination inhaled corticosteroid/LABA therapy for an average of three days a week over the past three months, record 3 for Q1073.

If Q1073 is answered 0, skip to Q8. If Q1073 is greater than or equal to 5, the participant is ineligible.

Question 1080. Record the number of days per week, on average, the participant has had daytime asthma symptoms over the past three months. For example, if the participant responds that he/she had daytime asthma symptoms an average of three days a week over the past three months, record 3 for Q1080. If the participant responds that he/she had daytime asthma symptoms an average of 10 times a month over the past 3 months, record 3 for Q1080 (10 times a month/4 weeks in a month = 2.5 days a week which rounds to 3). If unsure of the number of days per week, estimate to the nearest number of days.

Question 1100. Record the number of nighttime awakenings per month, on average, the participant has had due to asthma symptoms during the past three months. Note that regardless of the number of times a participant wakes up during a night, if he/she wakes up at least once in a night that counts as one nighttime awakening. For example, if the participant had nighttime awakenings 5 nights a month over the past three months, record 5 for Q1100.

If the participant responds that he/she had 1 night with awakenings per week during the past three months, record 4 for Q1120 (1 night a week x 4 weeks in a month = 4 awakenings per month). If unsure of the number of awakenings per month, estimate to the nearest number of awakenings.

Question 1120. Record the number of days per week, on average, the participant has used his/her short acting beta-agonist for relief of symptoms over the past three months. For example, if the participant responds that he/she used his/her short acting beta-agonist for relief of symptoms an average of three days a week over the past three months, record 3 for Q1120.

If the participant responds that he/she used his/her short acting beta-agonist for relief of symptoms an average of 10 times a month over the past 3 months, record 3 for Q1120 (10 times a month/4 weeks in a month = 2.5 days a week which rounds to 3). If unsure of the number of days per week, estimate to the nearest number of days.

If IRB approval for protocol version 4.1 has NOT yet been obtained:
Question 1140. The participant's prebronchodilator (baseline) FEV_1 (% predicted) value should be obtained from Q1040 on the Spirometry Testing (SPIRO) form completed at the visit. The participant is ineligible if FEV_1 % predicted ≤ 80%.

If IRB approval for protocol version 4.1 has been obtained:
Question 1145. The participant's prebronchodilator (baseline) FEV_1 (% predicted) value should be obtained from Q1040 on the Spirometry Testing (SPIRO) form completed at the visit. The participant is ineligible if FEV_1 % predicted ≤ 70%.

Question 1150. If the participant indicates historical evidence of a disease or medical condition, but has no current evidence, Q1150 should be answered 'No.' The participant must have current evidence of one of the medical conditions for Q1150 to be answered 'Yes.'

If a participant at Visit 0A has one of these exclusionary medical conditions and is being allowed to progress through the study per a DCC-approved protocol exception, then Q1150 should be answered 'Yes' and Q1190 should also be answered 'Yes' (if no other ineligibility critera are met). Resulting errors should be marked unresolvable, and the participant's condition and physician approval to proceed should be documented in the comment provided. Such cases will be treated as protocol exceptions.

Question 1160. If the participant is taking one of the drugs that are listed as exclusionary, and is allowed to progress through the study per a DCC-approved protocol exception, Q1160 should be answered 'Yes', Q1170 should be answered 'No' and Q1190 should also be answered 'Yes' (if no other ineligibility criteria are met). Resulting errors should be marked unresolvable, and the participant's SIENA-exclusionary medication and physician approval to proceed should be documented in the comment provided. Such cases will be tracked as protocol exceptions.

Question 1170. If Q1160 is answered Yes, complete Q1170 after reviewing the required washout periods found on the Exclusionary Drugs for SIENA reference card (P6_EXCLDRUG). If the participant is not able to go off his/her medication(s) for the required washout period(s), he/she is ineligible for the SIENA study.

When completing page 3 (questions a-m), the '10 months prior to today's date is' field should be completed first. This date will apply to questions h,i, k, and l. If any of the gray boxes are checked, the participant will be ineligible at Visit 1 and thus should stop completion of Visit 0A. Note these fields are not data entered, but will be reviewed at the DCC.

Question 1190. If any of the shaded boxes is completed, the participant is ineligible. The visit should be stopped and the visit packet should **not** be entered into the AsthmaNet database or sent to the DCC. File the visit packet in the participant's study folder at the clinic.

If the participant is eligible, continue with the rest of the Visit 0A visit procedures. For more details pertaining to eligibility, see the Eligibility Criteria discussion in Section 2.

General Instructions:

If an eligibility protocol exception was granted by the DCC, complete the question(s) that the exception was granted for accurately (i.e., complete the shaded box). Q1190 should be answered 'Yes' to indicate the participant is eligible to proceed and any entry errors that result from the exception should be marked unresolvable. In the unresolvable comment section, indicate that a protocol exception was granted, who granted it, and the justification for the exception. Also, complete the comment field (Q6000) provided on the last page of the form with additional information on the exception.

To verify that the information collected on this form is correct, have the participant initial and date the form in the shaded source documentation box provided (Q1200-1210) on the last page of the form.

4.1.17 SIENA Eligibility Checklist 0B (P6_ELIG0B)

Purpose: This form consists of questions that assist in determining if a participant is eligible to continue in the SIENA study.

Who: An AsthmaNet coordinator completes the form.

When: Visit 0B

Form Instructions:

For detailed information regarding eligibility criteria, see the Eligibility Criteria discussion in Section 2.

Questions 1000, 1020, 1040. These values are obtained from the Spirotel® SIENA Eligibility Report (P6_ELIG_RPT). The format of the report will match the field annotations and question text of the SIENA Eligibility Checklist 0B (P6_ELIG0B) form.

If IRB approval for protocol version 4.1 has NOT yet been obtained:
Question 1060. The participant's prebronchodilator (baseline) FEV_1 (% predicted) value should be obtained from Q1040 on the Spirometry Testing (SPIRO) form completed at the visit. The participant is ineligible if FEV_1 % predicted ≤ 80%.

If IRB approval for protocol version 4.1 has been obtained:
Question 1065. The participant's prebronchodilator (baseline) FEV_1 (% predicted) value should be obtained from Q1040 on the Spirometry Testing (SPIRO) form completed at the visit. The participant is ineligible if FEV_1 % predicted ≤ 70%.

Question 1080. If any of the shaded boxes is completed, the participant is ineligible. The visit should be stopped. Enter and submit all collected data, along with the SIENA Termination of Study Participation (P6_TERM) form.

If the participant is eligible, continue with the rest of the Visit 0B visit procedures.

General Instructions:

If an eligibility protocol exception was granted by the DCC, complete the question(s) that the exception was granted for accurately (i.e., complete the shaded box). Q1080 should be answered 'Yes' to indicate the participant is eligible to proceed and any entry errors that result from the exception should be marked unresolvable. In the unresolvable comment section, indicate that a protocol exception was granted, who granted it, and the justification for the exception. Also, complete the comment field

(Q6000) provided on the last page of the form with additional information on the exception.

4.1.18 SIENA Eligibility Checklist 1 (P6_ELIG1)

Purpose: This form consists of questions that assist in determining if a participant is eligible to continue in the SIENA study.

Who: An AsthmaNet coordinator completes the form.

When: Visit 1

Form Instructions:

For detailed information regarding eligibility criteria, see the Eligibility Criteria discussion in Section 2.

If the participant completed Supervised Washout Visits 0A and 0B, do not complete Q1000-Q1020.

Question 1000. Do not ask the participant this question.

Data can **only** be collected if the participant has signed an informed consent form for the SIENA study. See the Informed Consent discussion in Section 2 for further details.

Question 1010. The signature date should be the date the participant signed the consent document. If the consent was signed prior to the Visit 1, the consent should be reviewed by the participant on the day Visit 1 takes place. The date the consent form was signed should **not** be updated.

Question 1020. Do not ask the participant this question.

If the participant is between ages 12 and 17, data can **only** be collected if the participant has signed and dated the assent form or given verbal assent for the SIENA study. See the Informed Consent discussion in Section 2 for further details.

If IRB approval for protocol version 4.1 has NOT yet been obtained:
Question 1060. If answered yes, and participated in the Supervised Washout, the respiratory infection should be recorded on the Clinical Adverse Events (AECLIN) form. The respiratory infection should have occurred within the past 6 weeks for Q1060 to be answered Yes.

If IRB approval for protocol version 4.1 has been obtained:
Question 1065. If answered yes, and participants in the Supervised Washout, the respiratory infection should be recorded on the Clinical Adverse Events (AECLIN) form. The respiratory infection should have occurred within the past 4 weeks for Q1065 to be anwered Yes.

Questions 1070, 1090, 1110. If the participant had Supervised Washout visits, these values are obtained from the Spirotel® SIENA Eligibility Report (P6_ELIG_RPT). The format of the report will match the field annotations and question text of the SIENA Eligibility Checklist 1 (P6_ELIG1) form.
If Visit 1 is the first visit for the participant, these questions are answered based on participant report (see the next three paragraphs below).

Question 1070. Record the number of days per week, on average, the participant has had daytime asthma symptoms over the past four weeks. For example, if the participant responds that he/she had daytime asthma symptoms an average of three days a week over the past four weeks, record 3 for Q1070.

If unsure of the number of days per week, estimate to the nearest number of days.

Question 1090. Record the number of nighttime awakenings the participant has had due to asthma symptoms during the past four weeks. Note that regardless of the number of times a participant wakes up during a night, if he/she wakes up one or more times in a night that counts as one nighttime awakening. For example, if the participant responds that he/she had 1 night with awakenings a week during the past four weeks, record 4 for Q1090.

If unsure of the number of awakenings per month, estimate to the nearest number of awakenings.

Question 1110. Record the number of days per week, on average, the participant has used his/her short acting beta-agonist for relief of symptoms over the past four weeks. For example, if the participant responds that he/she used his/her short acting beta-agonist for relief of symptoms an average of three days a week over the past four weeks, record 3 for Q1110.

If unsure of the number of days per week, estimate to the nearest number of days.

Question 1140. If any of the shaded boxes is completed, the participant is ineligible. The visit should be stopped and a SIENA Termination of Study Participation (P6_TERM) form completed if the participant completed Supervised Washout visits.

All completed data collection forms for a Supervised Washout participant who terminates at Visit 1 should be entered and forwarded to the DCC.
If Visit 1 is the first visit for the participant, stop the visit and file the completed forms in the participant's folder.

If the participant is eligible, continue with the rest of the Visit 1 procedures.

General Instructions:

If an eligibility protocol exception was granted through the DCC, complete the question(s) that the exception was granted for accurately (i.e. complete the shaded box). Q1140 should be answered 'Yes' to indicate the participant is eligible to proceed and any entry errors that result from the exception should be marked unresolvable. In the unresolvable comment section, indicate that a protocol exception was granted, who granted it, and the justification for the exception. Also, complete the comment field (Q6000) provided on the last page of the form with additional information on the exception.

To verify that the information collected on this form is correct, have the participant initial and date the form in the shaded source documentation box provided (Q1150-1160) on the last page of the form.

4.1.19 SIENA Eligibility Checklist 2 (P6_ELIG2)

Purpose: This form consists of questions that assist in determining if a participant is eligible to continue in the SIENA study.

Who: An AsthmaNet coordinator completes the form.

When: Visit 1

Form Instructions:

For detailed information regarding eligibility criteria, see the Eligibility Criteria discussion in Section 2.

Question 1000. If the participant indicates historical evidence of a disease or medical condition, but has no current evidence, Q1000 should be answered 'No.' The participant must have current evidence of one of the medical conditions for Q1000 to be answered 'Yes.'

If a participant screened at Visit 1 has one of these exclusionary medical conditions and is being allowed to progress through the study per a DCC-approved protocol exception, then Q1000 should be answered 'Yes' and Q1210 should also be answered 'Yes' (if no other ineligibity criteria are met). Resulting errors should be marked unresolvable, and the participant's condition and physician approval to proceed should be documented in the comment provided. Such cases will be treated as protocol exceptions.

Questions 1010-1030. Review participant medical records (if available) and responses on the PRIOR_COND_ADULT (for 18+) when answering these questions.

Question 1040. If the participant has taken one of the drugs that are listed as exclusionary within the specified time periods, but is allowed to progress through the study per a DCC-approved protocol exception, Q1040 should be answered 'Yes' and Q1210 should also be answered 'Yes' (if no other ineligibility criteria are met). Resulting errors should be marked unresolvable, and the participant's SIENA-exclusionary medication and physician approval to proceed should be documented in the comment provided. Such cases will be tracked as protocol exceptions.

Question 1050. If the participant is currently taking prescription or OTC medications other than those listed on the Allowed Medications for SIENA (P6_MEDALLOW) reference card, the coordinator should confirm through the DCC that the medication is

allowed before continuing. If the medication is approved by the DCC, Q1050 should be answered 'No.' If the medication is not approved by the DCC, the participant is ineligible to continue in the study and Q1050 should be answered 'Yes.'

Questions 1060 and 1070. The participant must agree to either adhere to a specific dose of an intranasal steroid **OR** stop use of all intranasal steroids for the duration of the SIENA study, starting at or before Visit 1.

The intranasal steroid should be recorded on the Concomitant Medications for Asthma/Allergy and Adverse Events (CMED) form as an ongoing record.

Question 1080. The participant may enroll in the study if an established maintenance regimen was implemented continuously for a minimum of 3 months prior to Visit 1.

Question 1120 and 1130. 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. Pack-year history will be recorded on the Adult Asthma and Allergy History (ASTHMA_HX_ADULT for 18+) form at Visit 1.

If IRB approval for protocol version 4.1 has NOT yet been obtained:
Question 1140. If the participant received a physician diagnosis of asthma at least 12 months ago, Q1140 should be answered Yes.

If IRB approval for protocol version 4.1 has been obtained:
Question 1145. If the participant received a physician diagnosis of asthma at least 12 months ago OR had a history consistent with asthma for the previous 12 months, Q1145 should be answered Yes.

If IRB approval for protocol version 4.1 has NOT yet been obtained:
Question 1170. If Q1170 is anwered Yes, the participant is ineligible to proceed with Visit 1.

If the participant is taking ICS intermittently or using a low-dose ICS and is well controlled, he/she may be eligible for the Supervised ICS Washout. The coordinator can switch to the Visit 0A packet to assess eligibility for the Supervised ICS Washout.

If Q1170 is answered Yes for a participant that has already gone through Supervised ICS Washout visits (0A and 0B), complete a SIENA Termination of Study Participant (P6_TERM) form.

If IRB approval for protocol version 4.1 has been obtained:
Questions 1173 and Q1175. If Q1173 or Q1175 is answered Yes, the participant is ineligible to proceed with Visit 1.

If the participant is taking inhaled corticosteroid, combination inhaled corticosteroid/LABA (less than 5 days a week for the past 3 months) or a leukotriene modifier and is well controlled, he/she may be eligible for the Supervised Washout. The coordinator can switch to the Visit 0A packet to assess eligibility for the Supervised Washout.

If Q1175 is answered Yes for a participant that has already gone through Supervised Washout visits (0A and possibly 0B), complete a SIENA Termination of Study Participant (P6_TERM) form.

Question 1180. If there is any possibility that the participant is physically able to bear children, Q1180 should be answered 'Yes' (even if the participant indicates she is not currently engaging in heterosexual intercourse).

If the participant is pre-menarche, surgically sterile or post-menopausal for at least one year, Q1180 should be answered 'No.' If the participant is male, Q1180 should be answered 'N/A.'

Questions 1190 and 1200. Complete only if the participant is able to bear children. If the participant is currently pregnant or lactating, she is ineligible to participate in the study at this time.

Question 1200. Show the participant the Birth Control Methods (BIRTH_CTRL) reference card found on the AsthmaNet secure website in the Standard Forms: Reference Cards folder and ask if she is using one of the listed birth control methods.

A participant who is able to bear children **must** be using a birth control method listed on the reference card to be eligible for the study. If the participant is not engaging in heterosexual intercourse, abstinence applies as a legitimate birth control method.

If the participant is eligible, continue with the rest of the Visit 1 procedures.

General Instructions:

If an eligibility protocol exception was granted through the DCC, complete the question(s) that the exception was granted for accurately (i.e. complete the shaded box). The applicable eligibility question(s) should be answered 'Yes' to indicate the participant is eligible to proceed and any entry errors that result from the exception

should be marked unresolvable. In the unresolvable comment section, indicate that a protocol exception was granted, who granted it, and the justification for the exception. Also, complete the comment field (Q6000) provided on the last page of the form with additional information on the exception.

To verify that the information collected on this form is correct, have the participant initial and date the form in the shaded source documentation box provided (Q1220-1230) on the last page of the form.

4.1.20 SIENA Eligibility Checklist 3 (P6_ELIG3)

Purpose: This form consists of questions that assist in determining if a participant is eligible to continue in the SIENA study.

Who: An AsthmaNet coordinator completes the form.

When: Visit 1

Form Instructions:

For detailed information regarding eligibility criteria, see the Eligibility Criteria discussion in Section 2.

Question 1000. The participant's prebronchodilator (baseline) FEV_1 (% predicted) value should be obtained from Q1040 on the Spirometry Testing (SPIRO) form completed at the visit.

Question 1010. If the participant met the FEV_1 reversibility criterion at Visit 1 (Q1010 is answered Yes), questions regarding methacholine challenge source documentation (Q1020-Q1070) should not be completed and the coordinator should skip to Section 2.

If the participant did not meet FEV_1 reversibility criterion at Visit 1, the coordinator should continue with Section Q1020-Q1070.

To determine the % change in response to albuterol, calculate as follows:

> [(Post-bronchodilator FEV_1 – Pre-bronchodilator FEV_1) / Pre-bronchodilator FEV_1] x 100

Calculations must be based on FEV_1 in liters (not % of predicted scale).

Do not round the result to the nearest full percentage when assessing eligibility.

If the calculation is close, but less than 12.0%, contact the SIENA Scientific Coordinator at the DCC for an exception before assuming the asthma verification criteria have been met. The exception must be documented on P6_ELIG3 as explained below.

Question 1020. Valid source documentation is acceptable for a methacholine challenge performed within six months of the Visit 1 visit date, performed with the AsthmaNet systems, and completed by a certified technician or supervised by a

certified supervisor. The coordinator may use source documentation of a methacholine challenge from any AsthmaNet protocol. The source documentation methacholine challenge should be a test overread by AsthmaNet, and therefore a part of the export data from the Medgraphics system.

If the participant has valid source documentation (Q1020 is answered 'Yes'), complete Q1030-Q1060. If the participant does not have valid source documentation, skip to Q1070.

Question 1030. If the participant has source documentation of a PC_{20} in the past six months, the values should be transcribed onto the SIENA Eligibility Checklist 3 (P6_ELIG3) form only. Do **not** transcribe these values on the Methacholine Challenge Testing (METHA) form; no prior Spirometry Testing (SPIRO) form or Methacholine Challenge Testing (METHA) form should be submitted with the Visit 1 packet when providing source documentation.

A copy of the source documentation methacholine challenge report should be stored in the participant's study folder, as well as forwarded to the DCC along with the Visit 1 packet.

If the participant has source documentation of a PC_{20} in the past six months, do **not** mark the Methacholine Challenge Testing Report (METHA_RPT) as present when entering the Visit 1 packet.

Question 1040. Provide the date of the methacholine challenge used for source documentation.

Questions 1050 and 1060. Provide the Technician ID and Supervisor ID, if applicable, of the methacholine challenge used for source documentation.

Question 1070. This question should only be answered if the participant completed a Visit 1 continuation visit with methacholine challenge. If participant does not qualify for methacholine challenge per the Adult or Pediatric Methacholine Challenge Checklist form, this question should be answered No.

If a Continuation Visit is necessary, PREG_TEST, P6_PULMONARYCHK, ENO, SPIRO, METHACHK_ADULT or METHACHK_PED, and METHA single forms will be completed first. The rest of the P6_ELIG3 form and Visit 1 forms should then be completed as outlined by the visit procedure checklist, using the visit date of the continuation visit. For more information, refer to Section 4.4 below.

Question 1130. If any of the shaded boxes is completed, the participant is ineligible. The visit should be stopped and a SIENA Termination of Study Participation (P6_TERM) form completed.

If the participant is eligible, continue with the rest of the Visit 1 procedures.

General Instructions:

If an eligibility protocol exception was granted through the DCC, complete the question(s) that the exception was granted for accurately (i.e. complete the shaded box). The applicable eligibility question(s) should be answered 'Yes' to indicate the participant is eligible to proceed and any entry errors that result from the exception should be marked unresolvable. In the unresolvable comment section, indicate that a protocol exception was granted, who granted it, and the justification for the exception. Also, complete the comment field (Q6000) provided on the last page of the form with additional information on the exception.

4.1.21 SIENA Eligibility Checklist 4 (P6_ELIG4)

Purpose: This form consists of questions that assist in determining if a participant is eligible to continue in the SIENA study.

Who: An AsthmaNet coordinator completes the form.

When: Visits 2 and 2A

Form Instructions:

For detailed information regarding eligibility criteria, see the Eligibility Criteria discussion in Section 2.

Question 1030. If the participant has taken one of the drugs that are listed as exclusionary within the specified time periods, but is allowed to progress through the study per a DCC-approved protocol exception, Q1030 should be answered 'Yes' and Q1070 should also be answered 'Yes' (if no other ineligibility critera are met). Resulting errors should be marked unresolvable, and the participant's SIENA-exclusionary medication and physician approval to proceed should be documented in the comment provided. Such cases will be tracked as protocol exceptions.

General Instructions:

If an eligibility protocol exception was granted through the DCC, complete the question(s) that the exception was granted for accurately (i.e. complete the shaded box). The applicable eligibility question(s) should be answered 'Yes' to indicate the participant is eligible to proceed and any entry errors that result from the exception should be marked unresolvable. In the unresolvable comment section, indicate that a protocol exception was granted, who granted it, and the justification for the exception. Also, complete the comment field (Q6000) provided on the last page of the form with additional information on the exception.

4.1.22 SIENA Eligibility Checklist 5 (P6_ELIG5)

Purpose: This form consists of questions that assist in determining if a participant is eligible to continue in the SIENA study.

Who: An AsthmaNet coordinator completes the form.

When: Visit 3

Form Instructions:

For detailed information regarding eligibility criteria, see the Eligibility Criteria discussion in Section 2.

Question 1000. **Note: Prior to the Visit 3 date, review the Participant Status Report to verify that the participant has two acceptable sputum induction samples.**

If IRB approval for protocol version 4.1 has NOT yet been obtained:
Question 1030. If Visit 3 needs to be rescheduled due to Asmanex® use within past 6 weeks, file any of the data collected at the first Visit 3 in the participant's folder but do not enter the data or forward it to the DCC. At the rescheduled visit, complete a new Visit 3 packet.

If the participant was not instructed to take or did not take Asmanex® for the treatment failure, Q1030 should be left blank and a comment detailing this should be entered into Q6000.

If IRB approval for protocol version 4.1 has been obtained:
Question 1035. If Visit 3 needs to be rescheduled due to Asmanex® use within past 3 weeks, file any of the data collected at the first Visit 3 in the participant's folder but do not enter the data or forward it to the DCC. At the rescheduled visit, complete a new Visit 3 packet.

If the participant was not instructed to take or did not take Asmanex® for the treatment failure, Q1035 should be left blank and a comment detailing this should be entered into Q6000.

Question 1050. If the participant has taken one of the drugs that are listed as exclusionary within the specified time periods, but is allowed to progress through the study per a DCC-approved protocol exception, Q1050 should be answered 'Yes' and Q1180 should also be answered 'Yes' (if no other ineligibility criteria are met).

Resulting errors should be marked unresolvable, and the participant's SIENA-exclusionary medication and physician approval to proceed should be documented in the comment provided. Such cases will be tracked as protocol exceptions.

If IRB approval for protocol version 4.1 has NOT yet been obtained:
Question 1060. If answered yes, the respiratory infection should be recorded on the Clinical Adverse Events (AECLIN) form.

If Visit 3 needs to be rescheduled due to respiratory infection within past 6 weeks, file all data collected at the first Visit 3 in the participant's folder but do not enter the data or forward it to the DCC. At the rescheduled visit, complete a new Visit 3 packet.

If IRB approval for protocol version 4.1 has been obtained:
Question 1065. If answered yes, the respiratory infection should be recorded on the Clinical Adverse Events (AECLIN) form.

If Visit 3 needs to be rescheduled due to respiratory infection within past 4 weeks, file all data collected at the first Visit 3 in the participant's folder but do not enter the data or forward it to the DCC. At the rescheduled visit, complete a new Visit 3 packet.

If IRB approval for protocol version 4.1 has NOT yet been obtained:
Questions 1070, Q1080, Q1090, and 1100. Review the participant's Spirotel® SIENA Eligibility Report (P6_ELIG_RPT) to answer these questions. Note that Q1100 pertains to the compliance listed on the Eligibility Report, **not** the Compliance Report.

If IRB approval for protocol version 4.1 has been obtained:
Questions 1085, Q1090, and 1100. Review the participant's Spirotel® SIENA Eligibility Report (P6_ELIG_RPT) to answer these questions. Note that Q1100 pertains to the compliance listed on the Eligibility Report, **not** the Compliance Report.

Question 1110. See Dosing Compliance discussion in Section 2 for instructions on how to calculate Respimat® compliance during the run-in.

Question 1120. The participant's prebronchodilator (baseline) FEV_1 (% predicted) value should be obtained from Q1040 on the Spirometry Testing (SPIRO) form completed at the visit.

Questions 1130 and 1140 should only be completed if the participant is randomized to Twisthaler®.

Note: If the participant is terminated due to a question response in Q1000-Q1140, Q1150-Q1170 should still be completed.

General Instructions:

If an eligibility protocol exception was granted through the DCC, complete the question(s) that the exception was granted for accurately (i.e. complete the shaded box). The applicable eligibility question(s) should be answered 'Yes' to indicate the participant is eligible to proceed and any entry errors that result from the exception should be marked unresolvable. In the unresolvable comment section, indicate that a protocol exception was granted, who granted it, and the justification for the exception. Also, complete the comment field (Q6000) provided on the last page of the form with additional information on the exception.

4.1.23 SIENA Laboratory Results (P6_LAB)

Purpose: This form is completed after the local lab report is received.

Who: An AsthmaNet coordinator completes the form.

When: Visits 1, 2, 2A

Form Instructions:

Visit Date. Record the visit date as the date the blood is drawn (should match collection date on lab report).

Questions 1000-1060. Refer to the laboratory results printout generated at each clinical center's local laboratory to answer Q1000 – Q1060.

Round each value to the nearest tenth, where applicable, and record the value on the form. Ensure that measurement units match those on the form; otherwise, make the necessary conversions before submitting the data to the DCC.

Submit the original lab report with the participant's visit packet. The coordinator should record the participant's ID number in the upper right-hand corner of the report.

All identifying information (name, medical record number, etc.) should be blackened-out prior to forwarding the report to the DCC with the packet. If the DCC receives a report for which the identifying information has not been blackened-out, a protocol violation may be assigned.

4.1.24 SIENA Participant Study Treatment Questionnaire (P6_PARTTXQX/P6_PARTTXQX_2)

Purpose: Any observations the participant may have made during the SIENA study that may have compromised the study blind on the scheduled medications are recorded on this form.

Who: The participant completes the form.

When: Visits 3-9, 90A-92A

Form Instructions:

The SIENA Participant Study Treatment Questionnaire (P6_PARTTXQX) form should be completed at Visits 5, 7, and 9 or on the day of a randomized participant's last visit if he or she terminates prior to Visit 9.

If a randomized participant terminates:

- **during** a post-randomization visit, the SIENA Participant Study Treatment Questionnaire (P6_PARTTXQX) form should be completed at the end of a treatment period and entered as a packet form at Visits 5, 7, and 9. It should be entered as a single form if completed at Visits 4, 6, or 8.

- between visits, the SIENA Participant Study Treatment Questionnaire (P6_PARTTXQX) form should be entered as a single form with the number of the last visit completed in the upper right-hand corner. For instance, a participant could be terminated from the SIENA study following Visit 4 but before Visit 5. In this case, the SIENA Participant Study Treatment Questionnaire (P6_PARTTXQX) should be entered as a single form with the last visit number completed in the upper right-hand corner of the form, or Visit 4.

The visit date recorded on the form should be the date the form is completed.

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.

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

Question 1010. The participant should check the box that most closely represents his or her feelings about which type of scheduled Twisthaler®/MDI he/she used over the past 12 weeks.

Question 1030. If the participant chooses option 2, he or she can comment on the taste of, smell of, or physical sensations produced by the Twisthaler®/MDI in Q1030D.

Question 1040. The participant should check the box that most closely represents his or her feelings about which type of scheduled Respimat® he/she used over the past 12 weeks.

Question 1060. If the participant chooses option 2, he or she can comment on the taste of, smell of, or physical sensations produced by the Respimat® in Q1060D.

To verify that the information collected on this form is provided by the participant, have the participant initial and date the form in the shaded source documentation box provided (Q1070-1080) on the second page.

4.1.25 SIENA Pulmonary Procedure Checklist (P6_PULMONARYCHK)

Purpose: This form assists the coordinator in determining if the participant is eligible to proceed with pulmonary function testing.

Who: The Pulmonary Function Technician or an AsthmaNet coordinator interviews the participant and completes the form. The individual completing the form **must possess SIENA protocol certification**.

When: Visits 0A, 0B, 1-9

Form Instructions:

If the SIENA Pulmonary Procedure Checklist (P6_PULMONARYCHK) form is completed at an FEV_1 re-assessment visit, specify the number of the last visit completed and the current visit date in the upper right-hand corner. This form should be entered as a single form.

If any medications other than the study rescue ProAir® medication were used, record the medications on the Concomitant Medications for Asthma/Allergy and Adverse Events (CMED) form.

Question 1140. The participant is ineligible to perform pulmonary function testing if any of the shaded boxes are completed. However, two exceptions for an ineligible participant to continue with spirometry are as follows:

1. An ineligible participant may proceed with spirometry if this is an FEV_1 re-assessment visit for evaluation of a significant asthma exacerbation.

2. An ineligible participant may proceed with spirometry if he or she is already known to be a treatment failure at visits 1, 2, 3, 4, 6, or 8.

If the participant is not eligible to proceed with spirometry and is willing to reschedule the visit, file the collected data in his or her study folder; do not enter the data or forward it to the DCC.

If a spirometry eligibility protocol exception was granted through the DCC, complete the question(s) for which the exception was granted accurately (i.e. complete the shaded box). Q1140 should be answered 'Yes' to indicate the participant is eligible to proceed and any entry errors that result from the exception should be marked

unresolvable. In the unresolvable comment section, indicate that a protocol exception was granted, who granted it, and the justification for the exception. Also, complete the comment field (Q6000) provided on the last page of the form with additional information on the exception.

Question 1150. If participant is 18 to 20 years old, complete Q1150 at Visits 2-8, and 90A-92A. For Supervised Washout participants 18 to 20 years old, Q1150 should also be completed at Visits 0B and 1.

At Visits 0A, 1 (for non-Supervised Washout participants only) and 9, refer to height recorded on the Adult Body Measurements (BODYMEAS_ADULT) form; do not record on this form.

4.1.26 SIENA Scheduled Medications (P6_MED)

Purpose: The dispensation of post-randomization scheduled medications is recorded on this form.

Who: An AsthmaNet coordinator completes the form.

When: Visits 3-8

Note: This form must be completed every time scheduled inhalers are dispensed at regular visits (Visits 3-8) and in the event of backup dispensation for lost scheduled medication(s).

Form Instructions:

The SIENA Scheduled Medications (P6_MED) form must be completed **every** time scheduled medications are dispensed.

Following the loss of medications, complete a new SIENA Scheduled Medications (P6_MED) form with the current date and the visit number corresponding to the last visit completed in the upper right-hand corner. Indicate backup medication dispensation in Q1000.

For more information on backup drug procedures, see Section 5 of this MOP and the Study Medications discussion in Section 2.

If backup medications are dispensed, complete the SIENA Scheduled Medications (P6_MED) form and enter it as a single form (with Q1000 = 2). For example, when scheduled medications are dispensed at Visit 5, complete the packet Visit 5 SIENA Scheduled Medications (P6_MED) form. If the participant loses the vial dispensed at regular Visit 5, generate backup inhaler numbers and complete the SIENA Scheduled Medications (P6_MED) form for the backup medication dispensation. Enter this form as a Visit 5 single form at the time of backup medication dispensation.

Questions 1010 and 1040. If the P6_MED form is completed, these fields should always be answered. If medications were dispensed due to backup and only one of the medications needed dispensed, the other field should be completed with a ‘0’. For example, if only the Respimat® supply was lost by a participant and in need of refill, then Q1040 should be answered ‘0’.

Questions 1020, 1030 and Labels. At Visits 3-8, remove the label(s) from the dispensed Respimat® inhalers and affix to the SIENA Scheduled Medications (P6_MED) form in the box(es) next to Q1020 and Q1030. Copy the vial number(s) into fields Q1020 and Q1030.

Twisthaler®:
Questions 1050-1070 and Labels. At Visits 3-8, remove the label(s) from the dispensed Twisthalers® and affix to the SIENA Scheduled Medications (P6_MED) form in the box(es) next to the fields. Copy the inhaler number(s) into fields Q1050-Q1070.

MDI:
Question 1050 and Label. At Visits 3-8, remove the label from the dispensed MDI and affix to the SIENA Scheduled Medications (P6_MED) form in the box next to the field. Copy the inhaler number into field Q1050; fields Q1060-Q1070 should not be completed if only one MDI is dispensed.

After affixing the labels, the coordinator should sign and date the source documentation box provided (Q1090-1100).

4.1.27 SIENA Significant Asthma Exacerbation (P6_SIGEX)

Purpose: This form outlines the significant asthma exacerbation criteria to determine if a participant experienced an event during the SIENA study.

Who: An AsthmaNet coordinator completes the form.

When: Visits 0A, 0B, 1-3, 90A-92A

Form Instructions:

The SIENA Significant Asthma Exacerbation (P6_SIGEX) form is completed **only** if the participant experiences a significant asthma exacerbation as defined in the Significant Asthma Exacerbation discussion in Section 2.

The SIENA Significant Asthma Exacerbation (P6_SIGEX) form should be entered and forwarded to the DCC within one week of form completion. If this form is completed between visits prior to randomization, specify the number of the last visit completed and the current date in the upper right-hand corner. If the participant experiences a significant asthma exacerbation after randomization, this form should be entered as part of the V90A, 91A, or 92A packet (depending on number of previous significant asthma exacerbation events for the participant).

Question 1010. Refer to the Q19 column 'Number of RED RESCUE puffs taken during the past 24 hours' on the participant's Spirotel® Participant Visit Report (P6_SPIROTEL_RPT) to answer Q1010.

Question 1020. Refer to Q1030 on the participant's spirometry data collected on the Spirometry Testing (SPIRO) form(s) at two consecutive visits (a regular study visit and a FEV_1 re-assessment visit). The baseline value is Q1030 on the Spirometry Testing (SPIRO) form at Visit 1. If two consecutive FEV_1 values are below 50% of the baseline prebronchodilator value the criterion is met.

If the participant's FEV_1 is less than 50% of the baseline prebronchodilator value at the regular visit and a second spirometry session (FEV_1 re-assessment visit) is not completed, Q1020 should be answered 'Not evaluated.'

If the participant's prebronchodilator FEV_1 is less than 50% of baseline for the first time and the participant does not meet any other significant asthma exacerbation criteria according to the SIENA Significant Asthma Exacerbation form (P6_SIGEX), schedule the participant to return to the clinic for repeat spirometry within 1-4 days

(i.e., FEV_1 re-assessment visit). If the participant does not return for the re-assessment visit, or if he/she does not perform spirometry at the FEV_1 re-assessment visit, select 'Not evaluated'. The SIENA Asthma Monitoring Log (P6_ASTHMA_LOG) should be returned to the participant for use prior to the scheduled FEV_1 re-assessment visit.

For more information about FEV_1 re-assessment visits, refer to the gray box on the visit procedure checklists starting at Visit 2 and the FEV_1 re-assessment section of the SIENA MOP section 2.

Question 1030. Refer to Q1040 on the participant's spirometry data collected on the Spirometry Testing (SPIRO) form at two consecutive visits (a regular study visit and a FEV_1 re-assessment visit). If two consecutive FEV_1 values are below 40% of predicted according to Q1040, the criterion is met.

If the participant's FEV_1 is less than 40% of predicted at the regular visit and a second spirometry session (FEV_1 re-assessment visit) is not completed, Q1030 should be answered 'Not evaluated.'

Question 1040. If the study or treating physician prescribed the participant oral/parenteral corticosteroids for the treatment of his or her asthma, record the details on the Concomitant Medications for Asthma/Allergy and Adverse Events (CMED) form.

Question 1060. If any of the shaded boxes is completed in Q1000-1050, the participant experienced a significant asthma exacerbation. Complete Q1070 and record the event on the Clinical Adverse Events (AECLIN) form using ICD-9 code 493.92.

If non-study medication was taken for treatment of the significant asthma exacerbation, record the medication on the Concomitant Medications for Asthma/Allergy and Adverse Events (CMED) form and link the medication to the significant asthma exacerbation event. Do this by recording the event record ID in Q1020 on the Concomitant Medications for Asthma/Allergy and Adverse Events (CMED) form.

If the completed form indicates the participant did not experience a significant asthma exacerbation, do not complete Q1070 and do **not** enter or submit the form to the DCC.

Question 1070. Record the date when the exacerbation criteria is met. If multiple criteria were met to indicate a significant asthma exacerbation, record the earliest date criterion was confirmed.

If a criterion requires confirmation (i.e., a second spirometry session) and upon the second spirometry session, the participant experiences a significant exacerbation event, record the date conditions were met using the date of the second measurement.

Question 1150. If Q1150 is answered Yes, complete a SERIOUS form and forward to the SIENA scientific coordinator within 72 hours.

Question 1190-1240. Participants experiencing a significant asthma exacerbation will be treated with oral prednisone (dispensed at participant's first visit). Record oral prednisone, as well as non-study inhaled corticosteroids, nebulized bronchodilator, oral corticosteroids, IM or IV steroids, antibiotics, or other medications taken for the exacerbation on the Concomitant Medications for Asthma/Allergy and Adverse Events (CMED) form. Link the medication to the significant asthma exacerbation event on the Clinical Adverse Events (AECLIN) form.

Question 1250. This question should be completed by the study physician that saw the participant for significant asthma exacerbation conditions.

If the participant's study medications are changed as a result of the significant asthma exacerbation, link the change in study medications to the exacerbation event by recording the event record ID in Q1010 on the SIENA Change in Study Medications (P6_CHANGE_MEDS) form.

A significant asthma exacerbation should be recorded on the Clinical Adverse Events (AECLIN) form as both a treatment failure and a significant asthma exacerbation. Therefore, if a participant experienced a significant asthma exacerbation since the last visit, both the significant asthma exacerbation and treatment failure event ICD-9 codes should be recorded on the appropriate Clinical Adverse Events (AECLIN) form. The ICD-9 codes for a significant asthma exacerbation and a treatment failure are 493.92 and 000.00, respectively.

Oral prednisone taken for treatment of a significant asthma exacerbation (which also qualifies as a treatment failure, by definition), should be recorded on the Concomitant Medications for Asthma/Allergy and Adverse Events (CMED) form and linked to the significant asthma exacerbation event. Do this by recording the significant asthma exacerbation event record ID in Q1020 of the medication record on the Concomitant Medications for Asthma/Allergy and Adverse Events (CMED) form. Any treatment required should also be indicated in the significant asthma event record on the Clinical Adverse Events (AECLIN) form, not the treatment failure event record. In other words,

Q1110 should be answered ‘2,’ or ‘medication,’ for the significant asthma exacerbation event and ‘1,’ or ‘none,’ for the treatment failure event.
Participants taking oral prednisone for treatment of significant asthma exacerbation will be instructed to discontinue study medications while taking prednisone. In this case, link the change in study medications to the significant asthma exacerbation event, not the treatment failure event, by recording the significant asthma exacerbation event record ID in Q1010 on the SIENA Change in Study Medications (P6_CHANGE_MEDS) form. The change in study medications should also be indicated in the significant asthma event record on the Clinical Adverse Events (AECLIN) form, not the treatment failure event record. In other words, Q1090 should be answered ‘2,’ or ‘altered,’ for the significant asthma exacerbation event and ‘1,’ or ‘unchanged,’ for the treatment failure event.

4.1.28 SIENA Significant Asthma Exacerbation Phone Follow-Up (P6_SIGEX_FOLLOW)

Purpose: This form guides the coordinator in completing a significant asthma exacerbation phone contact with the participant. The questions assist in checking the participant's medication usage and medical care since the Asthma Exacerbation visit or last scheduled phone call for an exacerbation event.

Who: An AsthmaNet coordinator completes the form.

When: Visits 90B-92B, 90C-92C, 90D-92D

Form Instructions:

Question 1000. Write in the number between 0-2 that represents which visit this form is being completed for considering the participant's previously completed Asthma Exacerbation Kits. The visit written in here should match the visit ID in the header of the form.

Question 1080. If Q1080 is answered Yes, complete a SERIOUS form and forward to the SIENA scientific coordinator within 72 hours.

Question 1120-1170. If the participant required treatment with non-study inhaled corticosteroids, nebulized bronchodilator, oral corticosteroids, IM or IV steroids, antibiotics, or other medications since the last Asthma Exacerbation contact, record the details on the Concomitant Medications for Asthma/Allergy and Adverse Events (CMED) form. Link the medication to the significant asthma exacerbation event on the Clinical Adverse Events (AECLIN) form.

At Phone Contact #1, additional care and medications started since the Asthma Exacerbation visit should be recorded. At Phone Contact #2 and #3, additional care and medications started since the last Asthma Exacerbation phone contact should be recorded.

The new medication(s) obtained during the phone contacts should be recorded on the CMED form completed at the last regular visit. The new medication(s) should be updated in the Participant Data module within the data management application. The same applies for any new event(s) obtained; they should be recorded on the AECLIN form completed at the last regular visit and updated in the Participant Data module.

4.1.29 SIENA Termination of Study Participation (P6_TERM)

Purpose: The date and the primary reason for a participant's termination of study participation are recorded on this form.

Who: An AsthmaNet coordinator completes the form.

When: Visits 0A-9, 90A-92A

Note: This form is completed at Visit 9 for those participants who complete the entire SIENA study. It may be completed at regular study visits (Visits 0A-8) and significant asthma exacerbation visits (90A-92A) when the participant withdraws consent, becomes pregnant, or is terminated by performance site staff.

Form Instructions:

Visit Date: This date should be the date the form is completed. It may not necessarily be the same as the most recent regular visit date. For example, if the participant is being terminated due to loss to follow up, the visit date would be the date the coordinator completed this form to document the termination, NOT the visit date of the last regular visit.

If a participant withdraws consent or is terminated from the SIENA study during a visit, specify the number of the current visit and the current visit date in the upper right-hand corner. For example, if the participant terminates during Visit 5, then the visit number on the form should be '5.' This form will be entered into the AsthmaNet database as a single form.

If a participant withdraws between visits, submit the SIENA Termination of Study Participant (P6_TERM) form with the number of the last visit completed in the upper right-hand corner. For instance, a participant could be terminated from the SIENA study following Visit 8 due to moving out of the area. In this case, the SIENA Termination of Study Participant (P6_TERM) form should be entered as a single form with the last visit number completed in the upper right-hand corner of the form, Visit 8.

Question 1010. If Q1010 is answered 'Participant,' complete Q1020 and Q1030D, if applicable, and skip to the signatures section of the form. Otherwise, skip to Q1040 and complete the rest of the form.

Question 1030D. An explanation should be provided for Q1030D if Q1020 is answered 1, 2, 6, 7, 8, or 10. If an explanation is provided, enter the full explanation

(up to 100 characters) into the AsthmaNet database; otherwise, leave the field blank during data entry.

Questions 1040-1180. ALL applicable reasons for termination should be noted in these questions, even if not the primary reason for termination (Q1200). For example, if the participant is being terminated due to a significant asthma exacerbation during the run-in (Visits 1-3), but also had low medication dosing compliance, both Q1120 and Q1160 would be answered 'Yes'.

Question 1040. If the participant is male, Q1040 should be answered 'N/A.' If the participant is female and surgically sterile or postmenopausal, Q1040 should be answered 'No.' Q1040 should be answered 'Yes' if the participant becomes pregnant during the course of the SIENA study.

Question 1190D. An explanation should be provided for Q1190D if any of the following is answered 'Yes': Q1050, Q1080-Q1185. If an explanation is provided, enter the full explanation (up to 100 characters) into the AsthmaNet database. Otherwise, leave the field blank during data entry.

Question 1200. At least one of the questions in Q1040-1180 must be answered 'Yes' if clinical staff terminated the participant. Of the questions Q1040-1185 marked 'Yes', indicate the letter associated with the **primary** reason for termination in Q1200.

This form requires the signatures of the coordinator and AsthmaNet investigator to verify that all data collected for this participant are correct to the best of their knowledge.

Questions 1210 and 1230. If a signature is not present, this field should be left missing during data entry.

Any AsthmaNet investigator (site director, Principal Investigator, or other) may sign field Q1230 to verify that all data collected for this participant are correct to the best of their knowledge.

4.1.30 SIENA Treatment Failure Checklist (P6_TXFAIL_CHK)

Purpose: This form ensures that the participant is assessed thoroughly for treatment failure criteria at all applicable visits.

Who: An AsthmaNet coordinator completes the form.

When: Visits 1-9

Note: If this form is completed in between Visits 1 and 2, complete this form as a single form using visit number 1.

Form Instructions:

Question 1000. Reference the Q1 column on the participant's Spirotel® Participant Visit Report (P6_SPIROTEL_RPT) to determine if the participant awakened from asthma three or more times in a two-week period or on two consecutive nights.

Question 1010. Reference the Q20 column on the participant's Spirotel® Participant Visit Report (P6_SPIROTEL_RPT) to determine if the participant used albuterol for relief of symptoms four or more times/day for two or more consecutive days. **Note**: Q20 may be missing due to the response to Q19 for a trial date.

Question 1020. Reference the Q21 column on the participant's Spirotel® Participant Visit Report (P6_SPIROTEL_RPT) to determine if albuterol relieved symptoms for less than four hours after treatment. **Note**: Q21 may be missing due to the response to Q19 for a trial date.

Question 1030. Reference the Q20 column on the participant's Spirotel® Participant Visit Report (P6_SPIROTEL_RPT) and Q1010 on the SIENA Baseline PEF and Rescue Use Values (P6_BASELINE) form to determine if the participant used albuterol for relief of symptoms daily for seven days and if this use exceeded two times the baseline weekly use of albuterol.

At Visit 1, for non-Supervised Washout participants, you will need to calculate weekly high rescue use. For a participant with a rescue reference value of 2 puffs, multiply 2 puffs by 14 (2 x 14 = 28): weekly high rescue use = 28. At Visit 1 (for Supervised Washout participants) and Visit 2 (for non-Supervised Washout participants), the weekly high rescue use value will be printed on the SIENA Spirotel® Baseline Report (P6_BASELINE).

Question 1040. Reference the Q17 column on the participant's Spirotel® Participant Visit Report (P6_SPIROTEL_RPT) to determine if regular exercise caused unusually severe shortness of breath on two or more days during a seven day period.

Question 1050. If the participant experienced a significant asthma exacerbation, complete a SIENA Significant Asthma Exacerbation (P6_SIGEX) form and do **NOT** complete a SIENA Treatment Failure Information (P6_TXFAIL) form. The SIENA Treatment Failure Checklist (P6_TXFAIL_CHK) should still be completed.

Question 1060. If any of the shaded boxes is completed, the participant experienced a treatment failure. The rest of this form should be completed and the treatment failure event should be recorded on the Clinical Adverse Events (AECLIN) form using ICD-9 code 000.00 (the study specific treatment failure event code).

In addition, a SIENA Treatment Failure Information (P6_TXFAIL) form should be completed if Q1050 is answered No.

If it was determined the participant did not experience a treatment failure, do not complete the rest of the P6_TXFAIL_CHK form and continue on with the remaining visit procedures. Do **not** complete a SIENA Treatment Failure Information (P6_TXFAIL) form.

Question 1070. Record the date when the treatment failure criteria is met. If multiple criteria were met to indicate a treatment failure, record the earliest date criterion was confirmed.

Questions 1080-1110. If the participant experienced a significant asthma exacerbation that led to completion of the P6_TXFAIL_CHK form, the entire second page of the form does not need to be completed.

Questions 1080 and 1090. These questions are to be completed only at Visits 4 through 8. The treatment periods are defined as between Visits 3 and 5, between Visits 5 and 7, and between Visits 7 and 9.

For detailed information regarding treatment failures, see the Treatment Failure discussion in Section 2.

Question 1100. If Q1100 is answered Yes, record the high-dose ICS on the CMED form. If Q1100 is answered No, answer Q1110 and Q1110D, if necessary.

Participants should remain on scheduled medications during treatment failure; however, if the participant's study medications are changed as a result of the

treatment failure, link the change in study medications to the treatment failure event by recording the event record ID in Q1010 on the SIENA Change in Study Medications (P6_CHANGE_MEDS) form. The treatment failure AECLIN record – ICD9 code 000.00 – should have Q1090 = 2 to indicate change in study medications.

4.1.31 SIENA Treatment Failure Information (P6_TXFAIL)

Purpose: The details of each treatment failure event, including type of care, treatment, and physician assessment, are recorded on this form.

Who: An AsthmaNet coordinator completes the form.

When: Visits 1-9, as needed

Note: This form should be completed only when the SIENA Treatment Failure Checklist (P6_TXFAIL_CHK) form indicates that the participant met treatment failure criteria and did **NOT** meet significant asthma exacerbation criteria.

Form Instructions:

Question 1070-1120. If the participant required treatment with non-study inhaled corticosteroids, nebulized bronchodilator, oral corticosteroids, IM or IV steroids, antibiotics, or other medications, record the details on the Concomitant Medications for Asthma/Allergy and Adverse Events (CMED) form. Link the medication to the treatment failure event on the Clinical Adverse Events (AECLIN) form.

If oral corticosteroids and/or IM or IV steroids were taken, a SIENA Significant Asthma Exacerbation (P6_SIGEX) form should be completed.

4.1.32 SIENA Washout Form (P6_WASHOUT)

Purpose: To confirm that the participant meets washout requirements prior to proceeding with the visit.

Who: The coordinator completes the form.

When: Visits 5, 7, and 9

Form Instructions:

Question 1000. Treatment periods are defined as between Visits 3 and 5, between Visits 5 and 7, and between Visits 7 and 9. If Q1000 is answered No, the participant is eligible to complete Visit 5, 7 or 9. If Q1000 is answered Yes due to an asthma exacerbation, the participant is still eligible to complete Visit 5, 7 or 9. If Q1000 is answered Yes for a treatment failure (that is NOT also an asthma exacerbation), continue on with completion of Q1010.

Question 1010. If Q1010 is answered 'Yes' due to study physician feeling the study treatment contributed to treatment failure **alone** and **not** because of two or more treatment failures in a treatment period, please note this in Q6000. Doing so will prevent a query from being sent by Data Management staff.

Question 1020. If Q1010 is answered 'Yes,' Q1020 should be completed. Refer to the Concomitant Medications for Asthma/Allergy and Adverse Events (CMED) form for date of final dose.

If 2 weeks have not passed since the participant's final dose of open-label Asmanex®, the current visit should be rescheduled at least 14 days after treatment completion. The current P6_WASHOUT form should be filed in the participant folder and not entered or submitted to the DCC.

If Q1020 is answered Yes, the participant is eligible to complete Visit 5, 7, or 9.

If IRB approval for protocol version 4.1 has NOT yet been obtained:
Question 1040. The current visit date **must be at least 6 weeks** after the date of final dose of open-label Asmanex® to answer Q1040 'Yes.' Refer to the Concomitant Medications for Asthma/Allergy and Adverse Events (CMED)
form for date of final dose. For example, if the date of final dose of open-label Asmanex® is 05/01/2014, the minimum washout period would be met on 06/12/2014.

If Q1040 is answered 'No,' stop the current visit and reschedule for a date that meets the minimum 6 week washout requirement **but does not exceed the maximum 7**

weeks from the final dose (06/19/2014 at the latest for the above example). File the completed form in the participant folder and do not enter. The visit will have to be repeated from the beginning when the participant returns. The return visit number should remain unchanged.

If IRB approval for protocol version 4.1 has been obtained:
Question 1050. The current visit date **must be at least 3 weeks** after the date of final dose of open-label Asmanex® to answer Q1050 'Yes.' Refer to the Concomitant Medications for Asthma/Allergy and Adverse Events (CMED) form for date of final dose. For example, if the date of final dose of open-label Asmanex® is 05/01/2014, the minimum washout period would be met on 05/22/2014.

If Q1050 is answered 'No,' stop the current visit and reschedule for a date that meets the minimum 3 week washout requirement **but does not exceed the maximum 4 weeks** from the final dose (05/29/2014 at the latest for the above example). File the completed form in the participant folder and do not enter. The visit will have to be repeated from the beginning when the participant returns. The return visit number should remain unchanged.

4.1.33 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: Visits 0A, 0B, 1-9

Form Instructions:

Please note that at Visit 2A, the SPIROTELQC form should have a visit ID of 3 in the header of the form, as that should be the visit ID programmed into the spirotel® device.

4.1.34 Wisconsin Upper Respiratory Symptom Survey—21 Daily Symptom Report (WURSS_21)

Purpose: To record a participant's daily upper respiratory symptoms as part of the Asthma Exacerbation Kit.

Who: The participant completes the form.

When: Visits 90D-92D

Form Instructions:

Participants in the SIENA study will be given 21 copies of the Wisconsin Upper Respiratory Symptom Survey—21 Daily Symptom Report (WURSS_21) form at Visit 3 with the Asthma Exacerbation Kit.

When a set of Wisconsin Upper Respiratory Symptom Survey—21 Daily Symptom Report (WURSS_21) forms is returned to the clinic, the coordinator will complete the visit ID, return visit date, and coordinator ID fields on each form. The set of forms will be entered as a group, or "cold packet," under the single form entry type in the database.

For more information on the Wisconsin Upper Respiratory Symptom Survey—21 Daily Symptom Report (WURSS_21) form, see Section 10 of the AsthmaNet General MOP or the Wisconsin Upper Respiratory Symptom Survey—21 discussion in Section 2.

4.2 Administrative Forms

Administrative forms facilitate processing of the participant and visit flow by the performance sites and the DCC. They are not entered into the AsthmaNet database and they are not submitted to the DCC in most cases. The following is a list of all SIENA study administrative forms and related instructions[1]:

Administrative Form Name	Form Code
SIENA Asthma Monitoring Log	P6_ASTHMA_LOG
SIENA ImmunoCAP/Total IgE Serum Sample Log	P6_IGE_SAMPLE_LOG
SIENA Participant Assignment Log	P6_LOG
SIENA Periostin Serum Sample Log	P6_PERI_SAMP_LOG
SIENA Phone Contact Form	P6_CONTACT/P6_CONTACT_2
SIENA Serum Sample Log	P6_SERUM_SAMP_LOG
SIENA Visit Procedure Checklists	P6_VISITX

[1] Drug logs and related procedures are covered in the SIENA Pharmacy MOP

4.2.1 SIENA Asthma Monitoring Log (P6_ASTHMA_LOG)

Purpose: The participant's scheduled AM and PM peak flows (PEF) and daily RESCUE ProAir® inhaler puffs are recorded on this form as a reference. This form also collects information on adverse events and concomitant medications.

Who: The participant completes the form.

When: Return Visits 0B-9

Form Instructions:

The following information is recorded daily on the SIENA Asthma Monitoring Log (P6_ASTHMA_LOG) at each session performed on the spirotel device. This log will be used by the participant and coordinator as a reference because the spirotel® device will not allow the participant to go back and review data from previous days:

1. Nighttime awakenings due to asthma
2. Highest scheduled AM and PM peak flows (PEF)
3. Daily RED RESCUE ProAir® inhaler puffs
4. Total Daily RED RESCUE ProAir® times used

The last page of the SIENA Asthma Monitoring Log (P6_ASTHMA_LOG) is designed to record the following information that occurred since the last study visit:

1. Any non-study medications the participant took since the last study visit
2. Details of any medical problems the participant experienced since the last study visit (adverse events)

The first field of the Date column in the .pdf version of the SIENA Asthma Monitoring Log (P6_ASTHMA_LOG) is fillable. This form is available on the AsthmaNet secure website via the following path: Forms: SIENA: Admin Forms.

Before printing out this form to give to the participant, the coordinator can prefill all date fields on the form by entering the current date in the first field of the Date column and then clicking elsewhere in the form. The rest of the fields will prefill with subsequent dates up to 8 weeks from the current date.

The coordinator should complete the 65% baseline peak flow (PEF) reference value (65% Baseline PEF) in the "IMPORTANT" paragraph before giving the SIENA Asthma Monitoring Log (P6_ASTHMA_LOG) to the participant.

4.2.2 SIENA ImmunoCAP/Total IgE Serum Sample Log (P6_IGE_SAMPLE_LOG)

Purpose: To record information regarding a participant's specimen collection for ImmunoCAP and IgE tests.

Who: An AsthmaNet Coordinator completes the log.

When: Each time ImmunoCAP/Total IgE serum samples are collected.

Form Instructions:

When a blood sample (tiger top tube) is collected for ImmunoCAP and IgE tests, the Coordinator must complete a new row on the log for the participant ID. The log captures information on the collection of the tube as well as the processing. Storage conditions are also recorded.

SIENA sample barcodes do not contain participant identifiers. **It is important to record the barcodes on the log and enter the samples into Biological Sample Tracking as soon as possible after processing occurs.**

This log will be reviewed during AsthmaNet site visits.

For use only at the Clinical Center. This form is not data entered.

DO NOT forward to the DCC.

4.2.3 SIENA Participant Assignment Log (P6_LOG)

Purpose: This form is a log of all participants enrolled in the SIENA study.

Who: An AsthmaNet coordinator completes the log.

When: Visits 0A, 1, and 3

Form Instructions:

The SIENA Participant Assignment Log (P6_LOG) must be used each time a **new** participant ID number is assigned. A new participant ID number is assigned by completing the next available blank entry on the log at Visit 0A or 1. The protocol ID, site ID, and participant ID will be pre-filled on the assignment log printed from Forms: SIENA: Admin Forms section on the AsthmaNet secure website.

Participant initials must have three letters. The letter "X" should be used if a participant does not have a middle initial. The participant's initials must be the same initials entered in the AsthmaNet Registry module.

The participant's name should be written last name first, followed by first name on the SIENA Participant Assignment Log (P6_LOG).

At Visit 3, if the participant is randomized, mark the checkbox under the Randomized column.

This log, along with the corresponding medication logs, will be reviewed during AsthmaNet site visits.

4.2.4 SIENA Periostin Serum Sample Log (P6_PERI_SAMP_LOG)

Purpose: To record information regarding a participant's specimen collection for periostin testing.

Who: An AsthmaNet Coordinator completes the log.

When: Each time periostin serum samples are collected.

Form Instructions:

When a blood sample (tiger top tube) is collected for periostin testing, the Coordinator must complete a new row on the log for the participant ID. The log captures information on the collection of the tube as well as the processing. Storage conditions are also recorded.

SIENA sample barcodes do not contain participant identifiers. **It is important to record the barcodes on the log and enter the samples into Biological Sample Tracking as soon as possible after processing occurs.**

This log will be reviewed during AsthmaNet site visits.

For use only at the Clinical Center. This form is not data entered.

DO NOT forward to the DCC.

4.2.5 SIENA Phone Contact Form (P6_CONTACT/P6_CONTACT_2)

Purpose: This form guides the coordinator in completing a scheduled phone contact with the participant. The questions assist in checking the participant's asthma control, scheduled medication usage, and medical care.

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

When: At phone calls between study visits starting after Visit 1

Form Instructions:

When completing this form, specify the number of the last visit completed in the upper right-hand corner.

Complete the gray box with coordinator ID, date, time, and if contact occurred for each attempt made to contact the participant. Record any comments regarding the contact attempt in the Contact Occurred column.

When contact is made with the participant, ask him or her to refer to the SIENA Asthma Monitoring Log (P6_ASTHMA_LOG) as the coordinator will be asking the participant questions regarding RESCUE ProAir® use, compliance, and treatment failure assessment.

Question 1. Check only one box. If Q1 is answered 'Other', a description should be provided.

Questions 3 – 6. Indicate if the participant has been using his/her scheduled medications, completing the spirotel® e-diary, and performing three peak flow maneuvers every morning and evening.

If any of the questions are answered 'No,' review study adherence with the participant/guardian.

Question 7a. If the participant indicates that he or she has received the "Peak flow is low" spirotel alert, inquire as to his/her current asthma conditions and albuterol use.

Question 7b. If the participant indicates that he or she has received the "Rescue use high" spirotel alert, he/she has used greater than or equal to 16 puffs of albuterol per 24 hours for a period of 48 hours, meeting Significant Asthma Exacerbation criteria.

If YES to Question 7b or 8a,

- At Visit 1, 2, or 2A, complete a Significant Asthma Exacerbation (P6_SIGEX) form and update CMED and AECLIN forms. The participant is ineligible.

- At Visit 3-8, see Significant Asthma Exacerbation discussion in Section 2 of the SIENA MOP for further details, including completion of P6_SIGEX, CMED and AECLIN forms.

Question 7c. If the participant indicates that he or she has received the "E-diary indicates you need YELLOW inhaler" spirotel alert, he/she has met one of the Treatment Failure criteria. See Treatment Failure discussion in Section 2 of the MOP for further details, including completion of Treatment Failure Checklist (P6_TXFAIL_CHK), Treatment Failure Information (P6_TXFAIL), CMED and AECLIN forms.

Question 8. If the participant indicates that he or she took any new medications other than those given as part of the study since the last visit, record the medication on the Concomitant Medications for Asthma/Allergy and Adverse Events (CMED) form at the next visit.

Question 8a. If the participant was treated with prednisone or another systemic corticosteroid since the last study contact, he/she has met Significant Asthma Exacerbation criteria.

If YES to Question 7b or 8a,

- At Visit 1, 2, or 2A, complete a Significant Asthma Exacerbation (P6_SIGEX) form and update CMED and AECLIN forms. The participant is ineligible.
- At Visit 3-8, see Significant Asthma Exacerbation discussion in Section 2 of the SIENA MOP for further details, including completion of P6_SIGEX, CMED and AECLIN forms.

Question 9. If the participant indicates that he or she experienced a medical problem since the last visit, record the event on the Clinical Adverse Events (AECLIN) form at the next visit.

Question 10. If the participant indicates that he or she had any changes to non-study medications since the last visit, record the medication change on the Concomitant Medications for Asthma/Allergy and Adverse Events (CMED) form at the next visit. Depending on the type of medication that was changed, the Concomitant Medications for Non-Asthma Drugs (CMED_NON) form may instead need to be updated.

P6_CONTACT version only: Question 11. Complete the gray box above Q11 to verify the next visit date for the participant and whether this visit is before or after Twisthaler® expiration. If it is after expiration of the Twisthaler®, additional study medications should be dispensed.

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

4.2.6 SIENA Serum Sample Log (P6_SERUM_SAMP_LOG)

Purpose: To record information regarding a participant's specimen collection for serum testing.

Who: An AsthmaNet Coordinator completes the log.

When: Each time serum samples are collected.

Form Instructions:

When a blood sample (tiger top tube) is collected for serum testing, the Coordinator must complete a new row on the log for the participant ID. The log captures information on the collection of the tube as well as the processing. Storage conditions are also recorded.

SIENA sample barcodes do not contain participant identifiers. **It is important to record the barcodes on the log and enter the samples into Biological Sample Tracking as soon as possible after processing occurs.**

This log will be reviewed during AsthmaNet site visits.

For use only at the Clinical Center. This form is not data entered.

DO NOT forward to the DCC.

4.2.7 SIENA Visit Procedure Checklists (P6_VISIT0A, P6_VISIT0B, P6_VISIT1, P6_VISIT1_2, P6_VISIT1_SUP, P6_VISIT1_SUP_2, P6_VISIT2, P6_VISIT2A, P6_VISIT3, P6_VISIT3_2, P6_VISIT4_6_8, P6_VISIT5_7, P6_VISIT9, P6_VISIT90_92, P6_VISIT90A_92A, P6_VISIT90B_C-92B_C, P6_VISIT90D_92D, P6_VISIT_WASHOUT)

Purpose: To provide the coordinator with a checklist of all procedures and forms completed during a visit.

Who: An AsthmaNet coordinator completes the form.

When: At the specified visit

Form Instructions:

These checklists serve as guides for the coordinator and should be sent to the DCC, in front of the visit packet, with the other forms in the packet.

For all procedures and forms, indicate whether or not the procedure or form was completed. If it was not completed, indicate the reason in the comment field.

At Visits 4, 6, and 8: If a visit is missed, complete the checklist indicating the missed visit and document if any other actions were completed (i.e., dispensation of additional study medications, quality control testing of the spirotel® device, etc.). The completed checklist should be filed at the performance site and does not need to be sent to the DCC.

At Visits 90, 91, and 92: The visit checklist is not included in the Visits 90-92 packet printed from the website. The checklist should be printed from the Forms → SIENA → Admin forms section of the website upon receipt of the Visit 9X forms completed by the participant (which will occur at the in-clinic Visit 9XA visit) and prior to sending the packet to the DCC.

At extra study visits due to washout (from treatment failure or run-in respiratory infection), the P6_VISIT_WASHOUT visit checklist does not need to be forwarded to the DCC. It is for site purposes only and can be retained in the participant folder.

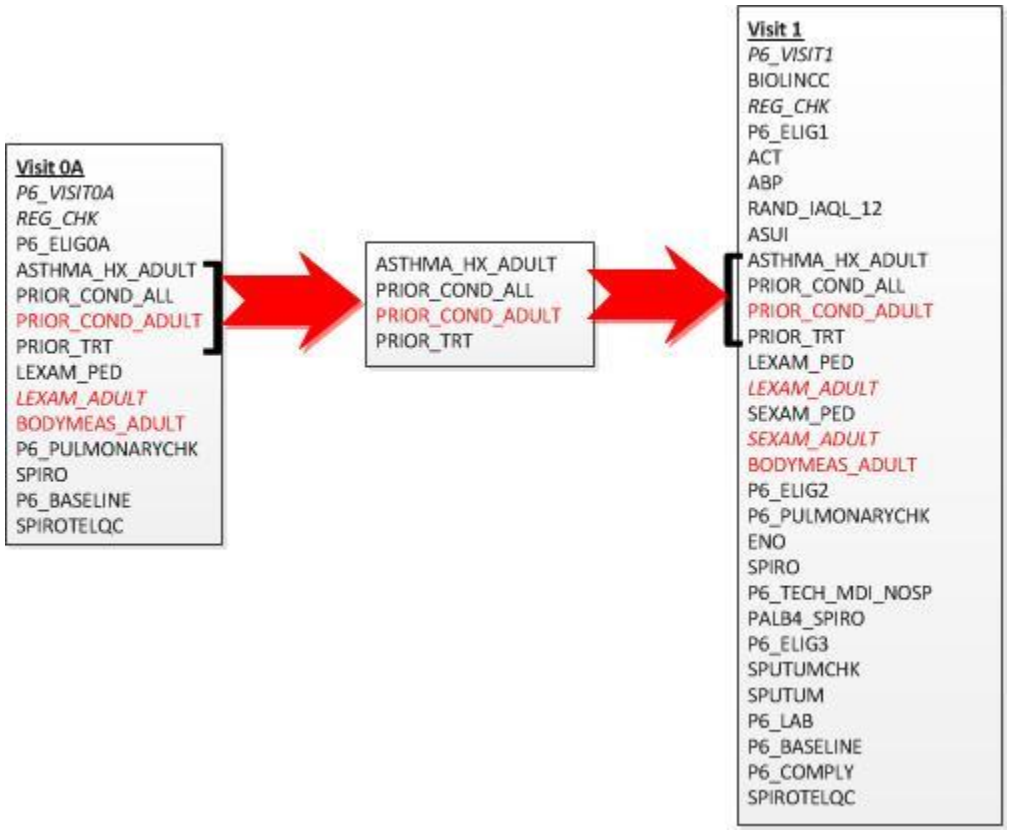
Procedures should be followed in the order they are presented on the visit checklist for applicable visits. If certain procedures, such as pulmonary function testing and questionnaire completion, are performed out of order, a protocol deviation will be assigned.

This form is not entered during data entry. Note: The asterisks present throughout the checklists are to indicate forms that should not be sent to the DCC. The checklists should be sent to the DCC with successful visit packets.

4.3 Handling forms from Visit 0A at Visit 1

For participants completing the Supervised Washout Visit 0A, the ASTHMA_HX_ADULT, PRIOR_COND_ALL, PRIOR_COND_ADULT (for 18+) and PRIOR_TRT forms will be completed at Visit 0A but not entered or forwarded to the DCC until Visit 1 (indicated by a † symbol on the Visit 0A checklist). If the participant completes Visit 0A but does not eventually complete Visit 1, these forms will be retained at the site in the participant folder but not entered nor forwarded to the DCC.

After Visit 0A is completed and prior to entry of the Visit 0A packet, remove the ASTHMA_HX_ADULT, PRIOR_COND_ALL, PRIOR_COND_ADULT (18+) and PRIOR_TRT forms from the packet, paper clip together, and store in participant folder until Visit 1. Prior to Visit 1, insert these forms into the '**Visit 1, SUP (Ages 12-17)**' or '**Visit 1, SUP (Ages 18+)**' Visit 1 packet printed from the website. The forms should then have the visit dates updated to the Visit 1 date and the data updated as necessary at Visit 1. Please use red ink for any updates, crossing out the previous response and circling the new, correct response with coordinator initials and date present. These forms will then be entered and forwarded to the DCC with the Visit 1 packet.



4.4 Visit Packet Organization

For participants ages 12-17, print the '(Ages 12-17)' packet versions posted on the website for Visits 0A, 0B, 1, 1 SUP, 2, 2A, 3, 4, 5, 6, 7, 8, 9, 90A-92A. These packets will contain the LEXAM_PED or SEXAM_PED data collection forms. The LEXAM_PED and SEXAM_PED data collection forms should be completed, entered and forwarded to the DCC for participants ages 12-17.

For participants ages 18+, print the '(Ages 18+)' packet versions posted on the website for Visits 0A, 0B, 1, 1 SUP, 2, 2A, 3, 4, 5, 6, 7, 8, 9, 90A-92A. These packets will contain the BODYMEAS_ADULT, PRIOR_COND_ADULT, LEXAM_ADULT and/or SEXAM_ADULT forms. The administrative forms LEXAM_ADULT and SEXAM_ADULT should be completed for participants ages 18 and older. These will be stored in the participant folders and are not entered nor forwarded to the DCC. These forms will be reviewed during site visits.

Please note that even though the visit packets are separated by age/Supervised Washout status on the website, all forms are available for entry in Participant Data. Therefore, the LEXAM_PED and SEXAM_PED forms will need to be set to missing for participants ages 18+. Similarly, the BODYMEAS_ADULT and PRIOR_COND_ADULT forms will need to be set to missing for participants ages 12-17.

For participants completing the Supervised Washout visits, Visits 0A, 0B, and 1 SUP packets from the form section of the website should be used. Non-Supervised ICS Washout participants will start with the Visit 1 packet.

Visit 1 Split Visit: If Visit 1 is being split across two days, complete the Visit 1 packet through the PALB4_SPIRO form. In Q6000 on the packet PALB4_SPIRO form, include a comment to indicate that this participant is having a split Visit 1 (this will prevent queries as a result of the different visit dates within a packet). On Day 2 of Visit 1, begin the visit with single P6_PULMONARYCHK, nitric oxide testing (single ENO), spirometry (single SPIRO form), 4 puffs of albuterol and post-albuterol spirometry (single PALB4_SPIRO form) and continue with the rest of the visit.

If a Washout participant needs to complete a Split visit, two Visit 1 SPIROTELQCs will be performed – one at the original Visit 1 and one at the Split visit. Both should be entered into the database. The original Visit 1 SPIROTELQC should be entered as a single form and the SPIROTELQC performed at the Split visit should be entered with the visit packet. At the original Visit 1 visit, return the spirotel® device to the participant with the same visit ID (1) and baseline values programmed. All Visit 1 spirotel® data (from the original Visit 1 and the Split visit) should be uploaded to the Central

Database. For the P6_ELIG_RPT, the spirotel report generated at the original Visit 1 visit (containing just the spirotel® data since Visit 0B) should be entered into the database (and used for the P6_ELIG1 form) and sent to the DCC. For the P6_COMPLY_RPT and P6_BASELINE form, only the spirotel reports generated at the Split visit (containing all of the Visit 1 spirotel® data) should be entered into the database and sent to the DCC.

Visit 1 Continuation visit packet: At a Continuation Visit, PREG_TEST, P6_PULMONARYCHK, ENO, SPIRO, METHACHK_ADULT/METHACHK_PED, and METHA single forms will be completed first. Two versions of the V1 Continuation Visit packet will be posted on the website: one for ages 12-17 and one for ages 18+. The rest of the P6_ELIG3 form and Visit 1 forms should then be completed as outlined by the visit procedure checklist, using the visit date of the continuation visit.

If a Washout participant needs to complete a Continuation visit, two Visit 1 SPIROTELQCs will be performed – one at the original Visit 1 and one at the Continuation visit. Both should be entered into the database. The original Visit 1 SPIROTELQC should be entered as a single form and the SPIROTELQC performed at the Continuation visit should be entered with the visit packet. At the original Visit 1 visit, return the spirotel® device to the participant with the same visit ID (1) and baseline values programmed. All Visit 1 spirotel® data (from the original Visit 1 and the Continuation visit) should be uploaded to the Central Database. For the P6_ELIG_RPT, the spirotel report generated at the original Visit 1 visit (containing just the spirotel® data since Visit 0B) should be entered into the database (and used for the P6_ELIG1 form) and sent to the DCC. For the P6_COMPLY_RPT and P6_BASELINE form, only the spirotel reports generated at the Continuation visit (containing all of the Visit 1 spirotel® data) should be entered into the database and sent to the DCC.

Visits 1 and 2 following IRB approval of protocol version 4.1: Once IRB approval for protocol version 4.1 has been obtained, the ABP, RAND_IAQL_12, and ASUI will no longer be completed at Visit 1 and ACT and ASUI will no longer be completed at Visit 2. These forms should be set to missing in Participant Data during entry.

FEV_1 re-assessment visit forms: At Visit 2 and 2A, single P6_PULMONARYCHK, ENO and SPIRO forms should be completed using the visit date of the re-assessment visit. If significant asthma exacerbation criteria are met, a P6_SIGEX and P6_TERM form should be completed. If criteria are not met, the rest of the visit can be completed. In either case, spirotel reports, the P6_COMPLY form and the P6_TXFAIL_CHK form should be updated at the re-assessment visit.

At Visit 3, single P6_PULMONARYCHK and SPIRO forms should be completed using the visit date of the re-assessment visit. If significant asthma exacerbation criteria are met, a P6_SIGEX and P6_TERM form should be completed. If significant asthma exacerbation and treatment failure criteria are not met, the rest of the visit can be completed. In either case, spirotel reports, the P6_COMPLY form and the P6_TXFAIL_CHK form should be updated at the re-assessment visit.

At Visits 4, 6, and 8, single P6_PULMONARYCHK and SPIRO forms should be completed using the visit date of the re-assessment visit. If significant asthma exacerbation criteria are met: With exception to P6_COMPLY, forms completed at the original visit and those updated at the re-assessment visit (P6_TXFAIL_CHK) will be entered with the initial visit packet. This includes the ACT, ASUI, CMED, AECLIN, P6_TXFAIL_CHK, SEXAM_PED, P6_PULMONARYCHK, and SPIRO. The P6_PULMONARYCHK and SPIRO forms completed during the re-assessment visit will be entered as single forms with the visit number of the initial visit. P6_SIGEX will be entered with the Exacerbation visit packet, and P6_COMPLY will be entered with the crossover visit (or Visit 9) packet. The visit ID of the spirotel data should be updated to that of the crossover visit (or Visit 9) prior to that crossover/last visit.

At Visits 5, 7, and 9, single P6_PULMONARYCHK and SPIRO forms should be completed using the visit date of the re-assessment visit. If significant asthma exacerbation criteria are met: Only the P6_PULMONARYCHK, SPIRO, P6_TXFAIL_CHK and SEXAM_PED (for 12-17 only) forms for the initial visit and re-assessment visit will be entered. These forms will all be single forms, with the visit number prior to the cross-over visit. No other forms from the initial visit should be entered. Day 0 (Visit 90-92) of the Asthma Exacerbation Kit should be completed. The visit will be rescheduled and Day 3-7 (Visit 90A-92A) of the Asthma Exacerbation Kit will be performed on the same day.

If significant asthma exacerbation criteria is not met at Visit 4-9: After spirometry testing is complete, the participant's spirotel® device should be uploaded and his/her P6_ASTHMA_LOG should be collected. The Spirotel® reports (Participant Visit Report and Compliance Report) should be regenerated so that they include the balance of the visit data collected over the past 1-4 days since the original visit took place. The SIENA Compliance Checklist (P6_COMPLY) should be updated to reflect the additional spirotel® data in Question 1, and additional medication taken between original visit and FEV_1 re-assessment visit in Questions 2 and 3. Dates on these forms should be updated to the re-assessment visit date to confirm that they have been reviewed and updated accordingly. At visits 4, 6 and 8, original visit should proceed as outlined following FEV_1 re-assessment section regardless of whether participant meets Treatment Failure criteria. At Visits 5, 7 and 9, original visit will need re-

scheduled to meet washout requirements if participant meets Treatment Failure criteria.
A single SPIRO_RPT generated from the Medgraphics laptop will accompany the single SPIRO form.

For refill packets (containing four AAAQ and four WPAI_ASTHMA forms for participant completion at home during exacerbation phone call visits), complete the visit ID by inserting the current Asthma Exacerbation visit ID (90, 91, or 92) for the first three forms and the next potential Asthma Exacerbation visit ID (91 or 92) for the last form.

For extra study visits as a result of washout from run-in respiratory infections or run-in/treatment period treatment failures, follow the Extra Visit due to Washout (P6_VISIT_WASHOUT) visit checklist (found on the website under Forms → SIENA → Admin Forms). A visit packet exists for these visits and contains this checklist and single forms to be completed. Note that this checklist is for your reference; it does not need to be forwarded to the DCC. spirotel® data should be uploaded to the Central Database following download and conversion. Single forms completed at this visit (P6_COMPLY, P6_TXFAIL_CHK, P6_TXFAIL, SPIROTELQC) should be entered with the visit ID of the most recently completed regular visit (2, 2A, 3, 4, 5, 6, 7, or 8). Any updated/new AECLIN and CMED records should be added to the database. Only the spirotel® Compliance report (P6_COMPLY_RPT) needs to be forwarded to the DCC with the single P6_COMPLY form. The other spirotel® report (P6_SPIROTEL_RPT) will be obtained again at the next regular visit. Note that the spirotel® reports will have the visit ID of the next regular visit and the single forms will have the visit ID of the last regular visit.

For combination/crossover visits as a result of significant exacerbation, follow the visit checklist of the next regular visit scheduled, and follow the prompts for where the Visit 9XA forms should be completed. All forms from the visit (including P6_TXFAIL_CHK, P6_PULMONARYCHK, and SPIRO) should be completed as part of the regular visit packet. Visit 9XA should contain AAAQ, P6_SIGEX, and LEXAM_PED/ADULT (where applicable). All other Visit 9XA forms (P6_TXFAIL_CHK, P6_PULMONARYCHK, and SPIRO) will be marked missing, as they were entered as part of the regular visit.

4.5 SIENA-Specific spirotel Tabs in Breeze

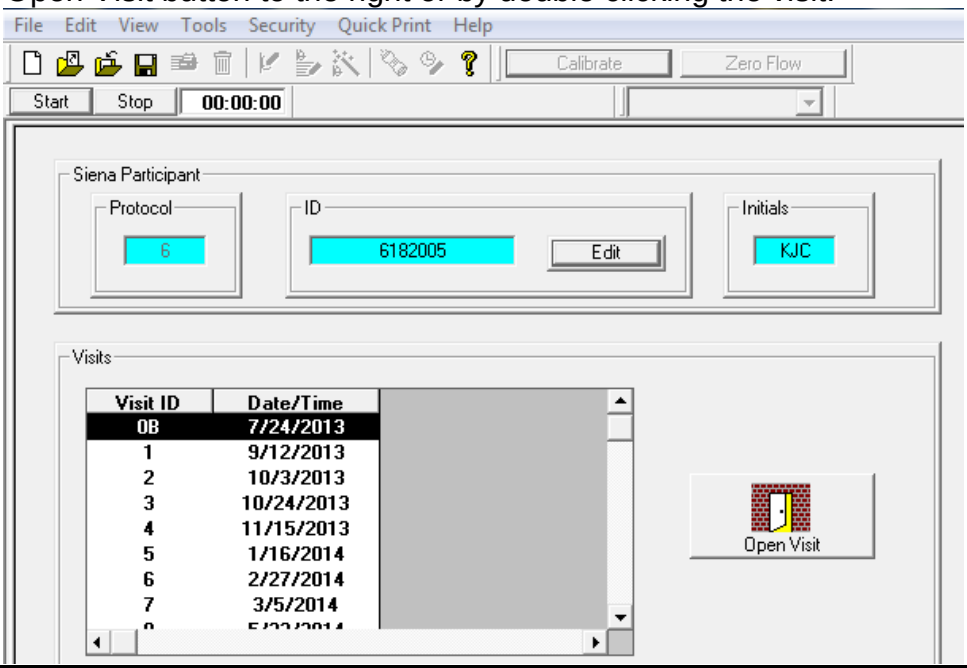
The SIENA Participant Visit Report, Participant Compliance Report, Eligibility Report, and Baseline Report are generated and printed from Breeze on the MedGraphics PC. For each visit, various tabs will be present to view. Viewing spirotel® data in Breeze is for reference purposes only, as the information necessary to complete data collection forms and to update the spirotel® device is contained on the printed reports generated by Breeze.

Please note that a participant's spirotel data should consistently be downloaded on the same MedGraphics machine as often as possible. Otherwise, values on the respective reports may be calculated incorrectly. Bold alert messages have been added to the Compliance and Eligibility reports to alert users to when this may have occurred. However, you should be reviewing the reports as they are generated to make sure the calculations are correct.

For detailed information on the content of these reports, see the spirotel® discussion in Section 2 of this MOP.

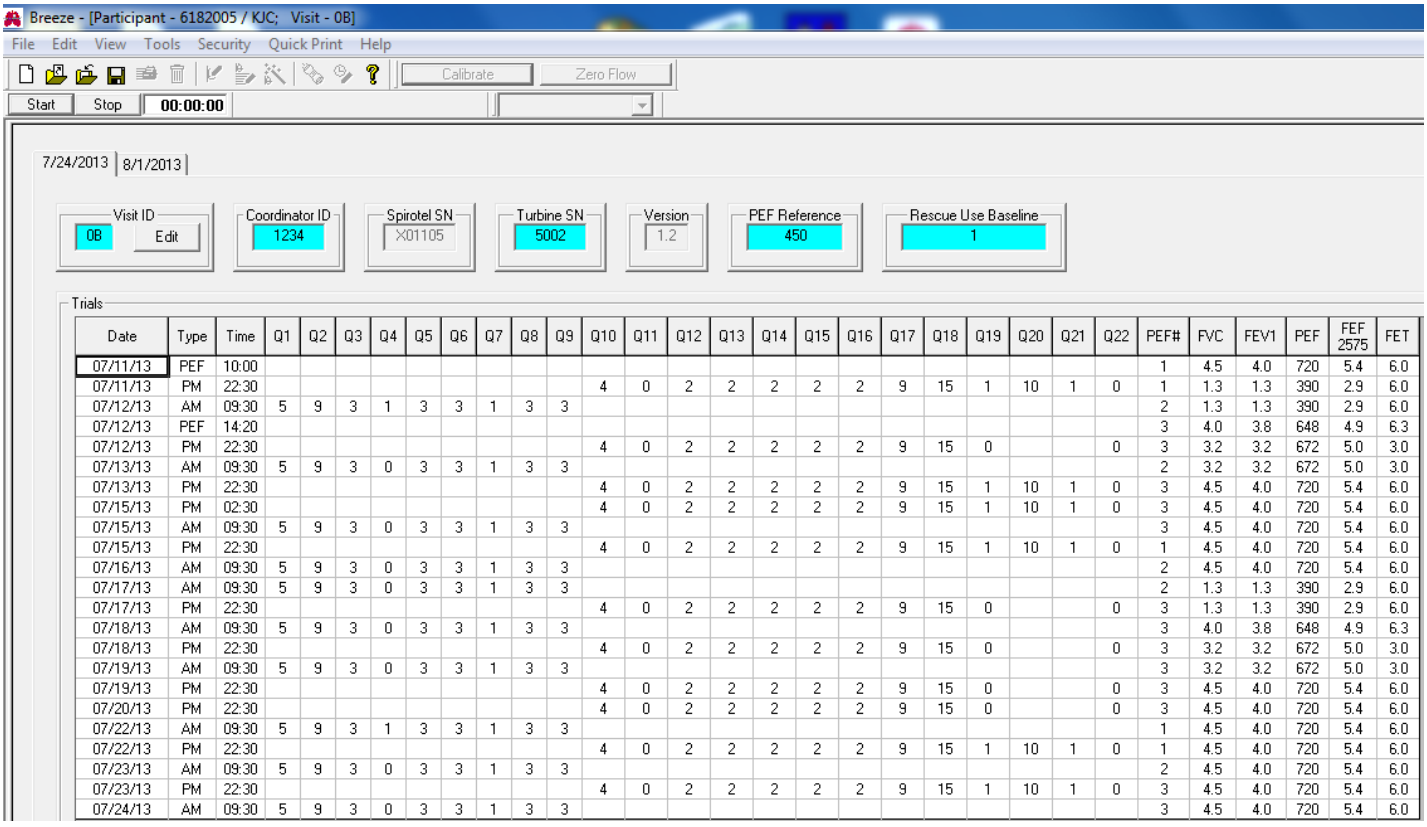
4.5.1 Participant Tab

The Participant Tab displays the Protocol ID number (6 for SIENA), the participant ID, and participant initials entered into the spirotel device during configuration. This tab also displays all downloaded visits, which can be opened by selecting a visit then clicking the Open Visit button to the right or by double clicking the visit.



4.5.2 Visit Tab

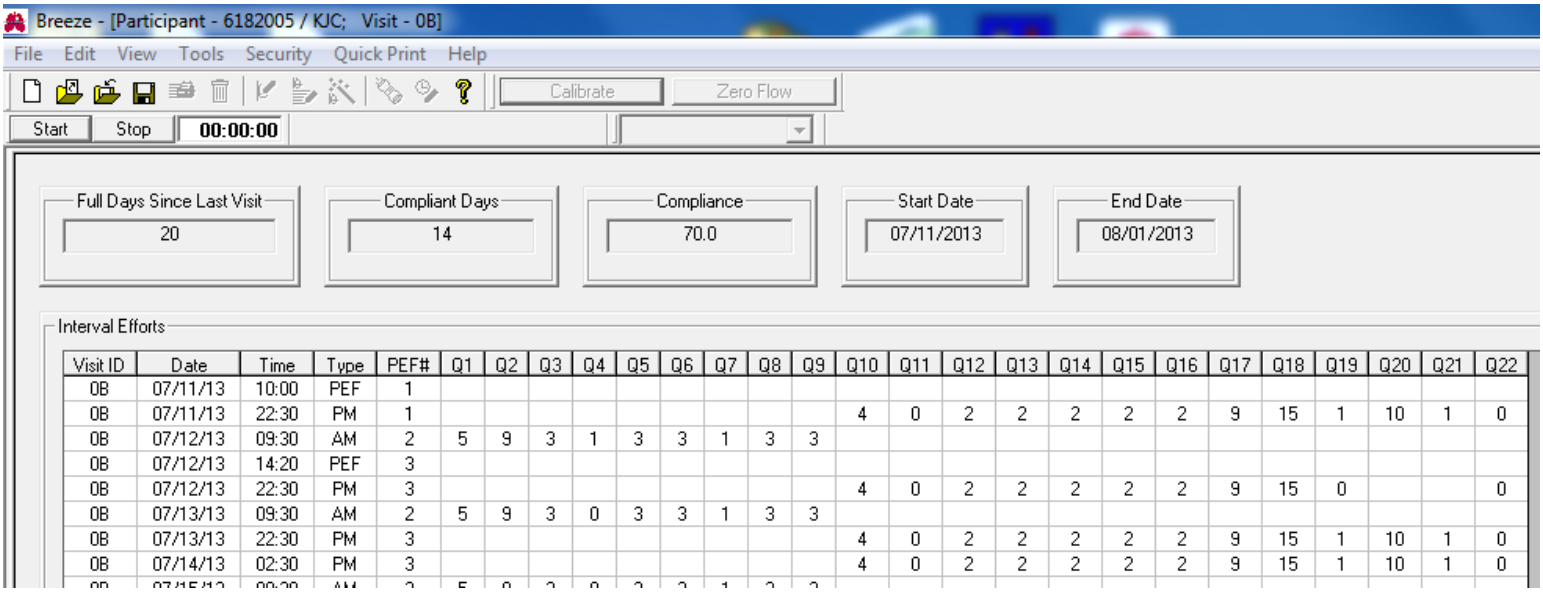
The Visit Tab will be available at all visits. The data on this screen will populate on the Participant Visit Report. This tab and accompanying report shows a 'data dump' of all information saved in the spirotel for each visit. The device configuration data (i.e., Visit ID, Coordinator ID, Spirotel Serial Number, Turbine Serial Number, Spirotel Version Number, Reference Peak Flow value, and Rescue Use Baseline value) are listed near the top of the screen. Each trial completed by the participant will be shown below the 'Trials' label. Each row represents one session with columns showing trial date, trial type (AM, PM, or unscheduled PEF), time the session started, participant response to diary questions, number of PEFs completed for the session, and the FVC, FEV_1, PEF, FEF_{25-75}, and FET values for the highest blow completed during the session. If the spirotel is downloaded more than once for a given visit, there will be a tab for each download at the top of the screen, labeled with the download date.



Date	Type	Time	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Q14	Q15	Q16	Q17	Q18	Q19	Q20	Q21	Q22	PEF#	FVC	FEV1	PEF	FEF 2575	FET
07/11/13	PEF	10:00																							1	4.5	4.0	720	5.4	6.0
07/11/13	PM	22:30										4	0	2	2	2	2	2	9	15	1	10	1	0	1	1.3	1.3	390	2.9	6.0
07/12/13	AM	09:30	5	9	3	1	3	3	1	3	3														2	1.3	1.3	390	2.9	6.0
07/12/13	PEF	14:20																							3	4.0	3.8	648	4.9	6.3
07/12/13	PM	22:30										4	0	2	2	2	2	2	9	15	0			0	3	3.2	3.2	672	5.0	3.0
07/13/13	AM	09:30	5	9	3	0	3	3	1	3	3														2	3.2	3.2	672	5.0	3.0
07/13/13	PM	22:30										4	0	2	2	2	2	2	9	15	1	10	1	0	3	4.5	4.0	720	5.4	6.0
07/15/13	PM	02:30										4	0	2	2	2	2	2	9	15	1	10	1	0	3	4.5	4.0	720	5.4	6.0
07/15/13	AM	09:30	5	9	3	0	3	3	1	3	3														3	4.5	4.0	720	5.4	6.0
07/15/13	PM	22:30										4	0	2	2	2	2	2	9	15	1	10	1	0	1	4.5	4.0	720	5.4	6.0
07/16/13	AM	09:30	5	9	3	0	3	3	1	3	3														2	4.5	4.0	720	5.4	6.0
07/17/13	AM	09:30	5	9	3	0	3	3	1	3	3														2	1.3	1.3	390	2.9	6.0
07/17/13	PM	22:30										4	0	2	2	2	2	2	9	15	0			0	3	1.3	1.3	390	2.9	6.0
07/18/13	AM	09:30	5	9	3	0	3	3	1	3	3														3	4.0	3.8	648	4.9	6.3
07/18/13	PM	22:30										4	0	2	2	2	2	2	9	15	0			0	3	3.2	3.2	672	5.0	3.0
07/19/13	AM	09:30	5	9	3	0	3	3	1	3	3														3	3.2	3.2	672	5.0	3.0
07/19/13	PM	22:30										4	0	2	2	2	2	2	9	15	0			0	3	4.5	4.0	720	5.4	6.0
07/20/13	PM	22:30										4	0	2	2	2	2	2	9	15	0			0	3	4.5	4.0	720	5.4	6.0
07/22/13	AM	09:30	5	9	3	1	3	3	1	3	3														1	4.5	4.0	720	5.4	6.0
07/22/13	PM	22:30										4	0	2	2	2	2	2	9	15	1	10	1	0	1	4.5	4.0	720	5.4	6.0
07/23/13	AM	09:30	5	9	3	0	3	3	1	3	3														2	4.5	4.0	720	5.4	6.0
07/23/13	PM	22:30										4	0	2	2	2	2	2	9	15	1	10	1	0	3	4.5	4.0	720	5.4	6.0
07/24/13	AM	09:30	5	9	3	0	3	3	1	3	3														3	4.5	4.0	720	5.4	6.0

4.5.3 Compliance Tab

The Compliance Tab is present at all visits. The data on this screen will be represented on the Participant Compliance Report. The top portion of the screen lists the number of full days since the previous visit, number of compliant days, percent compliance, and the start and end date of the calculation. The start and end date correspond to either the previous visit date or the earliest trial date for the current visit, and the current visit date. The interval efforts listed represent the AM and PM sessions completed (i.e. all diary questions answered and at least 1 PEF completed) between the start and end dates. Compliance is based on the number of full days where both the AM and the PM sessions are completed. There are no separate download tabs within the Compliance tab.



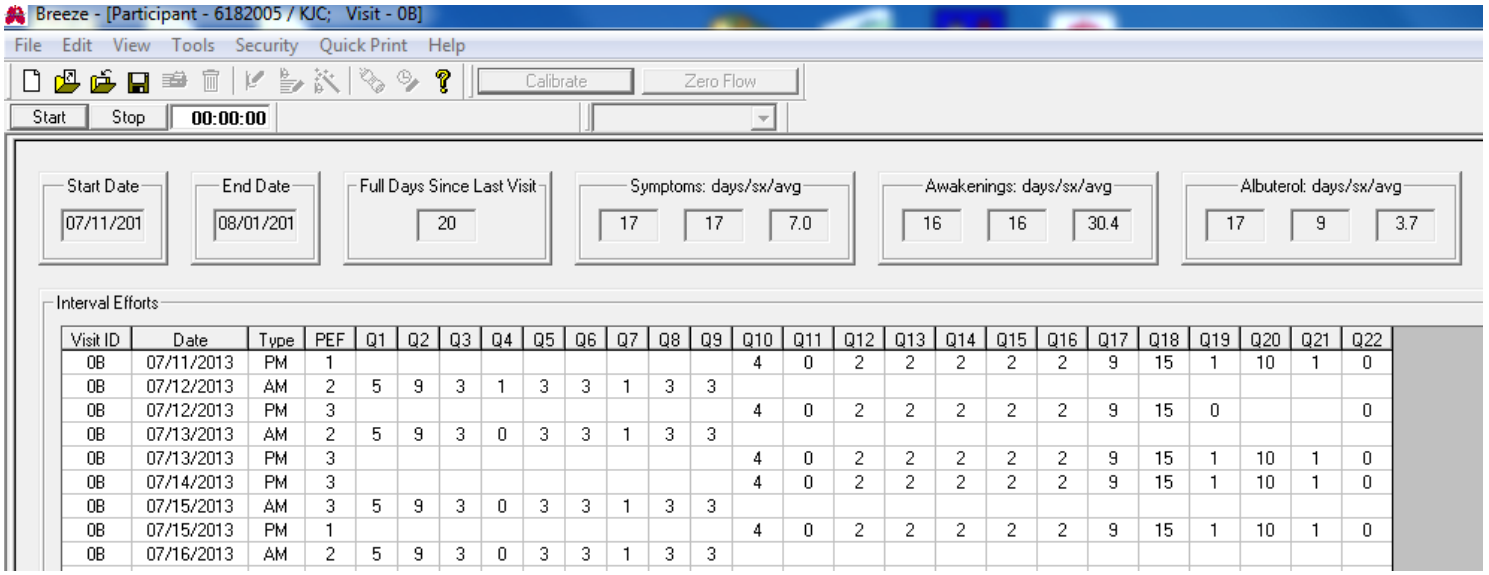
Visit ID	Date	Time	Type	PEF#	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Q14	Q15	Q16	Q17	Q18	Q19	Q20	Q21	Q22
0B	07/11/13	10:00	PEF	1																						
0B	07/11/13	22:30	PM	1										4	0	2	2	2	2	2	9	15	1	10	1	0
0B	07/12/13	09:30	AM	2	5	9	3	1	3	3	1	3	3													
0B	07/12/13	14:20	PEF	3																						
0B	07/12/13	22:30	PM	3										4	0	2	2	2	2	2	9	15	0			0
0B	07/13/13	09:30	AM	2	5	9	3	0	3	3	1	3	3													
0B	07/13/13	22:30	PM	3										4	0	2	2	2	2	2	9	15	1	10	1	0
0B	07/14/13	02:30	PM	3										4	0	2	2	2	2	2	9	15	1	10	1	0

4.5.4 Eligibility Tab

The Eligibility Tab is present for Visit 0B, 1, and 3 only. This tab displays eligibility assessment data, including compliance data using a definition that is different from that employed in the Compliance Tab. This data is represented on the Eligibility Report.

At Visit 0B and 1: The start and end date of the calculation are present, followed by the number of full days since the previous visit. Next are the average number of symptoms, awakenings and albuterol puffs recorded by the participant.

At Visit 3: The start and end date of the calculation are present, followed by the number of full days since Visit 1 – the Visit 3 report looks back at all of the data collected between Visits 1 and 3. Next are the average number of symptoms, awakenings and albuterol puffs recorded by the participant. Under the Eligibility info, the Compliance info for eligibility is present: start and end date of the calculation, followed by the number of full days since the previous visit, and the compliance calculation. Compliance is calculated based on the total number of AM and PM sessions completed (slightly different from the Compliance Tab).

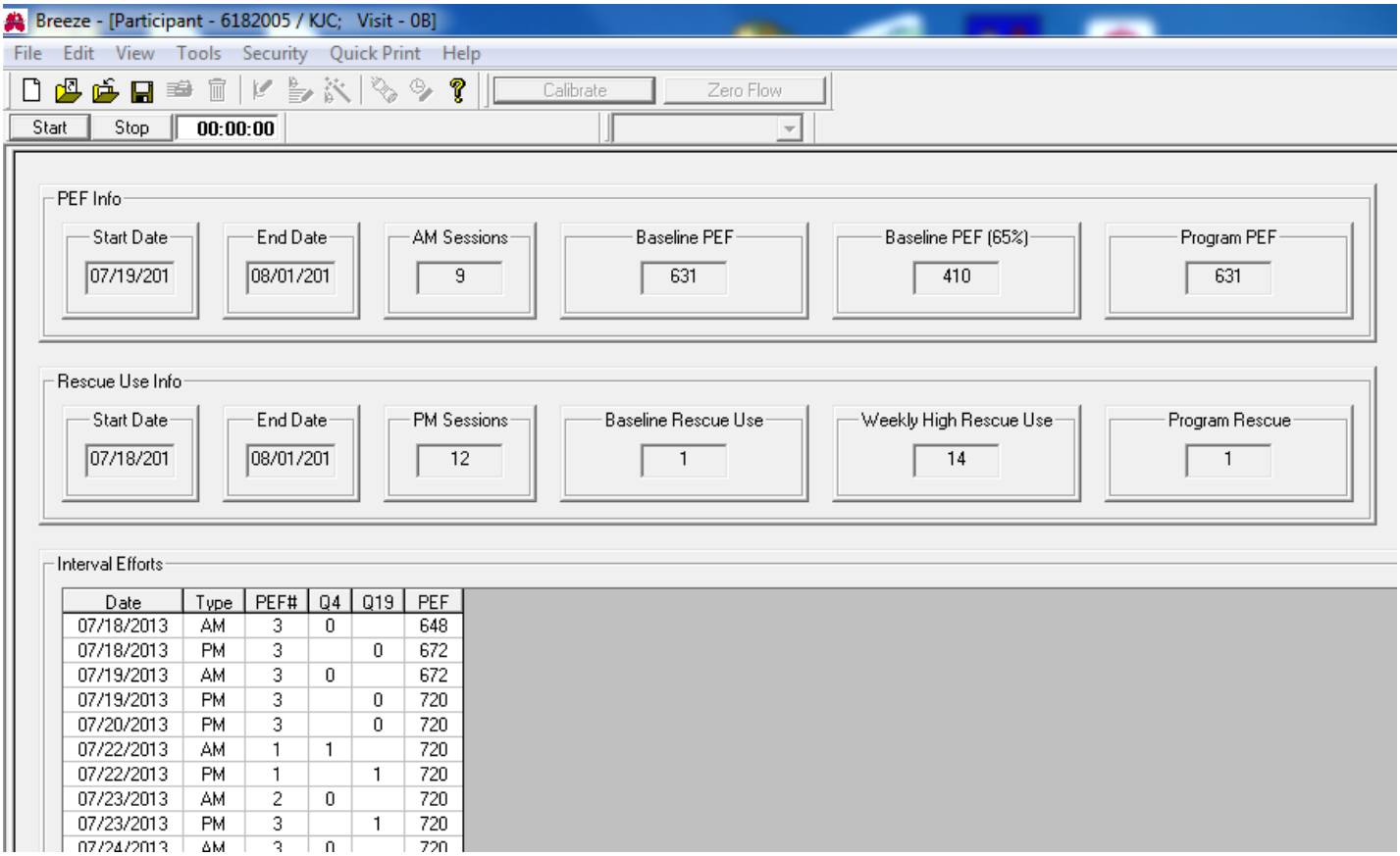


Visit ID	Date	Type	PEF	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Q14	Q15	Q16	Q17	Q18	Q19	Q20	Q21	Q22
0B	07/11/2013	PM	1										4	0	2	2	2	2	2	9	15	1	10	1	0
0B	07/12/2013	AM	2	5	9	3	1	3	3	1	3	3													
0B	07/12/2013	PM	3										4	0	2	2	2	2	2	9	15	0			0
0B	07/13/2013	AM	2	5	9	3	0	3	3	1	3	3													
0B	07/13/2013	PM	3										4	0	2	2	2	2	2	9	15	1	10	1	0
0B	07/14/2013	PM	3										4	0	2	2	2	2	2	9	15	1	10	1	0
0B	07/15/2013	AM	3	5	9	3	0	3	3	1	3	3													
0B	07/15/2013	PM	1										4	0	2	2	2	2	2	9	15	1	10	1	0
0B	07/16/2013	AM	2	5	9	3	0	3	3	1	3	3													

4.5.5 Baseline Tab

The Baseline tab is present at Visits 0B, 1, and 2 only. The data in this tab will be represented on the Baseline Report. While this tab is present at Visit 2, the report should not be generated/printed for a participant that completed Supervised Washout visits.

This tab first lists the PEF Info: start and end date of the calculation, number of AM sessions in the calculation, the Baseline PEF, 65% of the Baseline PEF, and the Baseline PEF to be programmed into the device before the participant leaves the current visit. Next, the Rescue Use Info is listed: start and end date of the calculation, number of PM sessions in the calculation, Baseline Rescue Use, Weekly High Rescue Use, and the Baseline Recue Use to be programmed into the the device before the participant leaves the current visit.



Date	Type	PEF#	Q4	Q19	PEF
07/18/2013	AM	3	0		648
07/18/2013	PM	3		0	672
07/19/2013	AM	3	0		672
07/19/2013	PM	3		0	720
07/20/2013	PM	3		0	720
07/22/2013	AM	1	1		720
07/22/2013	PM	1		1	720
07/23/2013	AM	2	0		720
07/23/2013	PM	3		1	720
07/24/2013	AM	3	0		720

4.6 SIENA spirotel® Troubleshooting

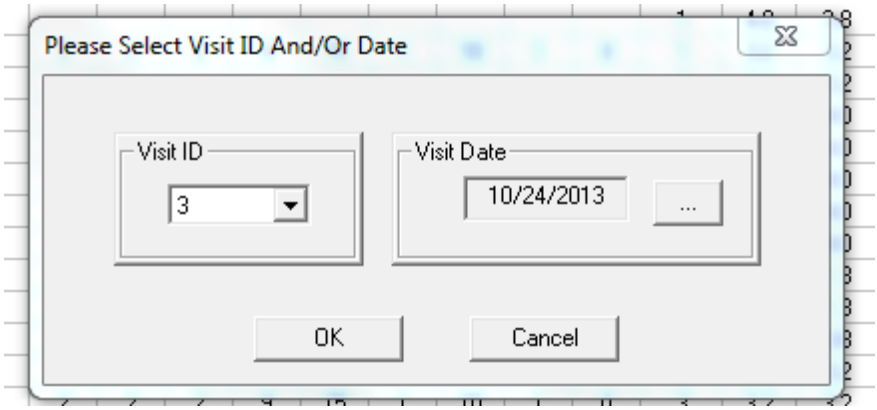
4.6.1 Updating Spirotel Visit ID

The Visit ID in the Spirotel device may need to be updated if:

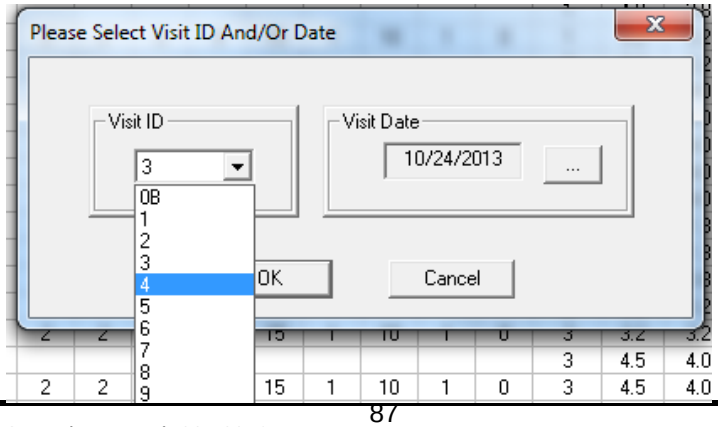
- the incorrect Visit ID was programmed at the previous visit or
- the participant experienced two treatment failures or a significant asthma exacerbation during the first half of a treatment period and is returning early for a crossover visit

To update the Visit ID of spirotel data, follow the normal steps to download and convert the data into Breeze. Once the data is in Breeze:

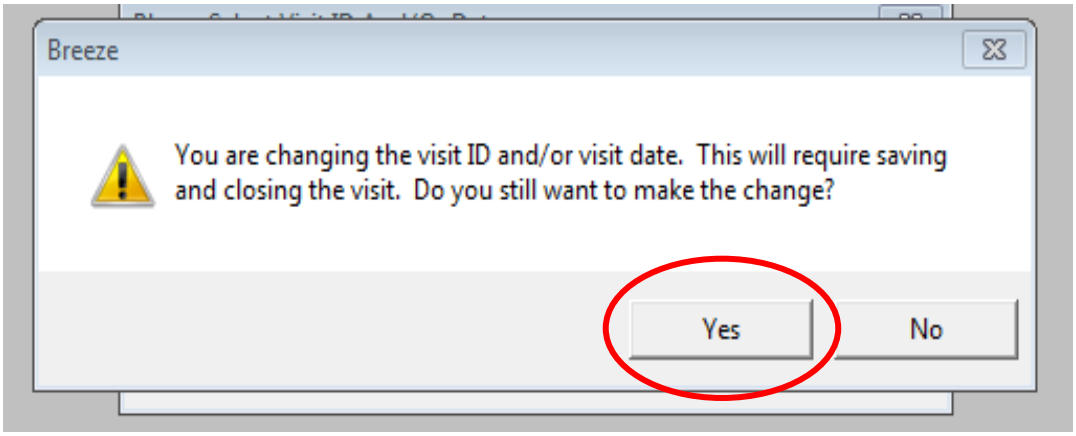
- Select the participant and open the visit you wish to change
- Click on the Visit Tab
- The Visit ID is listed in the upper left hand corner.
- To the right of the Visit ID, there is an edit button. Click Edit.
- Once you click Edit, a dialog box will pop up.



- Click the arrow next to the Visit ID to produce a dropdown list. Select the appropriate Visit ID, then, select OK.



- After selecting OK, a warning message will pop up. If you are confident with your change, select 'Yes.'



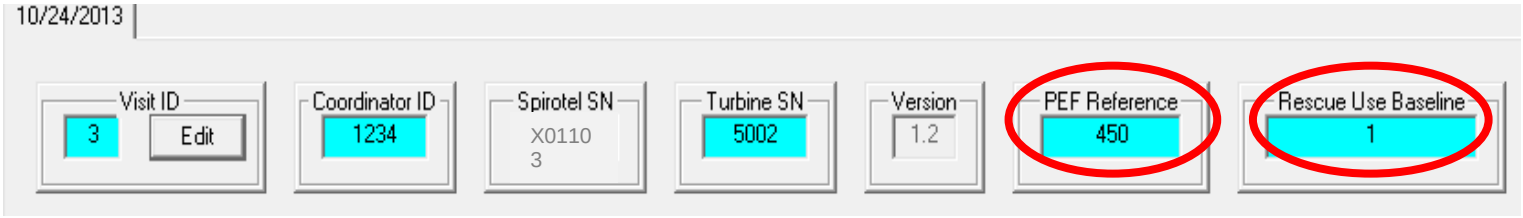
- After selecting 'Yes', you will automatically be navigated back to the main Open Patient Screen. Re-select the participant you were working with to verify that the Visit ID has been updated and to print any necessary reports.

4.6.2 Updating an Incorrect Reference PEF or Rescue Use value

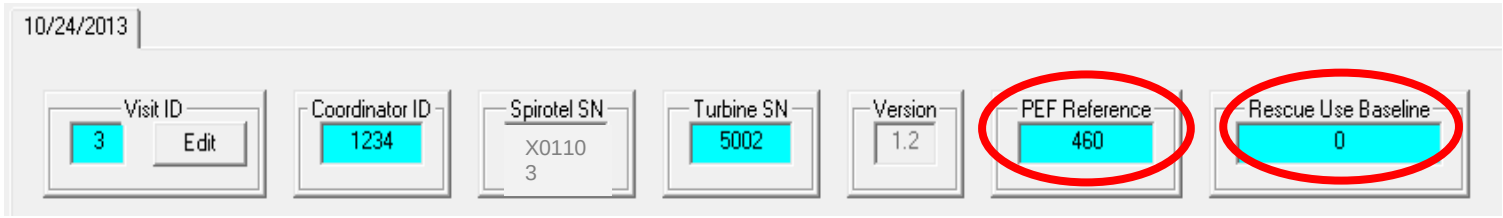
If an incorrect Reference PEF or Rescue Use value was programmed into the spirotel device and is discovered either during coordinator review or via query, this value can be updated in Breeze.

To update the Reference PEF value:

- Open the participant and Visit in Breeze
- Click on the Visit Tab
- The PEF Reference and/or Rescue Use Baseline values can be changed in the Visit Tab. They are the right-most teal fields at the top of the screen.



- Delete the incorrect value in this field and enter the correct value



4.6.3 SIENA spirotel® report error messages

If the following things are not done by the participant or coordinator, errors will appear on the various spirotel® reports generated from the Breeze Suite software.

SIENA Spirotel Participant Compliance Report

- "An unscheduled PEF was not done at the previous visit to start the visit interval in the spirotel®. Compliance metrics on this report may be incorrect. Check calculations closely before entering data." will appear on the Visit 0B or Visit 2 Participant Compliance Report if an unscheduled PEF is not performed at Visit 0A or Visit 1 as specified on the visit checklist. If this occurs, verify that the first trial date on the report matches the visit date of the previous visit. If not, then you will need to calculate the total number of days between visits to verify if the report is correct or updates will need to be noted. If corrections to the report are necessary, please make these in red ink on the P6_COMPLY_RPT generated and transcribe corrected value(s) onto the P6_COMPLY form. A comment should be added in P6_COMPLY Q6000 explaining the edits.

SIENA Spirotel Eligibility Report

- "Not all Visit 1 data is registered on this machine. Eligibility data will not be accurate. Please contact AsthmaNet_SIENA_DM@phs.psu.edu." will appear if there are not 31 trial dates present prior to the Visit 1 download date. 31 trial dates are needed for the report to calculate correctly. This may happen if more than one Visit 1 download exists and the downloads occurred on different machines. If so, contact the alias above and DM can generate a complete report from the Central Database **once all of the spirotel data is uploaded**.
    - **Please note that there may be a wait period of several hours to a day for the DCC to be able to see the newly uploaded spirotel data in the Central Database.**

- "No prior downloads at Visit 2 for this participant are registered on this machine. Eligibility data will not be accurate. Please contact AsthmaNet_SIENA_DM@phs.psu.edu." will appear if the Visit 2 and Visit 3 spirotel data are downloaded on different machines, since the Eligibility Report looks at data from Visit 1 to Visit 3. If this error appears, contact the alias above and DM can generate a complete report from the Central Database **once all of the spirotel data is uploaded**.
    - **Please note that there may be a wait period of several hours to a day for the DCC to be able to see the newly uploaded spirotel data in the Central Database.**

- "An unscheduled PEF was not done at the previous visit to start the visit interval in the spirotel®. Compliance metrics on this report may be incorrect. Check calculations closely before entering data." will appear if an unscheduled PEF is not performed at Visit 1 as specified on the visit checklist. If this occurs, verify that the first trial date on the report matches the visit date of the previous visit. If not, then you will need to calculate the total number of days between visits to verify if the report is correct or updates will need to be noted. If corrections to the report are necessary, please make these in red ink on the P6_COMPLY_RPT generated and transcribe corrected value(s) onto the P6_COMPLY form. A comment should be added in P6_COMPLY Q6000 explaining the edits.

SIENA Spirotel Baseline Report

- If no records are present to calculate either the PEF or Rescue Baseline Value, a message will appear to indicate no data is available and dashes (-) will appear on the report in place of values.

Note: spirotel® sessions completed between midnight and 3 AM will appear on the Participant Visit Report (P6_SPIROTEL_RPT) as the true date of completion (i.e. a PM session done at 2 AM on 2/19/2014 will appear with 2/19/2014 on the P6_SPIROTEL_RPT). For the rest of the reports, that session is considered a 2/18/2014 PM session given that the spirotel® PM window is 5 PM to 3 AM. When reviewing the P6_SPIROTEL_RPT, note that sessions completed between midnight and 3 AM should count as the PM session for the previous date.

Note: Do **NOT** select the 'All Reports' option when printing from Breeze. Not all of the reports print when this is selected and at Visit 2 the Baseline Report should not be printed for Supervised Washout participants even though it is available.