

**CLINICAL AND LABORATORY
ADVERSE EVENTS**

Subject ID: _____ - _____ - _____

Subject Initials: _____

Visit Number: _____

(Clinic Coordinator completed)

Complete this log if the subject experienced any clinical adverse events (including intercurrent events) since the last visit. Check the "None" box and instruct the subject to initial and date the source documentation box if the subject has not experienced any clinical adverse events since the last visit.

None

Subject's Initials: _____

Date: ____ / ____ / _____

* Please complete a Serious Adverse Event Reporting (SERIOUS) form.

** Please complete the appropriate Change in Medications form.

*** Please complete the Concomitant Medications (CMED) form.

DESCRIPTION OF ADVERSE EVENT (1000)	1. ICD9 CODE (1010)	2. DATE STARTED (Top Line) (1020)	4. ONGOING at current visit (1040)	5. TYPE (1050)	6. SEVERITY (1060)	7. SERIOUS (1070)	8. LIKELIHOOD OF RELATIONSHIP TO STUDY DRUG(S) (1080)	9. CHANGE IN STUDY DRUG(S) (1090)	10. OUTCOME (Skip if #3 is missing.) (1100)	11. TREATMENT REQUIRED (1110)	12. ONGOING at final visit (1120)
		3. DATE STOPPED (Bottom Line) (1030) MONTH / DAY / YEAR		1 - INTERMITTENT 2 - CONTINUOUS	1 - MILD 2 - MODERATE 3 - SEVERE	1 - YES * 0 - NO	1 - NONE 2 - UNLIKELY (REMOTE) 3 - POSSIBLE 4 - PROBABLE	1 - UNCHANGED 2 - ALTERED **	1 - COMPLETELY RECOVERED 2 - RECOVERED, BUT WITH LASTING EFFECTS 3 - DEATH *	1 - NONE 2 - MEDICATION *** 3 - HOSPITALIZATION * 4 - OTHER	
---	---	__ / __ / ____	<input type="checkbox"/> 1								<input type="checkbox"/> 1
---	---	__ / __ / ____	<input type="checkbox"/> 1								<input type="checkbox"/> 1
---	---	__ / __ / ____	<input type="checkbox"/> 1								<input type="checkbox"/> 1
---	---	__ / __ / ____	<input type="checkbox"/> 1								<input type="checkbox"/> 1
---	---	__ / __ / ____	<input type="checkbox"/> 1								<input type="checkbox"/> 1



(Technician completed)

1. Serial Number of AM1[®] being tested _____ (1000)
2. Serial Number of turbine being tested _____
(1010) - (1020)
3. Test date _____ / _____ / _____ (1030)
month day year
4. Is a new AM1[®] device being tested for this subject? ₁ Yes ₀ No (1040)
 If **YES**, indicate the primary reason. ₁ First issuing ₅ "Old" device was recalled
₂ "Old" device failed QC testing ₆ "Old" device was lost
₃ "Old" device had display problems ₇ Other (1050)
₄ "Old" device experienced battery failure

	AM1 [®] (L/Min)	Jones FVC (L/Min)
5. Trial 1 (1060/1070)	_____	_____ . _____
6. Trial 2 (1080/1090)	_____	_____ . _____
7. Trial 3 (1100/1110)	_____	_____ . _____
8. Trial 4 (1120/1130)	_____	_____ . _____
9. Trial 5 (1140/1150)	_____	_____ . _____

Clinic Use Only	
Relative Bias <small>(AM1 - Jones FVC) * 100 % Jones FVC</small>	Rank <small>smallest to largest</small>
_____ . _____ %	_____
_____ . _____ %	_____
_____ . _____ %	_____
_____ . _____ %	_____
_____ . _____ %	_____

Clinic Use Only

Median Relative Bias _____ . _____ % **Inter-quartile Range** _____ . _____ %

The Median Relative Bias is the third largest value of the 5 measures of relative bias.

The Inter-quartile Range is determined by subtracting the relative bias of rank 2 from the relative bias of rank 4.

When a subject receives a new AM1[®] or turbine for the first time, the median relative bias must be between -15% and +15%, AND the inter-quartile range must be less than 10%.

When a subject returns to the clinic with a used AM1[®]: (i) subtract the original median relative bias (the median relative bias when the AM1[®] or turbine was first dispensed) from the current median relative bias, and (ii) subtract the original inter-quartile range (the inter-quartile range when the AM1[®] or turbine was first dispensed) from the current inter-quartile range. The difference for (i) must be between -5% and +5% and the difference for (ii) must be less than +5% for the AM1[®] to be reissued to the subject.

10. Did the AM1[®] pass? ₁ Yes ₀ No (1160)
11. If **NO**, is this the second test with this turbine at this visit? ₁ Yes ₀ No (1170)
 ➔ If **NO**, retest the AM1[®] with the same turbine and complete another AM1[®] Quality Control form.
 ➔ If **YES**, issue a new turbine and complete another AM1[®] Quality Control form. If 2 turbines have been tested with this device, issue a new device and turbine and complete another AM1[®] Quality Control form.



ASTHMA HISTORY

Subject ID: _____ - _____ - _____
 Subject Initials: _____
 Visit Number: _____
 Visit Date: _____ / _____ / _____
Month Day Year
 Coordinator ID: _____

(Subject Interview completed)

1. Approximately how old were you when chest symptoms suggesting asthma first appeared? _____ years (1000)
(Enter '00' if subject was under 1 year.)

2. Think back to when a doctor first diagnosed you with asthma.
 2a. Approximately how old were you? _____ years (1010)

2b. What caused you to seek medical care?
₁ Acute Symptoms
₂ Chronic Symptoms
₃ Other _____ (1030)

3. How do you categorize your asthma symptoms throughout the course of the year?
₁ Relatively the same all year
₂ Vary by season(s) (1040)

➔ If 'vary by season(s)', do your asthma symptoms worsen during the...

3a. Winter? ₁ Yes ₀ No (1050)
 3b. Spring? ₁ Yes ₀ No (1060)
 3c. Summer? ₁ Yes ₀ No (1070)
 3d. Fall? ₁ Yes ₀ No (1080)

4. In the last 12 months, how many... *(Enter '00' if none)*
 4a. Asthma episodes have you had that required emergency care or an unscheduled office visit? _____ (1090)
 4b. Hospitalizations have you had due to asthma? _____ (1100)
 4c. Courses of oral corticosteroid therapy (eg., prednisone) for asthma have you taken? _____ (1110)



ASTHMA HISTORY

Subject ID: _____ - _____ - _____

Visit Number: _____

5. Have you missed any days of work or school due to asthma in the last 12 months? ₁ Yes ₀ No ₉ N/A (1120)

→ If **YES**, record your best estimate of the number of days missed. _____ (1130)

6. Have any of your immediate blood relatives been told by a physician that they have asthma? (Check the 'N/A' box if the subject does not have siblings or children.)

- 6a. Mother ₁ Yes ₀ No ₈ Don't Know (1140)
- 6b. Father ₁ Yes ₀ No ₈ Don't Know (1150)
- 6c. Brothers or Sisters ₁ Yes ₀ No ₈ Don't Know ₉ N/A (1160)
- 6d. Child(ren) ₁ Yes ₀ No ₈ Don't Know ₉ N/A (1170)

Subject Source Documentation

Subject's Initials: _____ (1180)

Date: ____ / ____ / _____ (1190)



**CONCOMITANT
MEDICATIONS FOR
ASTHMA/ALLERGY AND
ADVERSE EVENTS**

Subject ID: _____ - _____ - _____
Subject Initials: _____
Visit Number: _____

(Coordinator completed)

Instructions: Since signing the informed consent or last study visit, list all prescription and over-the-counter (OTC) concomitant medications used to treat asthma/allergy symptoms and adverse events. Do not list routine use of study drugs or rescue medications. Check the “None” box if the subject has not started taking any medications since signing the informed consent or last study visit. If the medication is not related to an adverse or laboratory event, leave the event number missing and check the “N/A” box. If the subject is still taking the medication at the end of the current visit, check the “ongoing at current visit” check box and leave the stop date missing. All ongoing medications should be reviewed at subsequent visits to document the stop date of a medication. At the last study visit or an early termination visit, review all ongoing medication and indicate a stop date or check the “ongoing at final visit” check box on the data collection form and update the medication data in the ACRN data entry application.

At the final study visit or early termination visit, forward all concomitant medications for asthma/allergy-related medications and adverse events forms to the DCC.

None

NAME OF MEDICATION (1000)	CODE (1010)	RELATED EVENT (1020)	DOSE (1030)	UNITS (1040)	FREQUENCY (1050)	ROUTE	START DATE (MM/DD/YYYY) (1060)	STOP DATE (MM/DD/YYYY) (1070)	ONGOING AT CURRENT VISIT (1080)	ONGOING AT FINAL VISIT (1090)
___		Event ___ <input type="checkbox"/> NA					___/___/___	___/___/___	<input type="checkbox"/>	<input type="checkbox"/>
___		Event ___ <input type="checkbox"/> NA					___/___/___	___/___/___	<input type="checkbox"/>	<input type="checkbox"/>
___		Event ___ <input type="checkbox"/> NA					___/___/___	___/___/___	<input type="checkbox"/>	<input type="checkbox"/>
___		Event ___ <input type="checkbox"/> NA					___/___/___	___/___/___	<input type="checkbox"/>	<input type="checkbox"/>
___		Event ___ <input type="checkbox"/> NA					___/___/___	___/___/___	<input type="checkbox"/>	<input type="checkbox"/>
___		Event ___ <input type="checkbox"/> NA					___/___/___	___/___/___	<input type="checkbox"/>	<input type="checkbox"/>



UNITS and FREQUENCY CODES FOR CONCOMITANT MEDICATIONS

Codes for Units	
Code	Units
1	mg
2	mcg (μ g)
3	ml
4	mg/ml
5	mEq
6	g
7	U
8	teaspoon
9	patch
10	puffs (oral inhalation)
11	nasal spray
12	no units
13	packet
14	1 drop
15	mm
16	other

Codes for Frequency		
Code	Frequency	
1	QD	1 time a day
2	BID	2 times a day
3	TID	3 times a day
4	QID	4 times a day
5	q4h	every 4 hours
6	q5h	every 5 hours
7	q6h	every 6 hours
8	q8h	every 8 hours
9	q12h	every 12 hours
10	q24h	every 24 hours
11	hs	every night at bedtime
12	PRN	as required
13	qod	every other day
14	qw	once a week
15	biw	2 times per week
16	tiw	3 times per week
17	5 times per week	
18	every 5 days	
19	once a month	
20	taper dose	
21	other	



**eDEM™ MONITOR
QUALITY CONTROL**

Subject ID: _____ - _____ - _____
 Subject Initials: _____
 Visit Number: _____
 Visit Date: ____/____/____
Month Day Year
 Technician ID: _____

(Technician completed)

1. Serial Number of eDEM™ monitor being tested _____ (1000)

2. Test date ____/____/____
month day year (1010)

3. Record monitor's validity ____ . ____
month (1020) year (1030)

4. Record battery voltage ____ . ____ volts (1040)

5. Is a new eDEM™ monitor being tested? ₁ Yes ₀ No (1050)

→ If **YES**, indicate the primary reason.

- ₁ First issuing
- ₂ "Old" device was recalled
- ₃ "Old" device experiencing low voltage (< 2.90 volts)
- ₄ "Old" device had downloading problems
- ₅ "Old" device experienced AC adaptor failure
- ₆ "Old" device experienced battery failure
- ₇ "Old" device was lost
- ₈ "Old" device validity expired
- ₉ Other _____ (1060)

6. Did the eDEM™ monitor pass? ₁ Yes ₀ No (1070)

→ If **NO**, issue a new eDEM™ monitor and complete another eDEM™ Monitor Quality Control form.



**EXHALED
NITRIC OXIDE**

Supervisor ID: _____

Subject ID: _____ - _____ - _____

Subject Initials: _____

Visit Number: _____

Visit Date: _____ / _____ / _____
Month Day Year

Technician ID: _____

(Technician completed)

Complete this form only if the subject is eligible according to the appropriate Pulmonary Procedures Checklist (PULMONARYCHK) form.

1. Was the exhaled nitric oxide (ENO) procedure performed? ₁ Yes ₀ No (1000)

→ **If NO, complete Question #1a and STOP.**

→ **If YES, proceed to Question #2 on the next page.**

1a. What was the reason the ENO procedure could not be performed?

₁ Equipment failure, please specify

₂ Equipment not calibrated

₃ Subject refusal

₄ Clinic oversight

₅ Other _____

(1010)



For each maneuver, record the time and FE_{NO} value. If the maneuver was not accepted by the NIOX machine, record the time and select the 'Maneuver Not Acceptable' check box. When TWO reproducible measurements are achieved, select the 'Reproducible Measurements' check box for both maneuvers. The two measurements are considered reproducible when they are within 5% of their mean or 1.25 ppb of their mean.

	Time (based on 24 - hour clock)	Measured FE _{NO}	Maneuver Not Acceptable	Clinic Use Only Reproducible Measurements
2. Maneuver #1	_____ (1020)	_____. ____ ppb (1030)	<input type="checkbox"/> ₁ (1050)	<input type="checkbox"/>
3. Maneuver #2	_____ (1060)	_____. ____ ppb (1070)	<input type="checkbox"/> ₁ (1090)	<input type="checkbox"/>
4. Maneuver #3	_____ (1100)	_____. ____ ppb (1110)	<input type="checkbox"/> ₁ (1130)	<input type="checkbox"/>
5. Maneuver #4	_____ (1140)	_____. ____ ppb (1150)	<input type="checkbox"/> ₁ (1170)	<input type="checkbox"/>
6. Maneuver #5	_____ (1180)	_____. ____ ppb (1190)	<input type="checkbox"/> ₁ (1210)	<input type="checkbox"/>
7. Maneuver #6	_____ (1220)	_____. ____ ppb (1230)	<input type="checkbox"/> ₁ (1250)	<input type="checkbox"/>
8. Maneuver #7	_____ (1260)	_____. ____ ppb (1270)	<input type="checkbox"/> ₁ (1290)	<input type="checkbox"/>
9. Maneuver #8	_____ (1300)	_____. ____ ppb (1310)	<input type="checkbox"/> ₁ (1330)	<input type="checkbox"/>
10. Maneuver #9	_____ (1340)	_____. ____ ppb (1350)	<input type="checkbox"/> ₁ (1370)	<input type="checkbox"/>

11. Did the subject achieve two reproducible outcomes? ₁ Yes ₀ No (1380)
 If **NO**, explain _____



**METHACHOLINE
CHALLENGE
TESTING**

Supervisor ID: _____

Subject ID: _____ - _____ - _____

Subject Initials: _____

Visit Number: _____

Visit Date: _____ / _____ / _____
Month Day Year

Technician ID: _____

(Technician completed)

Complete this form only if the subject is eligible according to the Methacholine Challenge Testing Checklist (METHACHK) form.

Clinic Use Only (Technician completed)

Use the FEV₁ value from the appropriate spirometry testing form as the baseline reference.

- A. Baseline FEV₁ prior to methacholine challenge ____ . ____ ____ L
- B. Methacholine Reversal Reference Value (Question A x 0.90 = ____ . ____ ____ L)
- C. Diluent FEV₁ Reference Value (Question 1000 x 0.8049 = ____ . ____ ____ L)

1. Post Diluent FEV₁ ____ . ____ ____ L (1000)
2. Did the subject drop \geq 20% at the diluent stage? ₁ Yes ₀ No (1010)
 → If **YES**, proceed to Question #5 and record 0 for Question #5a.
3. Last concentration of methacholine administered ____ . ____ ____ ____ mg/ml (1020)
4. FEV₁ after last concentration of methacholine administered ____ . ____ ____ L (1030)
5. Did the subject achieve a PC₂₀? ₁ Yes ₀ No (1040)
 → If **NO**, proceed to Question #6.
- 5a. PC₂₀ ____ . ____ ____ ____ mg/ml (1050)
6. Time methacholine challenge ended (based on 24-hour clock) ____ ____ ____ ____ (1060)
7. Subject's FEV₁ after standard reversal from methacholine challenge
If subject is continuing with sputum induction, standard reversal = 4 puffs albuterol.
If subject is not continuing with sputum induction, standard reversal = 2 puffs albuterol.
- 7a. FEV₁ ____ . ____ ____ L (1070)
- 7b. Time of FEV₁ in Question #7a (based on 24-hour clock) ____ ____ ____ ____ (1090)
- 7c. Was the FEV₁ from Question #7a \geq the methacholine reversal reference value (B) in the gray box above? ₁ Yes ₀ No (1100)
 → If **YES**, STOP HERE and continue with remaining visit procedures.
 → If **NO**, proceed to the Additional Treatment for Methacholine Challenge Testing (METHA_ADD_TRT) form.



**ADDITIONAL TREATMENT
POST METHACHOLINE
CHALLENGE TESTING**

Supervisor ID: _____

Subject ID: _____ - _____ - _____

Subject Initials: _____

Visit Number: _____

Visit Date: _____ / _____ / _____
Month Day Year

Technician ID: _____

(Technician completed)

Complete this form only if the subject did not reverse to 90% of baseline FEV₁ after the first post-challenge treatment of albuterol.

1. Was an additional treatment used in the first hour? ₁ Yes ₀ No (1000)
→ If NO, skip to Question #3.
 - 1a. Additional albuterol by MDI ₁ Yes ₀ No (1010)
→ If NO, skip to Question #1b.
 Number of additional puffs of albuterol administered ₁ two ₂ four ₃ > four (1020)
 - 1b. Nebulized Beta-agonist ₁ Yes ₀ No (1030)
 - 1c. Subcutaneous epinephrine ₁ Yes ₀ No (1040)
 - 1d. Implementation of clinic emergency protocol or algorithm ₁ Yes ₀ No (1050)
 - 1e. Other (specify) _____ ₁ Yes ₀ No (1060)

2. Subject's FEV₁ after additional treatment within first hour.
 - 2a. FEV₁ _____ . _____ L (1070)
 - 2b. FEV₁ (% predicted) _____ % predicted (1080)
 - 2c. Time of FEV₁ in Question #2a (based on 24-hour clock) _____ (1090)
 - 2d. Was the FEV₁ from Question #2a ≥ the methacholine reversal reference value (B) in the gray box on the Methacholine Challenge Testing (METHA) form? ₁ Yes ₀ No (1100)
→ If YES, STOP HERE and continue with remaining visit procedures.
→ If NO, proceed to Question #3.



**ADDITIONAL TREATMENT
POST METHACHOLINE**

Subject ID: _____ - _____ - _____

Site Number: _____

3. Was additional treatment used after one hour? ₁ Yes ₀ No (1110)
→ *If NO, skip to Question #4.*
- 3a. Additional albuterol by MDI ₁ Yes ₀ No (1120)
→ *If NO, skip to Question #3b.*
Number of additional puffs of albuterol administered ₁ two ₂ four ₃ > four (1130)
- 3b. Nebulized Beta-agonist ₁ Yes ₀ No (1140)
- 3c. Subcutaneous epinephrine ₁ Yes ₀ No (1150)
- 3d. Implementation of clinic emergency protocol or algorithm ₁ Yes ₀ No (1160)
- 3e. Treatment in the emergency room ₁ Yes ₀ No (1170)
- 3f. Overnight hospitalization ₁ Yes ₀ No (1180)
→ *If YES, please complete the Serious Adverse Event (SERIOUS) form.*
- 3g. Other (specify) _____ ₁ Yes ₀ No (1190)
4. Subject's final FEV₁ after methacholine challenge.
- 4a. FEV₁ _____ . _____ L (1200)
- 4b. FEV₁ (% predicted) _____ % predicted (1210)
- 4c. Time of FEV₁ from Question #4a (based on 24-hour clock) _____ (1220)
- 4d. Was the FEV₁ from Question #4a ≥ the methacholine reversal reference value (B) in the gray box on the Methacholine Challenge Testing (METHA) form? ₁ Yes ₀ No (1230)
→ *If NO, complete the source documentation box below.*

Physician Source Documentation
Physician's signature: _____ (1240)
Date: ____ / ____ / _____ (1250)
Time: _____ (based on 24-hour clock) (1260)



**METHACHOLINE
CHALLENGE
TESTING CHECKLIST**

Supervisor ID: _____

Subject ID: _____ - _____ - _____

Subject Initials: _____

Visit Number: _____

Visit Date: _____ / _____ / _____
Month Day Year

Technician ID: _____

(Technician completed)

Complete this form only if the subject is eligible according to the appropriate Pulmonary Procedure Checklist form and successfully completed baseline spirometry session(s).

1. Has the subject had any severe acute illness in the past 4 weeks? ₁ Yes ₀ No (1000)
- If **YES**, has the subject received permission from the supervising physician to proceed with the methacholine challenge testing?
Physician's Signature: _____ (1015) ₁ Yes ₀ No (1010)
2. Does the subject have a baseline (pre-diluent) FEV₁ less than 55% of predicted?
Use the FEV₁ value from the appropriate spirometry testing form as the baseline reference. ₁ Yes ₀ No (1020)
3. Does the subject have a history of urinary retention? ₁ Yes ₀ No (1030)
- ➔ If **NO**, proceed to Question #4.
- 3a. If **YES**, is the subject randomized? ₁ Yes ₀ No (1040)
- ➔ If **NO**, proceed to Question #4 and complete the appropriate Termination of Study Participation form.
- 3b. Was written medical clearance obtained from the study physician? ₁ Yes ₀ No (1050)
- If **YES**, obtain physician's signature:
_____ (1055)
4. Is there any other reason the subject should not proceed with the methacholine challenge testing? ₁ Yes ₀ No (1060)
- If **YES**, explain _____

5. Is the subject eligible to proceed with the diluent (solution #0) spirometry testing for the methacholine challenge? ₁ Yes ₀ No (1070)
- If any of the shaded boxes are completed, the subject is NOT eligible for the methacholine challenge.**
- ➔ **If YES, proceed to the Methacholine Challenge Testing (METHA) form.**



**MIA
ACTH STIMULATION
TESTS**

Subject ID: 1 5 - _____ - _____
 Subject Initials: _____
 Visit Number: _____
 Visit Date: _____ / _____ / _____
Month Day Year
 Coordinator ID: _____

(Clinic Coordinator completed)

1. In the past, has the subject had an ACTH stimulation test performed? ₁ Yes ₀ No (1000)
 - 1a. If **YES**, has the subject had a reaction to the test? ₁ Yes ₀ No (1010)

→ **If YES, the ACTH test cannot be performed and the subject cannot continue in the study. Complete the MIA Termination of Study Participation (P15_TERM) form and follow study termination procedures.**

2. Is the subject currently pregnant? ₁ Yes ₀ No ₉ N/A (1020)
 (If subject is male, check N/A)

→ **If YES, the subject must be terminated from the study. Complete the MIA Termination of Study Participation (P15_TERM) form and follow study termination procedures.**

3. Time blood was drawn for "Baseline Cortisol" tube *(based on 24-hour clock)* _____ (1030)
4. Record subject's baseline cortisol level _____ . _____ mcg/dL (1040)
5. Time blood was drawn for "30 Minute Post ACTH Cortisol" tube *(based on 24-hour clock)* _____ (1050)
6. Record subject's 30 minute post-ACTH cortisol level _____ . _____ mcg/dL (1060)
7. Time blood was drawn for "60 Minute Post ACTH Cortisol" tube *(based on 24-hour clock)* _____ (1070)
8. Record subject's 60 minute post-ACTH cortisol level _____ . _____ mcg/dL (1080)
9. Is the value in Question #6 or Question #8 \geq 20 mcg/dL? ₁ Yes ₀ No (1090)

→ **If NO, the subject cannot continue in the study. Complete the MIA Termination of Study Participation (P15_TERM) form and follow study termination procedures.**

Physician Source Documentation

Physician Signature: _____ (1100)

Date: ____ / ____ / _____ (1110)



**MIA
BRONCHOSCOPY
BIOPSY
RESULTS**

Date Completed: ___/___/___
Month Day Year

(Technician completed)

Instructions: Fax to Rosanne Pogash at the ACRN DCC at (717) 531-5779. Under Bronchoscopy PCR Assignment, Not Adequate should only be assigned if it is the final result.

Subject ID	Bronchoscopy PCR Assignment		
_____ - _____ - _____	Positive _A	Negative _B	Not Adequate _C
_____ - _____ - _____	Positive _A	Negative _B	Not Adequate _C
_____ - _____ - _____	Positive _A	Negative _B	Not Adequate _C
_____ - _____ - _____	Positive _A	Negative _B	Not Adequate _C
_____ - _____ - _____	Positive _A	Negative _B	Not Adequate _C
_____ - _____ - _____	Positive _A	Negative _B	Not Adequate _C
_____ - _____ - _____	Positive _A	Negative _B	Not Adequate _C
_____ - _____ - _____	Positive _A	Negative _B	Not Adequate _C
_____ - _____ - _____	Positive _A	Negative _B	Not Adequate _C
_____ - _____ - _____	Positive _A	Negative _B	Not Adequate _C
_____ - _____ - _____	Positive _A	Negative _B	Not Adequate _C
_____ - _____ - _____	Positive _A	Negative _B	Not Adequate _C
_____ - _____ - _____	Positive _A	Negative _B	Not Adequate _C
_____ - _____ - _____	Positive _A	Negative _B	Not Adequate _C
_____ - _____ - _____	Positive _A	Negative _B	Not Adequate _C
_____ - _____ - _____	Positive _A	Negative _B	Not Adequate _C
_____ - _____ - _____	Positive _A	Negative _B	Not Adequate _C
_____ - _____ - _____	Positive _A	Negative _B	Not Adequate _C



**MIA
BRONCHOSCOPY
CHECKLIST**

Subject ID: 1 5 - _____ - _____
 Subject Initials: _____
 Visit Number: 4
 Visit Date: _____ / _____ / _____
Month Day Year
 Coordinator ID: _____

(Clinic Coordinator completed)

The Bronchoscopy procedure and its related risks must be reviewed again at this visit. The subject must initial and date the appropriate consent to confirm that the bronchoscopy procedure has been reviewed one more time and that he/she is willing to undergo the procedure.

- | | | |
|---|--|--|
| 1. Is the subject's postbronchodilator FEV ₁ ≥ 60% predicted after 4 puffs of albuterol? | <input type="checkbox"/> ₁ Yes | <input checked="" type="checkbox"/> ₀ No (1000) |
| 2. Are any of the coagulation parameters out of range and preventing the subject to be eligible for bronchoscopy? | <input checked="" type="checkbox"/> ₁ Yes | <input type="checkbox"/> ₀ No (1010) |
| 3. Within the last 6 months , has the subject had intubation for asthma? | <input checked="" type="checkbox"/> ₁ Yes | <input type="checkbox"/> ₀ No (1020) |
| 4. Within the last 6 months , has the subject had more than 12 asthma exacerbations? | <input checked="" type="checkbox"/> ₁ Yes | <input type="checkbox"/> ₀ No (1030) |
| 5. Within the last 6 weeks , has the subject been hospitalized for asthma? | <input checked="" type="checkbox"/> ₁ Yes | <input type="checkbox"/> ₀ No (1040) |
| 6. Within the last 6 weeks , has the subject had a respiratory tract infection? | <input checked="" type="checkbox"/> ₁ Yes | <input type="checkbox"/> ₀ No (1050) |
| 7. Within the last 48 hours , did the subject experience an increase in cough, phlegm/mucus, chest tightness, wheezing, or shortness of breath along with an increase in rescue inhaler use of ≥ 8 puffs per 24 hours over baseline use? | <input checked="" type="checkbox"/> ₁ Yes | <input type="checkbox"/> ₀ No (1060) |
| 8. Within the last 48 hours , did the subject use an average of ≥ 16 puffs per 24 hours from his/her rescue inhaler? | <input checked="" type="checkbox"/> ₁ Yes | <input type="checkbox"/> ₀ No (1070) |
| 9. Is the subject's pulse oximetry demonstrating oxygen saturation of < 90% on room air? | <input checked="" type="checkbox"/> ₁ Yes | <input type="checkbox"/> ₀ No (1080) |

- | | | |
|--|---|--|
| 10. Is the subject eligible to proceed with the bronchoscopy procedure?
<i>If any of the shaded boxes are completed, the subject is ineligible for the bronchoscopy procedure.</i> | <input type="checkbox"/> ₁ Yes | <input checked="" type="checkbox"/> ₀ No (1090) |
|--|---|--|

- ➔ ***If YES, continue with the remaining visit procedures.***
- ➔ ***If NO, and the subject is not eligible due to Question #1 or #9 only, STOP HERE. DO NOT send this form to the DCC and reschedule Visit 4. If the subject is ineligible for any other reason, complete the MIA Termination of Study Participation (P15_TERM) form.***



**MIA
CLINIC COORDINATOR
STUDY TREATMENT
QUESTIONNAIRE
(Visits 5-9)**

Subject ID: 1 5 - ____ - ____
 Subject Initials: ____
 Visit Number: ____
 Visit Date: ____ / ____ / ____
Month Day Year
 Coordinator ID: _____

(Clinic Coordinator completed)

This questionnaire is to be completed at Visit 9 by the ACRN study coordinator who was primarily responsible for the subject's MIA visits during the preceding 16 weeks. If a randomized subject terminates prior to Visit 9, this form should be completed at the time of the termination visit.

1. Blinded Scheduled Pills

Subjects in the MIA study were randomized to receive either active clarithromycin pills or placebo pills. You were blinded to the actual treatment assignment. Please check the box that most closely represents your feelings about the treatment the subject received **during the randomized treatment period (Visit 5 through Visit 9)**.

- ₁ I am certain the pills contained placebo. (1000)
- ₂ I think the pills probably contained placebo.
- ₃ I have no idea which type of pills the subject received, but my best guess would be:
 - ₁ Placebo (1010)
 - ₂ Active Drug
- ₄ I think the pills probably contained active drug.
- ₅ I am certain the pills contained active drug.

2. Please comment with respect to any other observations you made that helped you make your choice in Question # 1.

Clinic Coordinator Source Documentation

Coordinator's Initials: ____ (1020)

Date: ____ / ____ / ____ (1030)



COMPLIANCE
CHECKLIST

Subject ID: 1 5 - _____ - _____
Visit Number: _____

Check the following compliance criteria at all scheduled Visits 2 - 11.

3. **Doser™ Compliance for Flovent® MDI**

If the interval between visits exceeds 30 days, complete Questions #3a - #3c using data for the 30 days prior to the visit.

3a. Total number of full days since the last visit _____ days (1090)

➔ Value obtained from Question #4 on P15_COMPLY_WKS

3b. Total number of compliant days _____ days (1100)

➔ Value obtained from Question #5 on P15_COMPLY_WKS

3c. Percent compliance = $\frac{\text{Question \#3b}}{\text{Question \#3a}} \times 100$ _____ % (1110)

➔ *If the subject took the correct daily dose less than 75% of the days, re-emphasize the importance of maintaining the daily dosing schedule.*

3d. Total number of scheduled puffs since the last visit _____ puffs (1120)

➔ Value obtained from Question #1 on P15_COMPLY_WKS

3e. Total number of puffs in Doser™ history _____ puffs (1130)

➔ Value obtained from Question #2 on P15_COMPLY_WKS

3f. Percent compliance = $\frac{\text{Question \#3e}}{\text{Question \#3d}} \times 100$ _____ % (1140)

➔ *If the subject took less than 75% of the scheduled Flovent® puffs, re-emphasize the importance of maintaining the daily dosing schedule.*



COMPLIANCE CHECKLIST

Subject ID: 15 - _____ - _____

Visit Number: _____

4. Diary Card Compliance

4a. Total number of full days since the last visit _____ days (1150)

4b. Total number of days where all 3 measurements (AM PEFR, PM PEFR, and complete symptom score) have been recorded _____ days (1160)

4c. Percent compliance = $\frac{\text{Question \#4b}}{\text{Question \#4a}} \times 100$ _____ % (1170)

4d. Total number of days where the subject measured both AM PEFR and PM PEFR on schedule and transcribed the measurements accurately on his/her diary cards _____ days (1180)

4e. Percent compliance on schedule = $\frac{\text{Question \#4d}}{\text{Question \#4a}} \times 100$ _____ % (1190)

➔ ***If the percent compliance for either Question #4c or #4e is less than 75%, re-emphasize the importance of accurately and regularly completing diary cards.***



**MIA
DIARY CARD**

Subject ID: 1 5 - _____ - _____

Subject Initials: _____

Return Visit Number: _____

Return Visit Date: _____ / _____ / _____
Month Day Year

Subject's Initials: _____

Date: ____ / ____ / _____

To the subject: If your peak flow is below _____ (1000) liters/minute, use your RESCUE inhaler as instructed in the handout "If Your Asthma Gets Worse." Contact study personnel if your peak flow does not increase to this value after 1 hour of RESCUE use, or if you are experiencing extreme symptoms. If you have taken at least _____ puffs/24 hours for the past 48 hours from your RESCUE inhaler, contact study personnel.

Please use black ink to complete.	Day 1: _____	Day 2: _____	Day 3: _____	Day 4: _____	Day 5: _____	Day 6: _____	Day 7: _____
Date (ddate)	____ / ____ month day	____ / ____ month day	____ / ____ month day	____ / ____ month day	____ / ____ month day	____ / ____ month day	____ / ____ month day

MORNING EVALUATION (Between 5 AM and 10 AM)

1. Number of times you woke up last night due to asthma (1010)	_____	_____	_____	_____	_____	_____	_____
2. Time of AM Peak Flow (within 15 minutes of awakening) (1020)	____ : ____	____ : ____	____ : ____	____ : ____	____ : ____	____ : ____	____ : ____
3. AM Peak Flow (liters/min)** (1030) / (1035)	_____	_____	_____	_____	_____	_____	_____
4. Total number of puff(s) from Flovent® Inhaler (AM) (1040)	_____	_____	_____	_____	_____	_____	_____
5. Number of pill(s) taken (AM) (1050)	_____	_____	_____	_____	_____	_____	_____
Symptoms⁺⁺ during the night	6. Shortness of Breath (1060)						
	7. Chest Tightness (1070)						
	8. Wheezing (1080)						
	9. Cough (1090)						
	10. Phlegm/Mucus (1100)						

NIGHT-TIME EVALUATION (Between 8 PM and 1 AM)

11. Time of PM Peak Flow (between 8 PM and 1 AM) (1110)	____ : ____	____ : ____	____ : ____	____ : ____	____ : ____	____ : ____	____ : ____
12. PM Peak Flow (liters/min)** (1120) / (1125)	_____	_____	_____	_____	_____	_____	_____
13. Total number of puff(s) from Flovent® Inhaler (PM) (1130)	_____	_____	_____	_____	_____	_____	_____
14. Number of pill(s) taken (PM) (1140)	_____	_____	_____	_____	_____	_____	_____
Symptoms⁺⁺ since you woke	15. Shortness of Breath (1150)						
	16. Chest Tightness (1160)						
	17. Wheezing (1170)						
	18. Cough (1180)						
	19. Phlegm/Mucus (1190)						

24 HOUR EVALUATION

20. Total number of puffs from albuterol (RESCUE) inhaler during past 24 hours. (Do not record preventive use.) (1200)	_____	_____	_____	_____	_____	_____	_____
--	-------	-------	-------	-------	-------	-------	-------

** Record the best of three attempts. Circle the value if you have taken any medication from your RESCUE inhaler in the last 2 hours.

++ Symptom Severity Rating Scale
 0 = Absent No symptom
 1 = Mild Symptom was minimally troublesome, i.e. not sufficient to interfere with normal daily activity or sleep.
 2 = Moderate Symptom was sufficiently troublesome to interfere with normal daily activity or sleep.
 3 = Severe Symptom was so severe as to prevent normal activity and/or sleep.



**MIA
DIARY CARD**

Subject ID: 15 - ____ - ____

Subject Initials: _____

Return Visit Number: _____

Return Visit Date: ____ / ____ / ____
Month Day Year

Subject's Initials: _____
Date: ____ / ____ / ____

To the subject: If your peak flow is below ____ (1000) liters/minute, use your RESCUE inhaler as instructed in the handout "If Your Asthma Gets Worse." Contact study personnel if your peak flow does not increase to this value after 1 hour of RESCUE use, or if you are experiencing extreme symptoms. If you have taken at least ____ puffs/24 hours for the past 48 hours from your RESCUE inhaler, contact study personnel.

Please use black ink to complete.	Day 1: ____	Day 2: ____	Day 3: ____	Day 4: ____	Day 5: ____	Day 6: ____	Day 7: ____
Date (ddate)	____ / ____ month day	____ / ____ month day	____ / ____ month day	____ / ____ month day	____ / ____ month day	____ / ____ month day	____ / ____ month day

MORNING EVALUATION (Between 5 AM and 10 AM)

1. Number of times you woke up last night due to asthma (1010)	____	____	____	____	____	____	____
2. Time of AM Peak Flow (within 15 minutes of awakening) (1020)	____ : ____	____ : ____	____ : ____	____ : ____	____ : ____	____ : ____	____ : ____
3. AM Peak Flow (liters/min)** (1030) / (1035)	____	____	____	____	____	____	____
4. Total number of puff(s) from Flovent® Inhaler (AM) (1040)	____	____	____	____	____	____	____
Symptoms ⁺⁺ during the night	5. Shortness of Breath (1060)						
	6. Chest Tightness (1070)						
	7. Wheezing (1080)						
	8. Cough (1090)						
	9. Phlegm/Mucus (1100)						

NIGHT-TIME EVALUATION (Between 8 PM and 1 AM)

10. Time of PM Peak Flow (between 8 PM and 1 AM) (1110)	____ : ____	____ : ____	____ : ____	____ : ____	____ : ____	____ : ____	____ : ____
11. PM Peak Flow (liters/min)** (1120) / (1125)	____	____	____	____	____	____	____
12. Total number of puff(s) from Flovent® Inhaler (PM) (1130)	____	____	____	____	____	____	____
Symptoms ⁺⁺ since you woke	13. Shortness of Breath (1150)						
	14. Chest Tightness (1160)						
	15. Wheezing (1170)						
	16. Cough (1180)						
	17. Phlegm/Mucus (1190)						

24 HOUR EVALUATION

18. Total number of puffs from albuterol (RESCUE) inhaler during past 24 hours. (Do not record preventive use.) (1200)	____	____	____	____	____	____	____
--	------	------	------	------	------	------	------

** Record the best of three attempts. Circle the value if you have taken any medication from your RESCUE inhaler in the last 2 hours.

++ Symptom Severity Rating Scale
 0 = Absent No symptom
 1 = Mild Symptom was minimally troublesome, i.e. not sufficient to interfere with normal daily activity or sleep.
 2 = Moderate Symptom was sufficiently troublesome to interfere with normal daily activity or sleep.
 3 = Severe Symptom was so severe as to prevent normal activity and/or sleep.



**MIA EXHALED
BREATH CONDENSATE
COLLECTION**

Supervisor ID: _____

Subject ID: 1 5 - _____ - _____

Subject Initials: _____

Visit Number: _____

Visit Date: _____ / _____ / _____
Month Day Year

Technician ID: _____

(Technician Completed)

1. Was EBC collection attempted at this visit?

Yes

No (1000)

→ If NO, complete Question #1a and STOP.

→ If YES, proceed to Question #2.

1a. Check the primary reason EBC collection was not attempted.

₁ Subject Refusal

₂ Equipment Unavailable

₃ Clinic Oversight

₄ Other _____ (1010)

2. Time EBC collection started (based on 24-hour clock).

_____ (1020)

3. Time EBC collection stopped (based on 24-hour clock).

_____ (1030)

→ If collection time exceeds ten minutes, please provide an explanation below.

4. Was at least one tube collected at this visit?

₁ Yes

₀ No (1040)

→ If NO, STOP HERE.

4a. If YES, record the number of tubes aliquoted.

_____ tubes (1050)

5. Were the tubes stored immediately at -70° Celsius or colder?

₁ Yes

₀ No (1060)

→ If YES, STOP HERE.

5a. At what temperature were the tubes stored?

_____ ° C (1070)



**MIA
ELECTROCARDIOGRAM
(ECG)**

Subject ID: 1 5 - _____ - _____
 Subject Initials: _____
 Visit Number: _____
 Visit Date: _____ / _____ / _____
Month Day Year
 Coordinator ID: _____

(Clinic Coordinator completed)

1. Record subject's QTc measurement _____ msec (1000)
- 1a. If FEMALE, is Question #1 \geq 450 msec? ₁ Yes ₀ No (1010)
- 1b. If MALE, is Question #1 \geq 430 msec? ₁ Yes ₀ No (1020)
2. Did the physician observe any other ECG result that would prevent the subject from taking clarithromycin for 16 weeks and/or having a bronchoscopy? ₁ Yes ₀ No (1030)

If **YES**, explain: _____

3. Are any of the shaded boxes completed? ₁ Yes ₀ No (1040)

If any of the shaded boxes are completed, the subject is ineligible.

→ *If NO, complete the MIA Termination of Study Participation (P15_TERM) form and follow study termination procedures.*

Physician Source Documentation
 Physician's signature: _____ (1050)
 Date: ____ / ____ / _____ (1060)



**MIA
ELIGIBILITY
CHECKLIST 1**

Subject ID: 1 5 - _____ - _____
 Subject Initials: _____
 Visit Number: 1
 Visit Date: _____ / _____ / _____
Month Day Year
 Interviewer ID: _____

(Subject Interview completed)

1. **Did the subject sign the MIA/Genetics Informed Consent?** ₁ Yes ₀ No (1000)
 1a. If **YES**, record the date the form was signed. _____ / _____ / _____ (1010)
month day year
2. Is the subject willing to undergo fiberoptic bronchoscopy with endobronchial biopsy for the PCR status determination? ₁ Yes ₀ No (1020)
3. Is the subject willing to give blood for safety variable measurements? ₁ Yes ₀ No (1030)
4. Is the subject between 18 and 60 years of age, inclusive? ₁ Yes ₀ No (1040)
5. Is the subject planning to move away from this clinical center in the next 9 months such that his/her ability to complete the study will be jeopardized? ₁ Yes ₀ No (1050)
6. Does the subject have current evidence of any of the conditions listed on the Exclusionary Medical Conditions reference card (P15_EXCLMED)? ₁ Yes ₀ No (1060)
 If **YES**, describe _____
7. Has the subject taken any medications listed on the Exclusionary Drugs reference card (P15_EXCLDRUG) within the specified time periods? ₁ Yes ₀ No (1070)
 If **YES**, describe _____
8. Is the subject currently taking any medications listed on the Clarithromycin Exclusionary Drugs reference card (P15_CLAR_EXCLD)? ₁ Yes ₀ No (1080)
 If **YES**, describe _____
9. Is the subject currently taking prescription or over-the-counter medication(s) other than those listed on the Allowed Medications reference card (P15_MEDALLOW)? ₁ Yes ₀ No (1090)
 If **YES**, describe _____

➔ **If YES and the drug is not listed on an exclusionary reference card (P15_EXCLDRUG, P15_CLAR_EXCLD), please contact the scientific coordinator to determine if the medication will be allowed.**
10. Has the subject used systemic corticosteroids during the past 6 weeks? ₁ Yes ₀ No (1100)



ELIGIBILITY CHECKLIST 1

Subject ID: 15 - _____ - _____Visit Number: 1

11. Has the subject had a change in the dose of controller therapy or therapies during the past 6 weeks? ₁ Yes ₀ No (1110)
12. Is the subject currently receiving hyposensitization therapy (e.g., allergy shots) other than an established maintenance regimen implemented continuously for a minimum of 3 months? ₁ Yes ₀ No (1120)
13. Has the subject used any smokeless tobacco products (e.g., chew, snuff) in the past year? ₁ Yes ₀ No (1130)
14. Has the subject smoked a pipe, cigar, marijuana, or any other substance in the past year? ₁ Yes ₀ No (1140)
15. Record smoking history in pack-years. (Enter '00.0' if none) _____ . _____ (1150)
- 15a. Is Question #15 \geq 10? ₁ Yes ₀ No (1160)
16. Has the subject had a respiratory tract infection in the past 6 weeks? ₁ Yes ₀ No (1170)
17. Has the subject experienced a significant asthma attack in the past 6 weeks? ₁ Yes ₀ No (1180)
18. Has the subject been hospitalized for asthma in the past 6 weeks? ₁ Yes ₀ No (1190)
19. Has the subject had more than 12 asthma exacerbations in the past 6 months? ₁ Yes ₀ No (1200)
20. Has the subject experienced a life-threatening asthma attack requiring intubation or mechanical ventilation in the past 10 years? ₁ Yes ₀ No (1210)
21. Does the subject work night shift or have an altered day/night cycle for other reasons? ₁ Yes ₀ No (1220)
22. Does the subject regularly consume grapefruit or grapefruit juice? ₁ Yes ₀ No (1230)
- 22a. If **YES**, is the subject willing to withhold consumption of grapefruit or grapefruit juice throughout the MIA study? ₁ Yes ₀ No (1240)

23. Is the subject eligible to proceed? ₁ Yes ₀ No (1250)
If any of the shaded boxes are completed, the subject is ineligible.
→ If YES, continue with remaining Visit 1 procedures.

Subject Source Documentation

Subject Initials: _____ (1260)

Date: ____ / ____ / _____ (1270)



**MIA
ELIGIBILITY
CHECKLIST 2**

Subject ID: 1 5 - _____ - _____
 Subject Initials: _____
 Visit Number: 1
 Visit Date: _____ / _____ / _____
Month Day Year
 Coordinator ID: _____

(Clinic Coordinator completed)

1. Record the subject's Average Score from the ACQ_JUN_SCORE form _____ . _____ (1000)
- 1a. Prior to Visit 1, was the subject on the controller therapy of ICS only or ICS/LABA? ₁ Yes ₀ No (1003)
- If NO, skip to Question #1b.**
- 1ai. Is Question #1 ≥ 1.25 OR in the opinion of the local investigator/clinic coordinator does the subject have a reasonable chance to have an ACQ score ≥ 1.25 at Visit 3? ₁ Yes ₀ No (1006)
- Skip to Question #2.**
- 1b. Is Question #1 ≥ 1.50 ? ₁ Yes ₀ No (1010)
2. Is the subject's postbronchodilator FEV₁ $\geq 60\%$ predicted after two puffs of albuterol? ₁ Yes ₀ No (1020)
3. According to the ECG results, is the subject eligible to enroll in the MIA study? ₁ Yes ₀ No (1030)
- Use Question #3 from the P15_ECG form to answer this question**
4. Is the subject potentially able to bear children? (If subject is male, check N/A and go to Question #5.) ₁ Yes ₀ No ₉ N/A (1040)
- 4a. If **YES**, is the subject currently pregnant or lactating? ₁ Yes ₀ No (1050)
- 4b. If **YES**, is the subject using an approved birth control method indicated on the Birth Control (BIRCTRL) reference card? ₁ Yes ₀ No (1060)
- The subject must use one non-barrier method with single barrier method OR double barrier method.**
5. Is the subject able to use a metered dose inhaler (MDI) properly, as evidenced by achieving a score of 6 on two consecutive, separate inhalations using the MDI Inhalation Technique Checklists (SCORE, TECH_MDI)? ₁ Yes ₀ No (1070)
6. Is the subject able to use the AM1[®] device correctly, as evidenced by achieving a satisfactory rating on the AM1[®] Performance Checklist (PERF_AM1)? ₁ Yes ₀ No (1080)



**ELIGIBILITY
CHECKLIST 2**

Subject ID: 1 5 - _____ - _____

Visit Number: 1

7. Is there any other reason why this subject should not be included in the study? ₁ Yes ₀ No (1090)

→ If **YES**, describe: _____

8. Is the subject eligible to proceed? ₁ Yes ₀ No (1100)
If any of the shaded boxes are completed, the subject is ineligible.

→ ***If NO, STOP HERE.***

9. Did the subject's FEV₁ improve \geq 12% in response to two puffs of albuterol? ₁ Yes ₀ No (1110)

→ ***If NO, the subject will have to meet methacholine criteria at Visit 2 to complete eligibility for the study. Proceed with Visit 1 according to the checklist.***



**MIA
ELIGIBILITY
CHECKLIST 4**

Subject ID: 1 5 - _____ - _____
 Subject Initials: _____
 Visit Number: 3
 Visit Date: _____ / _____ / _____
Month Day Year
 Coordinator ID: _____

(Clinic Coordinator completed)

1. Since Visit 1, has the subject received treatment with any excluded medications (P15_EXCLDRUG, P15_CLAR_EXCLD)? ₁ Yes ₀ No (1000)
2. Since Visit 2, did the subject experience a significant asthma exacerbation? ₁ Yes ₀ No (1010)
3. Since Visit 2, has the subject had a respiratory tract infection? ₁ Yes ₀ No (1020)
4. Record the subject's Average Score from the ACQ_JUN_SCORE form _____ . _____ (1030)
 - 4a. Is Question #4 \geq 1.25? ₁ Yes ₀ No (1040)
5. Using the pill count, did the subject take at least 75% of the required pills from his or her pill vial during the interval between Visits 2 and 3? ₁ Yes ₀ No (1050)

➔ Use Question #1e from P15_COMPLY to answer this question
6. Using the eDEM™ Monitor, did the subject take at least 75% of the required pills at the correct time-window during the interval between Visits 2 and 3? ₁ Yes ₀ No (1060)

➔ Use Question #2d from P15_COMPLY to answer this question
7. Using the history stored in the Doser™, did the subject take 4 puffs per day (correct daily dose) on at least 75% of the days during the interval between Visits 2 and 3? ₁ Yes ₀ No (1070)

➔ Use Question #3c from P15_COMPLY to answer this question
8. Using the history stored in the Doser™, did the subject take at least 75% of the required puffs from his or her Flovent® inhaler during the interval between Visits 2 and 3? ₁ Yes ₀ No (1080)

➔ Use Question #3f P15_COMPLY to answer this question
9. Did the subject record both AM and PM peak flow measurements and symptoms on his or her Diary Cards (P15_DIARY) on at least 75% of the days during the interval between Visits 2 and 3? ₁ Yes ₀ No (1090)

➔ Use Question #4c from P15_COMPLY to answer this question



ELIGIBILITY CHECKLIST 4

Subject ID: 1 5 - _____ - _____Visit Number: 3

10. Did the subject measure his or her AM and PM peak flow on schedule and accurately transcribe the measurements on his or her Diary Cards (P15_DIARY) on at least 75% of the days during the interval between Visits 2 and 3? ₁ Yes ₀ No (1100)
- ➔ Use Question #4e from P15_COMPLY to answer this question
11. Is the subject's postbronchodilator FEV₁ ≥ 60% of predicted after four puffs of albuterol? ₁ Yes ₀ No (1110)
12. Is the subject able to use a metered dose inhaler (MDI) properly, as evidenced by achieving a score of 6 on two consecutive, separate inhalations using the MDI Inhalation Technique Checklist (SCORE, TECH_MDI)? ₁ Yes ₀ No (1120)
13. Is the subject able to use the AM1[®] device correctly, as evidenced by achieving a satisfactory rating on the AM1[®] Performance Checklist (PERF_AM1)? ₁ Yes ₀ No (1130)
14. Does the subject wish to withdraw consent from the study? ₁ Yes ₀ No (1140)
15. Is there any new information that makes the subject ineligible according to the eligibility criteria?
If **YES**, describe: _____ ₁ Yes ₀ No (1150)
16. Is there any other reason why this subject should not be included in the study?
If **YES**, describe: _____ ₁ Yes ₀ No (1160)

17. Is the subject eligible? ₁ Yes ₀ No (1170)
- If any of the shaded boxes are completed, the subject is ineligible.***
- ➔ ***If NO, complete the MIA Termination of Study Participation (P15_TERM) form.***
- ➔ ***If YES, proceed with remaining Visit 3 procedures.***



**MIA
ELIGIBILITY
CHECKLIST 5**

Subject ID: 1 5 - _____ - _____
 Subject Initials: _____
 Visit Number: 5
 Visit Date: _____ / _____ / _____
Month Day Year
 Coordinator ID: _____

(Clinic Coordinator completed)

1. Since Visit 4, has the subject had a respiratory tract infection? ₁ Yes ₀ No (1000)
 → If **NO**, skip to Question #2.
- 1a. If **YES**, has the subject been free of infection-related symptoms for at least 6 weeks prior to Visit 5? ₁ Yes ₀ No (1010)
 → If **NO**, STOP HERE. DO NOT send this form to the DCC and reschedule Visit 5.
2. Since Visit 4, has the subject experienced a significant asthma exacerbation as defined in the protocol? ₁ Yes ₀ No (1020)
 → If **NO**, skip to Question #5.
- 2a. Has the subject received prednisone therapy? ₁ Yes ₀ No (1030)
 → If **NO** and the subject has NOT recovered, prednisone therapy should be prescribed and Visit 5 should be rescheduled 6 weeks after the last dose of prednisone.
 → If **NO**, and the subject has recovered, skip to Question #3.
- 2ai. If **YES**, record the date of the subject's last dose of prednisone from the Concomitant Medications for Asthma/Allergy and Adverse Events (CMED) form. _____ / _____ / _____ (1040)
month day year
- 2aai. Was the last dose taken at least 6 weeks prior to today's date? ₁ Yes ₀ No (1050)
 → If **NO**, STOP HERE. DO NOT send this form to the DCC and reschedule Visit 5 as above.
3. Record the subject's Average Score from the ACQ_JUN_SCORE form _____ . _____ (1060)
- 3a. In the opinion of the ACRN investigator, has the subject's clinical status and ACQ returned to the level similar to that observed during Visits 1 through 3? ₁ Yes ₀ No (1070)
- 3ai. Obtain the signature of the ACRN investigator who evaluated the subject. _____ (1075)
4. Is the subject's FEV₁ < 80% of the baseline? ₁ Yes ₀ No (1080)
 → Baseline is defined as the pre-bronchodilator FEV₁ value obtained at Visit 2.



ELIGIBILITY CHECKLIST 5

Subject ID: 1 5 - _____ - _____Visit Number: 5

5. Since Visit 4, has the subject received treatment with any excluded medications (P15_EXCLDRUG, P15_CLAR_EXCLD)? ₁ Yes ₀ No (1090)
6. Since Visit 4, has the subject experienced > 2 significant asthma exacerbations? ₁ Yes ₀ No (1100)
7. Since Visit 4, has the subject had > 2 respiratory tract infections? ₁ Yes ₀ No (1110)
8. Did the clinic receive confirmation via the Subject Status report that the subject is eligible for randomization? ₁ Yes ₀ No (1120)
→ If **NO**, reschedule Visit 5.
9. Is there any new information that makes the subject ineligible according to the eligibility criteria? ₁ Yes ₀ No (1130)
→ If **YES**, describe: _____
10. Is there any other reason why this subject should not be included in the study? ₁ Yes ₀ No (1140)
→ If **YES**, describe: _____

11. Is the subject eligible? ₁ Yes ₀ No (1150)
If any of the shaded boxes are completed, the subject is ineligible.
→ *If the subject is eligible and will participate in MIA, randomize the subject. Otherwise, please complete the MIA Termination of Study Participation (P15_TERM) form.*

12. Drug Packet Number (record on P15_LOG)

15 - -
(1160) (1170) (1180)

**MIA
FLUID PHASE
MEASUREMENTS**

Subject ID: 1 5 - _____ - _____
 Subject Initials: _____
 Visit Number: _____
 Visit Date: _____ / _____ / _____
Month Day Year
 Completed Date: _____ / _____ / _____
Month Day Year
 Technician ID: _____

(Technician completed)

		Non-detectable limit	Quantity not sufficient to dilute
Tryptase	_____ . _____ mcg/L (1000)	<input type="checkbox"/> (1010)	<input type="checkbox"/> (1020)

Complete at Visit 3 Only

IL-10	_____ . _____ pg/ml (1030)	<input type="checkbox"/> (1040)	<input type="checkbox"/> (1050)
-------	----------------------------	---------------------------------	---------------------------------



**MIA
LABORATORY
SAFETY CHECKLIST**

Subject ID: 1 5 - _____ - _____
 Subject Initials: _____
 Visit Number: _____
 Visit Date: _____ / _____ / _____
Month Day Year
 Coordinator ID: _____

(Clinic Coordinator completed)

(Visits 1, 3, 6-9 only)

1. CBC with differential cell count

**Lab Value
Out of Range**

- | | | |
|----------------------------------|-------------------------------|--|
| 1a. Eosinophils (absolute count) | _____ /mm ³ (1000) | <input type="checkbox"/> ₁ (1010) |
| 1b. WBC | _____ . _____ K/uL (1020) | <input type="checkbox"/> ₁ (1030) |
| 1c. HCT | _____ . _____ % (1040) | <input type="checkbox"/> ₁ (1050) |
| 1d. HGB | _____ . _____ g/dL (1060) | <input type="checkbox"/> ₁ (1070) |
| 1e. Platelet Count | _____ K/uL (1080) | <input type="checkbox"/> ₁ (1090) |
| 1f. Differential | | |
| 1fi. Lymphocytes | _____ . _____ % (1100) | <input type="checkbox"/> ₁ (1110) |
| 1fii. Monocytes | _____ . _____ % (1120) | <input type="checkbox"/> ₁ (1130) |
| 1fiii. Basophils | _____ . _____ % (1140) | <input type="checkbox"/> ₁ (1150) |
| 1fiv. Neutrophils | _____ . _____ % (1160) | <input type="checkbox"/> ₁ (1170) |
| 1fv. Eosinophils | _____ . _____ % (1180) | <input type="checkbox"/> ₁ (1190) |

(Visits 1, 6-9 only)

2. Liver Function Test (LFT)

- | | | |
|--------------------------------|-----------------------------|--|
| 2a. AST | _____ U/L (1200) | <input type="checkbox"/> ₁ (1210) |
| 2b. ALT | _____ U/L (1220) | <input type="checkbox"/> ₁ (1230) |
| 2c. Total Bilirubin | _____ . _____ mg/dL (1240) | <input type="checkbox"/> ₁ (1250) |
| 2d. Total Alkaline Phosphatase | _____ U/L (1260) | <input type="checkbox"/> ₁ (1270) |
| 3. Mg ⁺⁺ | _____ . _____ mg/dL (1280) | <input type="checkbox"/> ₁ (1290) |
| 4. K ⁺ | _____ . _____ mmol/L (1300) | <input type="checkbox"/> ₁ (1310) |
| 5. BUN + Creatinine | | |
| 5a. BUN | _____ mg/dL (1320) | <input type="checkbox"/> ₁ (1330) |
| 5b. Creatinine | _____ . _____ mg/dL (1340) | <input type="checkbox"/> ₁ (1350) |



**MIA LABORATORY
SAFETY CHECKLIST**

Subject ID: 1 5 - _____ - _____

Visit Number: _____

6. Are any lab values out of range? ₁ Yes ₀ No (1360)

→ ***If NO, STOP HERE.***

→ ***If YES, the supervising physician must evaluate the results immediately.***

6a. If YES, does the subject need to be evaluated? ₁ Yes ₀ No (1370)

→ ***If YES, the subject must be evaluated by the supervising physician within 24 hours.***

(Physician completed)

7. Is the subject allowed to continue in the study? ₁ Yes ₀ No (1380)

→ ***If NO, the subject cannot continue in the study. Complete the MIA Termination of Study Participation (P15_TERM) form and follow study termination procedures.***

Physician Source Documentation

Physician Signature: _____ (1390)

Date: ___ / ___ / _____ (1400)



MIA
SCHEDULED
MEDICATIONS
(Visits 5 - 8)

Subject ID: 1 5 - _____ - _____
Subject Initials: _____
Visit Number: _____
Visit Date: ____ / ____ / ____
 Month Day Year
Coordinator ID: _____

(Clinic Coordinator completed)

1. Type of scheduled medications dispensed

- ₁ Regular
₂ Backup (1000)

→ If backup medications were dispensed, fax this form immediately to the Project Coordinator at the DCC at (717) 531-4359. Explain circumstances:

2. Number of Flovent[®] MDIs dispensed

- ₀ None
₁ One
₂ Two (1010)

3. Number of Scheduled Pill Vials dispensed

- ₀ None
₁ One (1020)

Affix the drug log label below:

Copy the drug label number below:

1 5 - _____ - _____
(1030) (1040) (1050)

Coordinator's
Signature: _____ (1060)
Date: ____ / ____ / _____ (1070)

By signing in the source documentation box you are:

- 1) confirming that the label on the medications matches the number on the outside of the packet and the outside of the kit.
- 2) confirming that the subject name and ID number written on the outside of the kit correspond to the person receiving the medications.
- 3) confirming that the correct medications were distributed at this visit.



MEDICAL HISTORY

Subject ID: 1 5 - _____ - _____

Visit Number: 1

PRIOR ASTHMA TREATMENT

I will read a list of medications. Indicate if you have ever used each medication. If you have, please indicate, to the best of your knowledge, the date last taken.

If Yes, indicate date medication was last taken
month / day / year

- | | | | |
|--|--|---|---|
| <p>7. Non-long-acting Inhaled Beta-Agonists
(Bronkaid Mist, Duo-Medihaler, Medihaler-Epi, Primatene Mist, Alupent, Brethaire, Brethine, Bronkometer, Maxair, Metaprel, Proventil, Tornalate, Ventolin, Xopenex and others)</p> <p>7a. If YES, indicate average daily puffs in the past month. (Enter '00' if none used.)</p> | <input type="checkbox"/> ₁ Yes <input type="checkbox"/> ₀ No <input type="checkbox"/> ₈ Unknown | <p>(1150)</p> <p>_____ puffs (1190)</p> | <p>___ / ___ / _____
(1160) (1170) (1180)</p> |
| <p>8. Long-acting Inhaled Beta-Agonists
(Serevent, Foradil, Advair Diskus)</p> | <input type="checkbox"/> ₁ Yes <input type="checkbox"/> ₀ No <input type="checkbox"/> ₈ Unknown | <p>(1200)</p> | <p>___ / ___ / _____
(1210) (1220) (1230)</p> |
| <p>9. Asthma medication via a Nebulizer Machine</p> | <input type="checkbox"/> ₁ Yes <input type="checkbox"/> ₀ No <input type="checkbox"/> ₈ Unknown | <p>(1240)</p> | <p>___ / ___ / _____
(1250) (1260) (1270)</p> |
| <p>10. Oral Beta-Agonists
(Alupent, Brethine, Bricanyl, Metaprel, Proventil, Ventolin, Repetabs, Volmax and others)</p> | <input type="checkbox"/> ₁ Yes <input type="checkbox"/> ₀ No <input type="checkbox"/> ₈ Unknown | <p>(1280)</p> | <p>___ / ___ / _____
(1290) (1300) (1310)</p> |
| <p>11. Short-acting Oral Theophylline
(Aminophylline, Slo-Phyllin and others)</p> | <input type="checkbox"/> ₁ Yes <input type="checkbox"/> ₀ No <input type="checkbox"/> ₈ Unknown | <p>(1320)</p> | <p>___ / ___ / _____
(1330) (1340) (1350)</p> |
| <p>12. Sustained release Oral Theophylline
(Slo-bid, Theo-Dur, Uniphyll and others)</p> | <input type="checkbox"/> ₁ Yes <input type="checkbox"/> ₀ No <input type="checkbox"/> ₈ Unknown | <p>(1360)</p> | <p>___ / ___ / _____
(1370) (1380) (1390)</p> |
| <p>13. Inhaled Anticholinergic
(Atrovent, Combivent, Spiriva)</p> | <input type="checkbox"/> ₁ Yes <input type="checkbox"/> ₀ No <input type="checkbox"/> ₈ Unknown | <p>(1400)</p> | <p>___ / ___ / _____
(1410) (1420) (1430)</p> |
| <p>14. Anti-allergic Inhaled Medications
(Intal, Tilade and others)</p> | <input type="checkbox"/> ₁ Yes <input type="checkbox"/> ₀ No <input type="checkbox"/> ₈ Unknown | <p>(1440)</p> | <p>___ / ___ / _____
(1450) (1460) (1470)</p> |
| <p>15. Anti-allergic Nasal Medications
(Nasal crom, Astelin and others)</p> | <input type="checkbox"/> ₁ Yes <input type="checkbox"/> ₀ No <input type="checkbox"/> ₈ Unknown | <p>(1480)</p> | <p>___ / ___ / _____
(1490) (1500) (1510)</p> |



MEDICAL HISTORY

Subject ID: 1 5 - _____ - _____

Visit Number: 1

If Yes, indicate date medication was last taken month / day / year

- 16. Anti-allergic Oral Medications (Allegra, Claritin, Zyrtec, Chlor-Trimeton and others) ₁ Yes ₀ No ₈ Unknown (1520) ___ / ___ / _____ (1530) (1540) (1550)
- 17. Leukotriene Antagonist / 5LO Inhibitors (Accolate, Zyflo, Singulair) ₁ Yes ₀ No ₈ Unknown (1560) ___ / ___ / _____ (1570) (1580) (1590)
- 18. IgE Blocker (Xolair) ₁ Yes ₀ No ₈ Unknown (1600) ___ / ___ / _____ (1610) (1620) (1630)
- 19. Topical Steroids - Prescription (Synalar, Lidex, Dermacin, Fluocinonide and others) ₁ Yes ₀ No ₈ Unknown (1640) ___ / ___ / _____ (1650) (1660) (1670)
- 20. Topical Steroids - OTC (Hydrocortisone - multiple strengths and products) ₁ Yes ₀ No ₈ Unknown (1680) ___ / ___ / _____ (1690) (1700) (1710)
- 21. Nasal Steroids (Beconase, Vancenase, Flonase, Nasacort, Nasalide, Nasarel, Rhinocort, Nasonex and others) ₁ Yes ₀ No ₈ Unknown (1720) ___ / ___ / _____ (1730) (1740) (1750)
- 22. Oral Steroids (Prednisone, Medrol and others) ₁ Yes ₀ No ₈ Unknown (1760) ___ / ___ / _____ (1770) (1780) (1790)



MEDICAL HISTORY

Subject ID: 1 5 - _____ - _____Visit Number: 1

Next, I will read a list of inhaled steroid medications. Please indicate if you had used any of these medications prior to being screened for the MIA study. If you did, please indicate, to the best of your knowledge, the date last taken.

23. Inhaled Steroids (prior to MIA study) ₁ Yes ₀ No ₈ Unknown _____ / _____ / _____
(1800) (1810) (1820) (1830)
(Azmacort, Beclovent, Vanceril, AeroBid, QVAR, Flovent, Pulmicort, Advair Diskus and others)

- If NO or unknown, skip to Question #24.
- If YES, complete Questions #23a - 23c.

23a. Indicate most recent type of inhaled steroid taken prior to screening for MIA

- ₁ beclomethasone MDI (1 puff = 42 µg) (e.g., **Beclovent, Vanceril**)
- ₂ beclomethasone MDI (1 puff = 84 µg) (e.g., **Vanceril-DS**)
- ₃ beclomethasone HFA (1 puff = 40 µg) (e.g., **QVAR**)
- ₄ beclomethasone HFA (1 puff = 80 µg) (e.g., **QVAR**)
- ₅ budesonide DPI (1 puff = 200 µg) (e.g., **Pulmicort Turbuhaler**)
- ₆ flunisolide MDI (1 puff = 250 µg) (e.g., **Aerobid, Aerobid - M**)
- ₇ fluticasone MDI (1 puff = 44 µg) (e.g., **Flovent**)
- ₈ fluticasone MDI (1 puff = 110 µg) (e.g., **Flovent**)
- ₉ fluticasone MDI (1 puff = 220 µg) (e.g., **Flovent**)
- ₁₀ fluticasone DPI (1 puff = 50 µg) (e.g., **Flovent Rotadisk**)
- ₁₁ fluticasone DPI (1 puff = 100 µg) (e.g., **Advair Diskus**)
- ₁₂ fluticasone DPI (1 puff = 250 µg) (e.g., **Advair Diskus**)
- ₁₃ fluticasone DPI (1 puff = 500 µg) (e.g., **Advair Diskus**)
- ₁₄ triamcinolone acetonide MDI (1 puff = 100 µg) (e.g., **Azmacort**)
- ₁₅ other _____ (1840)

23b. Indicate number of daily inhaled steroid puffs used prior to screening for MIA

_____ puffs (1850)

23c. Indicate how long you had used the inhaled steroid prior to screening for MIA

- ₁ less than 1 month
- ₂ 1 - 6 months
- ₃ greater than 6 months (1860)



MEDICAL HISTORY

Subject ID: 1_5 - _____ - _____

Visit Number: 1

PRIOR DISEASES, ILLNESSES AND SURGERIES

Have you had any diseases, illnesses, or surgeries related to the following areas?

- | | | | If Yes, Comment |
|-------------------------------------|---|--|------------------------|
| 24. Skin | <input type="checkbox"/> ₁ Yes | <input type="checkbox"/> ₀ No | _____ (1870) |
| 25. Blood, Lymph, or Immune Systems | <input type="checkbox"/> ₁ Yes | <input type="checkbox"/> ₀ No | _____ (1880) |
| 26. Eyes | <input type="checkbox"/> ₁ Yes | <input type="checkbox"/> ₀ No | _____ (1890) |
| 27. Ears, Nose, or Throat | <input type="checkbox"/> ₁ Yes | <input type="checkbox"/> ₀ No | _____ (1900) |
| 28. Breasts | <input type="checkbox"/> ₁ Yes | <input type="checkbox"/> ₀ No | _____ (1910) |
| 29. Endocrine Systems | <input type="checkbox"/> ₁ Yes | <input type="checkbox"/> ₀ No | _____ (1920) |
| 30. Lung - other than asthma | <input type="checkbox"/> ₁ Yes | <input type="checkbox"/> ₀ No | _____ (1930) |
| 31. Heart and Blood Vessels | <input type="checkbox"/> ₁ Yes | <input type="checkbox"/> ₀ No | _____ (1940) |
| 32. Liver or Pancreas | <input type="checkbox"/> ₁ Yes | <input type="checkbox"/> ₀ No | _____ (1950) |
| 33. Kidneys or Urinary Tract System | <input type="checkbox"/> ₁ Yes | <input type="checkbox"/> ₀ No | _____ (1960) |
| 34. Reproductive System | <input type="checkbox"/> ₁ Yes | <input type="checkbox"/> ₀ No | _____ (1970) |
| 35. Stomach or Intestines | <input type="checkbox"/> ₁ Yes | <input type="checkbox"/> ₀ No | _____ (1980) |
| 36. Muscles or Bones | <input type="checkbox"/> ₁ Yes | <input type="checkbox"/> ₀ No | _____ (1990) |
| 37. Nervous System | <input type="checkbox"/> ₁ Yes | <input type="checkbox"/> ₀ No | _____ (2000) |
| 38. Psychiatric | <input type="checkbox"/> ₁ Yes | <input type="checkbox"/> ₀ No | _____ (2010) |
| 39. Other _____ | <input type="checkbox"/> ₁ Yes | <input type="checkbox"/> ₀ No | _____ (2020) |

SUBJECT'S WEIGHT

(Clinic Coordinator completed)

40. Weight (without shoes or heavy clothing) _____ kg (2030)

Subject Source Documentation

Subject's Initials: _____ (2040)

Date: ____ / ____ / _____ (2050)



**PULMONARY PROCEDURE
CHECKLIST**

Subject ID: 1 5 - _____ - _____

Visit Number: _____

11. Have you used any nasal steroids in the past **48** hours? ₁ Yes ₀ No (1100)
Examples: Flonase, Rhinocort, Nasonex

12. Have you used any cough medicines, anti-tussives, or expectorants in the past **24** hours? ₁ Yes ₀ No (1110)
Examples: guaifenesin, dextromethorphan, Duratuss, Benylin, Triaminic expectorant, Dayquil Anti-Cough

13. Have you used any other asthma controller medication in the past **6** weeks? ₁ Yes ₀ No (1120)
Examples: Singulair, Accolate

14. At this time, is your asthma worse because of recent exposure to triggers? ₁ Yes ₀ No (1130)
Examples: cold air, smoke, allergens, recent exercise, a recent respiratory tract infection, or other pulmonary infection

15. **(Complete at Visits 5-11 only)**
Since the last visit, have you experienced or been treated for a bacterial infection? ₁ Yes ₀ No (1140)

Examples: pneumonia, bronchitis, sinusitis, UTI, skin, ear

If **YES**, please indicate the type of infection(s):

16. Is there any other reason you should not proceed with spirometry testing? ₁ Yes ₀ No (1150)

If **YES**, explain _____

17. Is the subject eligible to proceed with the spirometry testing? ₁ Yes ₀ No (1160)

If any of the shaded boxes are completed, the subject is ineligible for spirometry and exhaled nitric oxide testing.

➔ ***If YES, proceed to Question #18 or the next form/procedure listed on the visit procedure checklist.***

➔ ***If NO, reschedule the visit. If the new visit falls outside the visit window, contact the MIA scientific coordinator.***

Complete for all subjects at Visit 1. If subject is less than 21 years old, complete Question #18 at each visit.

18. Height (without shoes) _____ cm (1170)



(Clinic Coordinator completed)

Complete at Visit 1 only

1. Record subject's a.m. cortisol value _____ . _____ mcg/dL (1000)
- 1a. Was the subject taking steroids at the time of Visit 1? ₁ Yes ₀ No (1010)
 → **If YES, STOP HERE.**
- 1b. Is Question #1 < 5 mcg/dL? ₁ Yes ₀ No (1020)
 → **If NO, STOP HERE.**
 → **If YES, bring the subject in, prior to the next shipment, and obtain blood for new a.m. cortisol analysis.**
- 1c. Record subject's new a.m. cortisol value _____ . _____ mcg/dL (1030)
- 1ci. Is Question #1c < 5 mcg/dL? ₁ Yes ₀ No (1040)
 → **If YES, bring the subject in and perform ACTH stimulation tests. Complete the MIA ACTH Stimulation tests (P15_ACTH) form.**

Complete at Visit 3 only

2. Record subject's a.m. cortisol value _____ . _____ mcg/dL (1050)
- 2a. Is Question #2 < 5 mcg/dL? ₁ Yes ₀ No (1060)
 → **If NO, STOP HERE.**
 → **If YES, bring the subject in, prior to the next shipment, and obtain blood for new a.m. cortisol analysis.**
- 2b. Record subject's new a.m. cortisol value _____ . _____ mcg/dL (1070)
- 2bi. Is Question #2b < 5 mcg/dL? ₁ Yes ₀ No (1080)
 → **If YES, bring the subject in and perform ACTH stimulation tests. Complete the MIA ACTH Stimulation tests (P15_ACTH) form.**



**MIA
SIGNIFICANT ASTHMA
EXACERBATION**

Subject ID: 1 5 - _____ - _____
 Subject Initials: _____
 Visit Number: _____
 Visit Date: ____/____/____
 Month Day Year
 Coordinator ID: _____

(Clinic Coordinator completed)

This form must be completed each time a subject experiences an asthma exacerbation according to the definition below.

1. Did the subject experience an increase in cough, phlegm/mucus, chest tightness, wheezing, or shortness of breath along with any of the following conditions?
 - 1a. An increase in rescue inhaler use of ≥ 8 puffs per 24 hours over baseline rescue inhaler use for a period of 48 hours? ₁ Yes ₀ No (1000)
 - 1b. Use of rescue inhaler ≥ 16 total puffs per 24 hours for a period of 48 hours? ₁ Yes ₀ No (1010)
 - 1c. A fall in prebronchodilator PEFR to $\leq 65\%$ of baseline on 2 of 3 consecutive scheduled morning or evening measurements? ₁ Yes ₀ No (1020)
 - 1d. A fall in prebronchodilator FEV₁ to $< 80\%$ of baseline? ₁ Yes ₀ No ₉ N/A (1030)
 - 1e. A fall in postbronchodilator FEV₁ to $< 60\%$ predicted? ₁ Yes ₀ No ₉ N/A (1040)
2. Were oral or parenteral corticosteroids given to the subject for his/her asthma exacerbation as a result of rescue intervention or by the opinion of the treating physician? ₁ Yes ₀ No (1050)

➔ ***If YES, please complete the CMED form.***

3. Did the subject experience a significant asthma exacerbation? ₁ Yes ₀ No (1060)
If any of the shaded boxes are completed, the subject experienced a significant asthma exacerbation.

➔ ***If NO, STOP HERE. DO NOT SUBMIT THIS FORM TO THE DCC.***
 ➔ ***If YES, but the subject did not undergo bronchoscopy, complete this form, then STOP. The subject is ineligible for the study. Please complete the MIA Termination of Study Participation (P15_TERM) form.***



**SIGNIFICANT ASTHMA
EXACERBATION**

4. Date significant asthma exacerbation occurred _____ / _____ / _____
month day year (1070)

5. Did the subject seek care for the asthma exacerbation? ₁ Yes ₀ No (1080)
→ **If NO, skip to Question #8.**

6. What type of care was sought?
6a. Study Investigator? ₁ Yes ₀ No (1090)

If **YES**, indicate type of contact.
₁ Scheduled clinic visit
₂ Unscheduled clinic visit
₃ Phone contact (1100)

6b. Primary Care or Other Physician? ₁ Yes ₀ No (1110)
Name of physician: _____

If **YES**, indicate type of contact.
₁ Scheduled clinic visit
₂ Unscheduled clinic visit
₃ Phone contact (1120)

6c. Emergency Room visit? ₁ Yes ₀ No (1130)
Name of hospital: _____

7. Was the subject hospitalized? ₁ Yes ₀ No (1140)
→ **If YES, please complete the Serious Adverse Event Reporting Form (SERIOUS).**

If **YES**,
7a. Name of hospital: _____

7b. Duration of hospital stay? _____ . _____ days (1150)

7c. Was intubation or ventilation assistance required? ₁ Yes ₀ No (1160)

8. Did the subject receive treatment with inhaled, oral, or intravenous corticosteroids? ₁ Yes ₀ No (1170)

→ **If YES, please complete the CMED form.**

9. Was the asthma exacerbation resolved solely by increasing PRN use of the rescue inhaler? ₁ Yes ₀ No (1180)



**SIGNIFICANT ASTHMA
EXACERBATION**

5 - ____ - ____

10. Was the asthma exacerbation treated as outlined in the protocol?

1 Yes

0 No (1190)

If **NO**, describe _____

11. Was the significant asthma exacerbation related to the routine pulmonary function testing, including the collection of exhaled nitric oxide? (*Check one box only*)

1 Definitely related

2 Probably related

3 Relationship undetermined

4 Probably not related

5 Definitely not related (1200)

12. Was the significant asthma exacerbation related to the methacholine challenge testing? (*Check one box only*)

1 Definitely related

2 Probably related

3 Relationship undetermined

4 Probably not related

5 Definitely not related (1210)

13. Was the significant asthma exacerbation related to the sputum induction procedure? (*Check one box only*)

1 Definitely related

2 Probably related

3 Relationship undetermined

4 Probably not related

5 Definitely not related (1220)

14. Was the significant asthma exacerbation related to the collection of exhaled breath condensate? (*Check one box only*)

1 Definitely related

2 Probably related

3 Relationship undetermined

4 Probably not related

5 Definitely not related (1230)



(Subject completed)

This questionnaire is to be completed by the MIA subject at the end of Visit 9. If a randomized subject terminates prior to Visit 9, please ask him or her to complete this form during the termination visit.

1. Scheduled Pills

As a MIA study participant you were randomized to receive either a real (i.e., active) clarithromycin pill or a look-alike placebo (i.e., inactive) pill. Please check the box that most closely represents your feelings about the **scheduled pills** you took **over the past 16 weeks**.

- ₁ I am certain the pills contained placebo. (1000)
- ₂ I think the pills probably contained placebo.
- ₃ I have no idea which type of pills I received, but my best guess would be:

- ₁ Placebo (1010)
- ₂ Active Drug

- ₄ I think the pills probably contained active drug.
- ₅ I am certain the pills contained active drug.

2. Please comment with respect to the **taste of the medication you received from your **scheduled pills over the past 16 weeks**.**

- ₁ Tasted good (1020)
(Describe) _____

₂ No noticeable taste

- ₃ Tasted bad
(Describe) _____

3. Please comment with respect to the **smell of the medication you received from your **scheduled pills over the past 16 weeks**.**

- ₁ Smelled good (1030)
(Describe) _____

₂ No noticeable smell

- ₃ Smelled bad
(Describe) _____



**SUBJECT
STUDY TREATMENT
QUESTIONNAIRE**

Subject ID: 1 5 - _____ - _____

Visit Number: _____

4. Please comment with respect to any **physical sensations** produced by the medication you received from your **scheduled pills** over the past 16 weeks.

₁ Pleasant sensations (1040)

(Describe) _____

₂ No noticeable sensations

₃ Unpleasant sensations

(Describe) _____

5. Please comment with respect to any other observations you may have made regarding your **scheduled pills**.

₁ I have no further comments (1050)

₂ I observed the following: (Describe below)

Subject Source Documentation

Subject's Initials: _____ (1060)

Date: ___ / ___ / _____ (1070)



**MIA
TERMINATION OF
STUDY PARTICIPATION**

Subject ID: 1 5 - ____ - ____
 Subject Initials: ____
 Visit Number: ____
 Visit Date: ____ / ____ / ____
 Month Day Year
 Coordinator ID: ____

(Clinic Coordinator completed)

Complete this form only for those subjects who have successfully completed Visit 1 and have been terminated or deemed ineligible.

1. Has the subject completed the study through Visit 11? ₁ Yes ₀ No (1000)
 → ***If YES, skip to the SIGNATURES section.***

2. Who initiated termination of the subject? ₁ Subject ₂ Clinical Staff (1010)
 → ***If subject withdrew due to impending clinical staff termination, please indicate termination by clinical staff.***
 → ***If Clinical Staff, skip to Question #4.***

3. Indicate the **primary** reason the subject has withdrawn from the study.

- ₁ no longer interested in participating *
- ₂ no longer willing to follow protocol *
- ₃ difficult access to clinic (location, transportation, parking)
- ₄ unable to make visits during clinic hours
- ₅ moving out of the area
- ₆ unable to continue due to personal constraints *
- ₇ unable to continue due to medical condition unrelated to asthma *
- ₈ side effects of study medications *
- ₉ dissatisfied with asthma control
- ₁₀ other * (1020)

*** Additional explanation required:**

→ ***Skip to the SIGNATURES section.***

(1030)



**TERMINATION OF
STUDY PARTICIPATION**

Subject ID: 1_5 - _____ - _____

Visit Number: _____

4. Did clinical staff terminate the subject due to ...
- 4a. pregnancy? ₁ Yes ₀ No ₉ N/A (1040)
(Check N/A if the subject is male.)
 - 4b. ineligibility during the run-in period (Visits 1-4) * ₁ Yes ₀ No (1050)
 - 4c. ineligibility during the stratification period (after bronchoscopy and prior to randomization) * ₁ Yes ₀ No (1060)
 - 4d. loss to follow-up? * ₁ Yes ₀ No (1070)
 - 4e. a respiratory tract infection ₁ Yes ₀ No (1080)
 - 4f. an asthma-related adverse event? * ₁ Yes ₀ No (1090)
 - 4g. a medication-related adverse event? * ₁ Yes ₀ No (1100)
 - 4h. an adverse event not related to asthma or medications? * ₁ Yes ₀ No (1110)
 - 4i. non-compliance with Flovent[®] dosing? * ₁ Yes ₀ No (1120)
 - 4j. non-compliance with taking scheduled pills? * ₁ Yes ₀ No (1130)
 - 4k. non-compliance with diary completion? * ₁ Yes ₀ No (1140)
 - 4l. non-compliance with visit attendance? * ₁ Yes ₀ No (1150)
 - 4m. non-compliance with peak flow monitoring? * ₁ Yes ₀ No (1160)
 - 4n. subject experienced > 2 asthma exacerbations during stratification phase (after bronchoscopy and prior to randomization) ₁ Yes ₀ No (1170)
 - 4o. subject experienced > 2 respiratory tract infections during stratification phase (after bronchoscopy and prior to randomization) ₁ Yes ₀ No (1180)
 - 4p. other reason? * ₁ Yes ₀ No (1190)

*** If Yes, additional explanation required:**

- 4q. Indicate the letter corresponding to the primary reason the subject was terminated. _____ (1210)

(1200)



**TERMINATION OF
STUDY PARTICIPATION**

Subject ID: 1 5 - ____ - ____

Visit Number: ____

SIGNATURES

Please complete the following section regardless of the reason for termination of study participation.

I verify that all information collected on the ACRN MIA data collection forms for this subject is correct to the best of my knowledge and was collected in accordance with the procedures outlined in the ACRN MIA Protocol.

Clinic Coordinator Signature (1220) ____ / ____ / ____ (1230)
month day year

Principal Investigator Signature (1240) ____ / ____ / ____ (1250)
month day year



**POST-ALBUTEROL
(2 puffs)
SPIROMETRY TESTING**

Supervisor ID: _____

Subject ID: _____ - _____ - _____

Subject Initials: _____

Visit Number: _____

Visit Date: _____ / _____ / _____
Month Day Year

Technician ID: _____

(Technician completed)

Complete this form only if the subject is eligible according to the appropriate Pulmonary Procedure Checklist form and successfully completed baseline spirometry session(s).

➔ **Administer 2 puffs of albuterol and wait 15 minutes, then perform spirometry.**

1. Time albuterol administered (*based on 24-hour clock*) _____ (1000)

2. Time post-albuterol spirometry started _____ (1010)
(*based on 24-hour clock*)

The best effort reflects the trial where the sum of FEV₁ and FVC is maximized.

3. Results of best effort post-albuterol:

3a. FVC _____ L (1020)

3b. FEV₁ _____ L (1030)

3c. FEV₁ (% predicted) _____ % predicted (1040)

3d. PEF_R _____ L/S (1050)

3e. FEF₂₅₋₇₅ _____ L/S (1060)

4. In your judgment, was the subject's spirometry technique acceptable? ₁ Yes ₀ No (1070)

4a. If **NO**, why was it unacceptable?

Inadequate inspiratory effort ₁ Yes ₀ No (1080)

Inadequate expiratory effort ₁ Yes ₀ No (1090)

Inadequate duration of expiration ₁ Yes ₀ No (1100)

Cough during procedures ₁ Yes ₀ No (1110)

Other (*specify*) _____ ₁ Yes ₀ No (1120)



**POST-ALBUTEROL
(4 puffs)
SPIROMETRY TESTING**

Supervisor ID: _____

Subject ID: _____ - _____ - _____

Subject Initials: _____

Visit Number: _____

Visit Date: _____ / _____ / _____
Month Day Year

Technician ID: _____

(Technician completed)

Complete this form only if the subject is eligible according to the appropriate Pulmonary Procedure Checklist form and successfully completed baseline spirometry session(s).

➔ **Administer 4 puffs of albuterol and wait 15 minutes, then perform spirometry.**

1. Time albuterol administered (*based on 24-hour clock*) _____ (1000)

2. Time post-albuterol spirometry started _____ (1010)
(*based on 24-hour clock*)

The best effort reflects the trial where the sum of FEV₁ and FVC is maximized.

3. Results of best effort post-albuterol:

3a. FVC _____ L (1020)

3b. FEV₁ _____ L (1030)

3c. FEV₁ (% predicted) _____ % predicted (1040)

3d. PEF_R _____ L/S (1050)

3e. FEF₂₅₋₇₅ _____ L/S (1060)

4. In your judgment, was the subject's spirometry technique acceptable? ₁ Yes ₀ No (1070)

4a. If **NO**, why was it unacceptable?

Inadequate inspiratory effort ₁ Yes ₀ No (1080)

Inadequate expiratory effort ₁ Yes ₀ No (1090)

Inadequate duration of expiration ₁ Yes ₀ No (1100)

Cough during procedures ₁ Yes ₀ No (1110)

Other (*specify*) _____ ₁ Yes ₀ No (1120)



"Attach Registry Form Label Here"

ACRN REGISTRY

Subject's Last Name: _____

Subject's First Name: _____

Subject's Initials: _____

Social Security Number: _____
(Last 4 digits)

Coordinator ID: _____

(Clinic Coordinator/Subject Interview Completed)

Search the ACRN Registry. If the subject is either incomplete or not found in the Registry, complete the Registry form and enter/update the subject's information appropriately.

ADMINISTRATIVE

- 1. Did the subject sign an ACRN Protocol Informed Consent and HIPAA Authorization form?

₁ Yes ₀ No (1000)

If **NO**, stop here. Data cannot be entered into the ACRN Registry.

If **YES**, record the signature date.

____ / ____ / _____ (1010)
Month Day Year

DEMOGRAPHICS

- 2. Subject's date of birth
(Ask the subject his/her date of birth.)

____ / ____ / _____ (1020)
Month Day Year

- 3. Subject's gender

₁ Male
₂ Female (1030)

- 4. Subject's Race and Ethnicity

- 4a. Subject's ethnic background
(Ask the subject to identify his/her ethnic background.)

₁ Hispanic or Latino
₂ Not Hispanic or Latino (1040)

- 4b. Subject's racial background
(Ask the subject to identify all that apply.)

American Indian or Alaskan Native

₁ Yes ₀ No (1050)

Asian

₁ Yes ₀ No (1060)

Black or African American

₁ Yes ₀ No (1070)

White

₁ Yes ₀ No (1080)

Native Hawaiian or Other Pacific Islander

₁ Yes ₀ No (1090)

Other *(specify)* _____

₁ Yes ₀ No (1100)



REGISTRY

Subject's Initials: _____

5. Subject's primary racial identification
(This identification will be used for spirometry testing. Ask the subject which category best describes him or her and check only one box.)

- ₁ American Indian or Alaskan Native
- ₂ Asian or Pacific Islander
- ₃ Black, not of Hispanic Origin
- ₄ White, not of Hispanic Origin
- ₅ Hispanic
- ₆ Other _____ (1110)

Subject Source Documentation

Subject's Initials: _____

Date: ____ / ____ / _____

Administrative Use Only

Does the subject recall participating in any of the ACRN I protocols? *(Circle all that apply)*

- | | | | | |
|-----------|------------|---------------|--------------|------------|
| BAGS (1) | CIMA (2) | SOCS/SLIC (3) | DICE (6) | MICE (7) |
| BARGE (8) | IMPACT (9) | SMOG (10) | SLiMSIT (11) | PRICE (12) |

Registry Form Storage Instructions:

Upon printing the subject's label sheet, print the subject's name on the upper right hand label. Attach the Registry form label to the upper left hand corner of the form. Lastly, attach the Registry Log label to the next available row on the Registry Log and complete the required fields. The Registry form should be stored alphabetically by subject's last name in the ACRN Registry Binder. The label sheet should then be filed directly behind the Registry form.

REGISTRY FORMS SHOULD NOT BE SENT TO THE DCC.



SERIOUS ADVERSE EVENT

Subject ID: _____ - _____ - _____

Visit Number: _____

6. What, in your opinion, caused the event?

6a. Toxicity of study drug(s)

₁ Yes

₀ No (1160)

6b. Withdrawal of study drug(s)

₁ Yes

₀ No (1170)

6c. Concurrent medication

₁ Yes

₀ No (1180)

If **YES**, describe _____

6d. Concurrent disorder

₁ Yes

₀ No (1190)

If **YES**, describe _____

6e. Other event

₁ Yes

₀ No (1200)

If **YES**, describe _____

DO NOT ENTER QUESTIONS #7 - 8: FOR REPORTING PURPOSES ONLY.

7. If subject died, cause of death: _____

8. Was an autopsy performed?

₁ Yes

₀ No

If YES, attach report or send as soon as possible.

REPORTING INVESTIGATOR:

Comments (discuss any relevant laboratory data or other assessments which help explain the event):

Name: _____

Signature: _____

Date: ___ / ___ / _____



**ALLERGY SKIN
TEST RESULTS**

Subject ID: _____ - _____ - _____
 Subject Initials: _____
 Visit Number: _____
 Visit Date: ____ / ____ / ____
Month Day Year
 Coordinator ID: _____

(Clinic Coordinator completed)

1. Since August 2004, has the subject had an acceptable skin test for an ACRN protocol within three years of the visit date?

₁ Yes ₀ No (1000)

→ If **NO**, proceed to Question #2.

1a. Date of previous skin test

____ / ____ / ____ (1010)
month day year

1b. Coordinator ID who performed the skin test

____ (1020)

1c. Time test sites pricked/punctured *(based on 24-hour clock)*

____ (1030)

1d. Time test sites evaluated *(based on 24-hour clock)*

____ (1040)

→ **STOP HERE** and attach a photocopy of pages 3 and 4 from the previous Allergy Skin Test Results (SKIN) form to this page for data entry purposes.

2. Has the subject had dermatographia **or** a significant adverse reaction to skin testing previously (e.g., anaphylaxis, angioedema, asthma, hypotension, etc.)?

₁ Yes ₀ No (1050)

→ If **YES**, do not proceed with allergy skin testing.

→ If **YES**, and the subject has acceptable ACRN skin testing results from a prior ACRN protocol (ACRN I or II), record Subject ID associated with the most recent acceptable test.

____ - ____ - ____
 (1052) (1054) (1060)

3. Has the subject taken any of the medications listed in the ACRN Skin Testing MOP within the exclusionary periods?

₁ Yes ₀ No (1070)

→ If **YES**, the allergy skin testing procedure should be rescheduled.



**ALLERGY SKIN
TEST RESULTS**

Subject ID: _____ - _____ - _____

Visit Number: _____

4. Was the subject's most recent FEV1 below 60% predicted? ₁ Yes ₀ No (1072)

→ If **NO**, proceed to Question #5.

4a. Has the subject received permission from the supervising physician to proceed with the skin testing? ₁ Yes ₀ No (1074)

→ If **YES**, obtain physician's signature:

_____ (1076)

→ If **NO**, allergy skin testing procedure should be rescheduled.

5. Is the subject eligible for allergy skin testing? ₁ Yes ₀ No (1080)

If any of the shaded boxes are completed, the subject is ineligible for allergy skin testing. STOP HERE.

→ Allergy Skin testing may be rescheduled for the next visit if the subject is ineligible due to Question #3 or Question #4a.

6. Time test sites pricked/punctured (based on 24-hour clock) _____ (1090)

7. Time test sites evaluated (based on 24-hour clock) _____ (1100)



ALLERGY SKIN TEST RESULTS

Subject ID: _____ - _____ - _____

Visit Number: _____

Transfer the tracing of each measurable wheal and record the longest diameter and the diameter at the perpendicular midpoint in mm. If the wheal is not measurable, record '0' for both diameters.

1. Positive Control	Largest Wheal Diameter: _____ mm (1110) Perpendicular Wheal Diameter: _____ mm (1120)	2. Negative Control	Largest Wheal Diameter: _____ mm (1130) Perpendicular Wheal Diameter: _____ mm (1140)
3. Mite Mix	Largest Wheal Diameter: _____ mm (1150) Perpendicular Wheal Diameter: _____ mm (1160)	4. Cockroach Mix	Largest Wheal Diameter: _____ mm (1170) Perpendicular Wheal Diameter: _____ mm (1180)
5. Mouse	Largest Wheal Diameter: _____ mm (1190) Perpendicular Wheal Diameter: _____ mm (1200)	6. Rat	Largest Wheal Diameter: _____ mm (1210) Perpendicular Wheal Diameter: _____ mm (1220)
7. Penicillium	Largest Wheal Diameter: _____ mm (1230) Perpendicular Wheal Diameter: _____ mm (1240)	8. Alternaria	Largest Wheal Diameter: _____ mm (1250) Perpendicular Wheal Diameter: _____ mm (1260)



ALLERGY SKIN TEST RESULTS

Subject ID: _____ - _____ - _____

Visit Number: _____

9. Aspergillus	Largest Wheal Diameter: _____ mm (1270) Perpendicular Wheal Diameter: _____ mm (1280)	10. Cladosporium	Largest Wheal Diameter: _____ mm (1290) Perpendicular Wheal Diameter: _____ mm (1300)
11. Cat	Largest Wheal Diameter: _____ mm (1310) Perpendicular Wheal Diameter: _____ mm (1320)	12. Dog	Largest Wheal Diameter: _____ mm (1330) Perpendicular Wheal Diameter: _____ mm (1340)

13. Is the mean diameter for the 'Negative Control' < 3 mm? ₁ Yes ₀ No (1350)

➔ If **YES**, go to Question #14.
 ➔ If **NO**, administer the negative control on the opposite hand and complete Question #13a and #13b.

13a. Record the measurements for the 'Negative Control' administered on the opposite hand:

Largest Wheal Diameter: _____ mm (1352)
 Perpendicular Wheal Diameter: _____ mm (1354)

13b. Is the mean diameter calculated from the measurements in Question #13a < 3 mm? ₁ Yes ₀ No (1360)

➔ If **NO**, go to Question #15. The subject has dermatographia and therefore, do not repeat skin testing on this subject.

14. Is the mean diameter for 'Positive Control' ≥ 3 mm more than the mean diameter from the 'Negative Control'? ₁ Yes ₀ No (1370)

15. Was this test acceptable? ₁ Yes ₀ No (1380)

If any of the gray shaded boxes are checked, this test was not acceptable.

➔ ***Allergy Skin testing may be rescheduled for the next visit if the subject's test was unacceptable due to the use of exclusionary medications.***



SPIROMETRY TESTING

Subject ID: _____ - _____ - _____
 Subject Initials: _____
 Visit Number: _____
 Visit Date: ____ / ____ / ____
Month Day Year
 Technician ID: _____

Supervisor ID: _____

(Technician completed)

Complete this form only if the subject is eligible according to the appropriate Pulmonary Procedure Checklist form.

1. Time spirometry started *(based on 24-hour clock)* _____ (1000)

The best effort reflects the trial where the sum of FEV₁ and FVC is maximized.

2. Results of best effort:

2a. FVC _____ L (1010)

2b. FEV₁ _____ L (1020)

2c. FEV₁ (% predicted) _____ % predicted (1030)

2d. PEFr _____ L/S (1040)

2e. FEF₂₅₋₇₅ _____ L/S (1050)

3. In your judgment, was the subject's spirometry technique acceptable? ₁ Yes ₀ No (1060)

3a. If **NO**, why was it unacceptable?

Inadequate inspiratory effort ₁ Yes ₀ No (1070)

Inadequate expiratory effort ₁ Yes ₀ No (1080)

Inadequate duration of expiration ₁ Yes ₀ No (1090)

Cough during procedures ₁ Yes ₀ No (1100)

Other *(specify)* _____ ₁ Yes ₀ No (1110)



**SPUTUM INDUCTION
LAB VALUES**

Subject ID: _____
 Subject Initials: _____
 Visit Number: _____
 Current Date: ____/____/____
Month Day Year
 Slide #: ____

(Technician completed)

Processing Sample

- 1. Technician ID _____ (1000)
- 2. Processing Date ____/____/____ (1010)
month day year
- 3. Time processing started *(based on 24-hour clock)* _____ (1020)
- 4. Total Cell Count _____ x 10⁴ cells/ml (1030)

Differential Cell Counts

- 5. Technician ID _____ (1040)
- 6. Read Date ____/____/____ (1050)
month day year
- 7. Squamous Cells _____ % (1060)

8. Did the subject's sputum sample reveal $\geq 80\%$ squamous cells? ₁ Yes ₀ No (1070)

➔ ***If NO, please complete Question #9 through Question #14 and send the sputum sample for overreading.***

➔ ***If YES, STOP HERE and mark the samples as excluded from shipment to San Francisco in the Sample Tracking Module.***

The parameters below are calculated following exclusion of squamous cells.

- 9. Total Cell Count _____ x 10⁴ cells/ml (1080)
- 10. Epithelial Cells _____ % (1090)
- 11. Macrophages _____ % (1100)
- 12. Neutrophils _____ % (1110)
- 13. Eosinophils _____ % (1120)
- 14. Lymphocytes _____ % (1130)



**SPUTUM INDUCTION
UCSF OVER-READ**

Subject ID: _____ - _____ - _____
 Subject Initials: _____
 Visit Number: _____
 Current Date: _____ / _____ / _____
Month Day Year
 Slide #: _____
 Technician ID: _____

(Technician completed)

1. Date of Over-Read _____ / _____ / _____ (1000)
month day year

2. Is the slide quality acceptable? ₁ Yes ₀ No (1010)
 → If **NO**, please comment below. If a back-up slide is required, update the Sample Tracking Module.

Differential Cell Counts

3. Squamous Cells _____ . _____ % (1020)

The parameters below are calculated following exclusion of squamous cells.

4. Epithelial Cells _____ . _____ % (1030)

5. Macrophages _____ . _____ % (1040)

6. Neutrophils _____ . _____ % (1050)

7. Eosinophils _____ . _____ % (1060)

8. Lymphocytes _____ . _____ % (1070)



SPUTUM INDUCTION

Supervisor ID: _____

Subject ID: _____

Subject Initials: _____

Visit Number: _____

Visit Date: ____ / ____ / ____
Month Day Year

Technician ID: _____

(Technician completed)

Complete this form only if the subject is eligible according to the Sputum Induction Checklist (SPUTUMCHK) form.

1. *(If attempting sputum induction for the first time in this protocol or subject has not had an adequate sample at prior attempts, do not complete Question #1.)*

What was the duration of sputum induction the first time the subject's sample was processed and had < 80% squamous cells for this protocol?

_____ . _____ minutes (1000)

Duration of sputum induction at current visit should not exceed this.

2. Sputum induction start time (based on 24-hour clock)

_____ (1010)

3. Sputum induction stop time (based on 24-hour clock)

_____ (1020)

4. Duration of sputum induction collection phase at this visit

_____ . _____ minutes (1030)

- 4a. Was the duration \geq 4 minutes?

₁ Yes ₀ No (1040)

5. Volume of sputum sample at this visit

_____ . _____ ml (1050)

- 5a. Is the volume of the sample \geq 1 ml?

₁ Yes ₀ No (1060)

6. Is the sample adequate for laboratory analysis?

₁ Yes ₀ No (1070)

If either shaded box in Question #4a or #5a are completed, the sputum sample is not adequate and should not be sent for analysis of squamous cell counts.

→ If YES, the technician reading the slide should complete the Sputum Induction Lab Values (SPUTLAB) form.



SPUTUM INDUCTION

Subject ID: _____

Visit Number: _____

7. Subject's FEV₁ immediately after completion of sputum induction

7a. FEV₁ _____ . _____ L (1080)

7b. FEV₁ (% predicted) _____ % predicted (1090)

7c. Time of FEV₁ in Question #7a (*based on 24-hour clock*) _____ (1100)

7d. Percent difference in FEV₁ $\frac{(\text{Reference} - \text{Question \#7a})}{\text{Reference}} \times 100$ _____ . _____ % (1110)

Reference = FEV₁ used for assessment of eligibility for SI.

7e. Did the subject's FEV₁ drop > 10% (from post-albuterol baseline) as indicated in Question #7d? ₁ Yes ₀ No (1120)

→ **If NO, STOP HERE and continue with remaining visit procedures.**

→ **If YES, proceed to the Additional Treatment for Sputum Induction (SPUTUM_ADD_TRT) form.**



**SPUTUM INDUCTION
CHECKLIST**

Supervisor ID: _____

Subject ID: _____

Subject Initials: _____

Visit Number: _____

Visit Date: ____ / ____ / ____
Month Day Year

Technician ID: _____

(Technician completed)

Complete this form only if the subject is eligible according to the appropriate Pulmonary Procedure Checklist form and successfully completed baseline spirometry session(s).

1. ***(If attempting Sputum Induction for the first time in this protocol, do not complete Question #1)***

Was the subject's sputum sample processed and had < 80% squamous cells the first time a sputum induction was attempted for this protocol?

₁ Yes ₀ No (1000)

2. ***(Only for subjects who completed a methacholine challenge at this visit.)***

Was the subject's FEV₁ after reversal from the methacholine challenge ≥ the methacholine reversal reference value (B) in the gray box on the Methacholine Challenge Testing (METHA) form?

₁ Yes ₀ No (1010)

2a. If **NO**, has the subject received permission from the supervising physician to proceed with sputum induction testing?

₁ Yes ₀ No (1020)

Physician's Signature: _____ (1030)

3. Subject's FEV₁ used for assessment of eligibility for sputum induction

____ . ____ ____ L (1040)

4. Subject's FEV₁ (% predicted) used for assessment of eligibility for sputum induction

____ ____ ____ % predicted (1050)

5. Was the subject's FEV₁ (% predicted) from Question #4 ≥ 60% predicted?

₁ Yes ₀ No (1060)

6. Is there any other reason the subject should not proceed with sputum induction?

₁ Yes ₀ No (1070)

If **YES**, explain _____

7. Is the subject eligible for sputum induction?

₁ Yes ₀ No (1080)

If any of the shaded boxes are completed, the subject is NOT eligible for sputum induction.

→ If YES, proceed to the Sputum Induction (SPUTUM) form.

