Asthma Clinical Research Network
NIH/NHLBI

CLINICAL AND LABORATORY ADVERSE EVENTS

(Clinic Coordinator completed)

Subject ID: ___ ___ - ___ ___ - ___ ___ ___
Subject Initials: ___ ___ ___
Visit Number: ___ ___ ___

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.

☐$_0$ None

Subject 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)** 3. DATE STOPPED (Bottom Line) **(1030)** MONTH / DAY / YEAR	4. ONGOING at current visit **(1040)**	5. TYPE **(1050)** 1 - INTERMITTENT 2 - CONTINUOUS	6. SEVERITY **(1060)** 1 - MILD 2 - MODERATE 3 - SEVERE	7. SERIOUS **(1070)** 1- YES * 0 - NO	8. LIKELIHOOD OF RELATIONSHIP TO STUDY DRUG(S) **(1080)** 1 - NONE 2- UNLIKELY (REMOTE) 3 - POSSIBLE 4 - PROBABLE	9. CHANGE IN STUDY DRUG(S) **(1090)** 1 - UNCHANGED 2 - ALTERED**	10. OUTCOME *(Skip if #3 is missing.)* **(1100)** 1 - COMPLETELY RECOVERED 2 - RECOVERED, BUT WITH LASTING EFFECTS 3 - DEATH *	11. TREATMENT REQUIRED **(1110)** 1 - NONE 2 - MEDICATION *** 3 - HOSPITALIZATION * 4 - OTHER	12. ONGOING at final visit **(1120)**
___ ___	_ _ _ . _ _	_ _ / _ _ / _ _ _ _ _ _ / _ _ / _ _ _ _	☐$_1$								☐$_1$
___ ___	_ _ _ . _ _	_ _ / _ _ / _ _ _ _ _ _ / _ _ / _ _ _ _	☐$_1$								☐$_1$
___ ___	_ _ _ . _ _	_ _ / _ _ / _ _ _ _ _ _ / _ _ / _ _ _ _	☐$_1$								☐$_1$
___ ___	_ _ _ . _ _	_ _ / _ _ / _ _ _ _ _ _ / _ _ / _ _ _ _	☐$_1$								☐$_1$
___ ___	_ _ _ . _ _	_ _ / _ _ / _ _ _ _ _ _ / _ _ / _ _ _ _	☐$_1$								☐$_1$

Asthma Clinical Research Network
NIH/NHLBI

AM1® QUALITY CONTROL

Subject ID: __ __ - __ __ - __ __ __
Subject Initials: __ __ __
Visit Number: __ __ __
Visit Date: __ __ / __ __ / __ __ (Month / Day / Year)
Technician ID: __ __ __ __ __ __

(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
   - ❑2 "Old" device failed QC testing
   - ❑3 "Old" device had display problems
   - ❑4 "Old" device experienced battery failure
   - ❑5 "Old" device was recalled
   - ❑6 "Old" device was lost
   - ❑7 Other **(1050)**

		AM1® (L/Min)	Jones FVC (L/Min)	Clinic Use Only: Relative Bias (AM1 − Jones FVC) / Jones FVC * 100 %	Clinic Use Only: Rank (smallest to largest)
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

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 Clinical Research Network
NIH/NHLBI

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? *(Enter '00' if subject was under 1 year.)* ____ ____ years **(1000)**

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)**

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 **(1140)**	
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 **(1160)**

Subject Source Documentation

Subject's Initials: __ __ __ **(1180)**

Date: __ __ / __ __ / __ __ __ __ **(1190)**

Asthma Clinical Research Network
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ASTHMA SEVERITY QUESTIONNAIRE

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

(Subject Interview completed)

The subject should be asked to review their last month of asthma control in answering these questions. Please check the box next to the response that best describes the subject's symptoms.

1. In the past month, how often have you experienced asthma symptoms?

- ❑0 less than or equal to 2 days a week
- ❑1 greater than 2 days a week but not daily
- ❑2 daily but not continual
- ❑3 continual **(1000)**

2. In the past month, how often have you used your rescue beta-agonist medicine (e.g., albuterol (Proventil, Ventolin)) other than to pretreat prior to exercise?

- ❑0 less than or equal to 2 times a week
- ❑1 greater than 2 times a week but not daily
- ❑2 daily but less than 4 times a day
- ❑3 greater than or equal to 4 times a day **(1010)**

3. In the past month, how often have you woken up at night due to asthma symptoms?

- ❑0 less than or equal to 2 nights a month
- ❑1 greater than 2 nights a month but less than or equal to 1 night a week
- ❑2 greater than 1 night a week but not most nights
- ❑3 most nights **(1020)**

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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.

❑0 None

NAME OF MEDICATION **(1000)**	CODE **(1010)**	RELATED EVENT **(1020)**	DOSE **(1030)**	UNITS **(1040)**	FREQ UENCY **(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 ___ ___ ❑0 NA					___ / ___ / _____	___ / ___ / _____	❑1	❑1
___ ___		Event ___ ___ ❑0 NA					___ / ___ / _____	___ / ___ / _____	❑1	❑1
___ ___		Event ___ ___ ❑0 NA					___ / ___ / _____	___ / ___ / _____	❑1	❑1
___ ___		Event ___ ___ ❑0 NA					___ / ___ / _____	___ / ___ / _____	❑1	❑1
___ ___		Event ___ ___ ❑0 NA					___ / ___ / _____	___ / ___ / _____	❑1	❑1
___ ___		Event ___ ___ ❑0 NA					___ / ___ / _____	___ / ___ / _____	❑1	❑1

UNITS and FREQUENCY CODES FOR CONCOMITANT MEDICATIONS

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Codes for Units	
Code	Units
1	mg
2	mcg (μg)
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	

Asthma Clinical Research Network
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EXHALED BREATH CONDENSATE COLLECTION

Supervisor ID: ___ ___ ___ ___ ___ ___

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

(Technician Completed)

1. Has the subject had anything other than water to drink or eat in the past hour? ❑1 Yes ❑0 No **(1000)**

   ➔ ***If YES, STOP HERE. Subject is ineligible to continue with ebc collection. If possible, wait until the full hour has passed, then proceed with collection.***

2. Was ebc collection attempted at this visit? ❑1 Yes ❑0 No **(1010)**

   ➔ ***If NO, complete Question #2a and STOP.***
   ➔ ***If YES, proceed to Question #3***

   2a. Check the primary reason ebc collection was not attempted.
   ❑1 Subject Refusal
   ❑2 Equipment Unavailable
   ❑3 Clinic Oversight
   ❑4 Other_____ **(1020)**

3. Time ebc collection started (based on 24-hour clock). ___ ___ ___ ___ **(1030)**

4. Time ebc collection stopped (based on 24-hour clock). ___ ___ ___ ___ **(1040)**

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

_____
_____
_____
_____
_____

5. Did the subject experience any of the following during the collection process...
   5a. Sneezing? ❑1 Yes ❑0 No **(1050)**
   5b. Coughing? ❑1 Yes ❑0 No **(1060)**
   5c. Burping? ❑1 Yes ❑0 No **(1070)**

6. Were six eppendorf tubes aliquoted at this visit? ☐ 1 Yes ☐ 0 No **(1080)**

If YES, proceed to Question #7.

6a. Which of the following explain why six tubes were not collected?

Equipment Malfunction ☐ 1 Yes ☐ 0 No **(1090)**
If YES, explain _____

Low Yield ☐ 1 Yes ☐ 0 No **(1100)**

Subject could not tolerate procedure ☐ 1 Yes ☐ 0 No **(1110)**

Other ☐ 1 Yes ☐ 0 No **(1120)**
If YES, explain _____

6b. Record the number of tubes aliquoted. ___ tubes **(1130)**

➔ ***If '0', STOP HERE.***

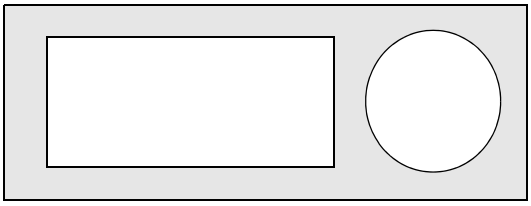
7. Was nitrogen gas layered on the tubes before closing them? ☐ 1 Yes ☐ 0 No **(1150)**

8. Were the tubes stored immediately at -70° Celsius or colder? ☐ 1 Yes ☐ 0 No **(1160)**

➔ ***If YES, STOP HERE.***

8a. At what temperature were the tubes stored? ___ ___ ___ ° C **(1170)**

9. Attach one barcode label/dot pair from the subject's visit-specific strip here. Write the barcode number from the label in the spaces provided.



___ ___ ___ ___ ___ ___ ___ ___ **(1180)**

Comments:_____

_____

_____

_____

Asthma Clinical Research Network
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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)**	☐ 1 **(1050)**	☐
3.	Maneuver #2	___ ___ ___ ___ **(1060)**	___ ___ ___ . ___ ppb **(1070)**	☐ 1 **(1090)**	☐
4.	Maneuver #3	___ ___ ___ ___ **(1100)**	___ ___ ___ . ___ ppb **(1110)**	☐ 1 **(1130)**	☐
5.	Maneuver #4	___ ___ ___ ___ **(1140)**	___ ___ ___ . ___ ppb **(1150)**	☐ 1 **(1170)**	☐
6.	Maneuver #5	___ ___ ___ ___ **(1180)**	___ ___ ___ . ___ ppb **(1190)**	☐ 1 **(1210)**	☐
7.	Maneuver #6	___ ___ ___ ___ **(1220)**	___ ___ ___ . ___ ppb **(1230)**	☐ 1 **(1250)**	☐
8.	Maneuver #7	___ ___ ___ ___ **(1260)**	___ ___ ___ . ___ ppb **(1270)**	☐ 1 **(1290)**	☐
9.	Maneuver #8	___ ___ ___ ___ **(1300)**	___ ___ ___ . ___ ppb **(1310)**	☐ 1 **(1330)**	☐
10.	Maneuver #9	___ ___ ___ ___ **(1340)**	___ ___ ___ . ___ ppb **(1350)**	☐ 1 **(1370)**	☐

11. Did the subject achieve two reproducible outcomes? ☐ 1 Yes ☐ 0 No **(1380)**

If ***NO***, explain _____

_____

_____

_____

Asthma Clinical Research Network
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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 FEV_1 value from the appropriate spirometry testing form as the baseline reference.

A. Baseline FEV_1 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 FEV_1 ___ . ___ ___ L **(1000)**

2. Did the subject drop ≥ 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. FEV_1 after last concentration of methacholine administered ___ . ___ ___ L **(1030)**

5. Did the subject achieve a PC_{20}? ❑ 1 Yes ❑ 0 No **(1040)**
   If ***NO***, proceed to Question #6.

   5a. PC_{20} ___ ___ ___ . ___ ___ ___ ___ mg/ml **(1050)**

6. Time methacholine challenge ended *(based on 24-hour clock)* ___ ___ ___ ___ **(1060)**

7. Subject's FEV_1 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. FEV_1 ___ . ___ ___ L **(1070)**

   7b. Time of FEV_1 in Question #7a (*based on 24-hour clock*) ___ ___ ___ ___ **(1090)**

   7c. Was the FEV_1 from Question #7a ≥ 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.***

Asthma Clinical Research Network
NIH/NHLBI

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 FEV_1 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 FEV_1 after additional treatment within first hour.

   2a. FEV_1 ___ . ___ ___ L **(1070)**

   2b. FEV_1 (% predicted) ___ ___ ___ % predicted **(1080)**

   2c. Time of FEV_1 in Question #2a (*based on 24-hour clock*) ___ ___ ___ ___ **(1090)**

   2d. Was the FEV_1 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.***

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 FEV_1 after methacholine challenge.

4a. FEV_1 ___ . ___ ___ L **(1200)**

4b. FEV_1 (% predicted) ___ ___ ___ % predicted **(1210)**

4c. Time of FEV_1 from Question #4a (*based on 24-hour clock*) ___ ___ ___ ___ **(1220)**

4d. Was the FEV_1 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)**

Asthma Clinical Research Network
NIH/NHLBI

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? ☐ 1 Yes ☐ 0 No **(1010)**
   Physician's Signature: _____ **(1015)**

2. Does the subject have a baseline (pre-diluent) FEV_1 less than 55% of predicted? ☐ 1 Yes ☐ 0 No **(1020)**
   Use the FEV_1 value from the appropriate spirometry testing form as the baseline reference.

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.***

Asthma Clinical Research Network
NIH/NHLBI

LARGE CLINIC COORDINATOR STUDY TREATMENT QUESTIONNAIRE (Visits 4-9 and 12-17)

Subject ID: 1 4 - __ __ - __ __ __
Subject Initials: __ __ __
Visit Number: __ __
Visit Date: __ __ / __ __ / __ __ (Month / Day / Year)
Coordinator ID: __ __ __ __ __ __

(Clinic Coordinator completed)

This questionnaire is to be completed at visits 9 and 17 by the ACRN study coordinator who was primarily responsible for the subject's LARGE visits during the preceding 18 weeks. If a randomized subject terminates prior to Visit 17, this form should be completed at the time of the termination visit. Do not complete this form for subjects terminating between Visits 9 and 12.

1. **Blinded Scheduled Diskus**

Subjects in the LARGE study were randomized to receive either an active salmeterol Diskus or a placebo Diskus. You were blinded to the actual treatment assignment. Please check the box that most closely represents your feelings about the treatment the subject received **over the past 18 weeks.**

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

Asthma Clinical Research Network
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LARGE CHANGE IN MEDICATIONS

(Visits 1 - 20 and 11A-11H)

Subject ID: 1 4 - ___ ___ - ___ ___ ___
Subject Initials: ___ ___ ___
Visit Number: ___ ___ ___
Visit Date: ___ ___ / ___ ___ / ___ ___ (Month / Day / Year)
Coordinator ID: ___ ___ ___ ___ ___ ___

(Clinic Coordinator completed)

Complete this form if the subject has experienced an adverse event that resulted in altering the dose of any of the subject's study medications.

1. Related Adverse Event Number ___ . ___ **(1000)**

2. QVAR MDI
   - ☐ 1 Discontinued
   - ☐ 2 Reduced
   - ☐ 3 Increased
   - ☐ 4 Unchanged **(1010)**

➔ If ***Unchanged***, proceed to Question # 3.

2a. Date change began ___ ___ / ___ ___ / ___ ___ ___ ___ (Month / Day / Year) **(1020)**

2b. Date change ended ___ ___ / ___ ___ / ___ ___ ___ ___ (Month / Day / Year) **(1030)**

2c. Ongoing at current visit ☐ 1 **(1035)**

3. Scheduled Diskus®
   - ☐ 1 Discontinued
   - ☐ 2 Reduced
   - ☐ 3 Increased
   - ☐ 4 Unchanged
   - ☐ 5 Not Applicable **(1040)**

➔ If ***Unchanged or Not Applicable***, stop here.

3a. Date change began ___ ___ / ___ ___ / ___ ___ ___ ___ (Month / Day / Year) **(1050)**

3b. Date change ended ___ ___ / ___ ___ / ___ ___ ___ ___ (Month / Day / Year) **(1060)**

3c. Ongoing at current visit ☐ 1 **(1065)**

Asthma Clinical Research Network
NIH/NHLBI

LARGE COMPLIANCE CHECKLIST

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

(Clinic Coordinator completed)

Check the following compliance criteria at all scheduled Visits 2 - 21 and 11A - 11H.

1. **Doser™ Compliance for QVAR MDI**

If the interval between visits exceeds 30 days, complete Questions #1a - #1f using data for the 30 days prior to the visit.

1a. Total number of scheduled puffs since the last visit ___ ___ ___ puffs **(1000)**

➔ Value obtained from Question #1 on P14_COMPLY_WKS

1b. Total number of puffs in Doser™ history ___ ___ ___ puffs **(1010)**

➔ Value obtained from Question #2 on P14_COMPLY_WKS

1c. Percent compliance = $\frac{\textit{Question \#1b}}{\textit{Question \#1a}}$ *x 100* ___ ___ ___ . ___ % **(1020)**

➔ ***If the subject took less than 80% of the scheduled QVAR puffs, re-emphasize the importance of maintaining the daily dosing schedule.***

1d. Total number of full days since the last visit ___ ___ **(1030)**

➔ Value obtained from Question #4 on P14_COMPLY_WKS

1e. Total number of compliant days ___ ___ **(1040)**

➔ Value obtained from Question #5 on P14_COMPLY_WKS

1f. Percent compliance = $\frac{\textit{Question \#1e}}{\textit{Question \#1d}}$ *x 100* ___ ___ ___ . ___ % **(1050)**

➔ ***If the subject took the correct daily dose less than 70% of the days, re-emphasize the importance of maintaining the daily dosing schedule.***

2. **Scheduled Diskus® Compliance (Visits 5 - 9 and 13 - 17 ONLY*)***

2a. Number of scheduled puffs since the last visit ___ ___ ___ puffs **(1060)**

➔ ***To calculate the number of scheduled puffs, do not count puffs during the 24 hour withhold period prior to the visit.***

2b. Number of remaining puffs reflected on scheduled Diskus® counter ___ ___ ___ puffs **(1070)**

➔ At Visits 6 - 9 and 14 - 17: Total the values reflected on two returned scheduled Diskuses®

2c. Number of puffs taken ___ ___ ___ puffs **(1080)**

➔ At Visits 5, 13: 60 - Question #2b

➔ At Visits 6 - 9 and 14 - 17: 120 - Question #2b

2d. Percent compliance = $\frac{\textit{Question \#2c}}{\textit{Question \#2a}}$ *x 100* ___ ___ ___ . ___ % **(1090)**

➔ ***If the subject took less than 80% of the scheduled Diskus puffs, re-emphasize the importance of maintaining daily dosing schedule.***

Asthma Clinical Research Network
NIH/NHLBI

LARGE DIARY CARD

Subject's Initials: _ _ _
Date: _ _ / _ _ / _ _ _ _

Subject ID: 1 4 - _ _ - _ _ _
Subject Initials: _ _ _
Return Visit Number: _ _ _
Return Visit Date: _ _ / _ _ / _ _
Month Day Year

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 QVAR Inhaler **(AM)** (1040)		___	___	___	___	___	___	___
Symptoms++ during the night	5. Shortness of Breath (1050)							
	6. Chest Tightness (1060)							
	7. Wheezing (1070)							
	8. Cough (1080)							
	9. Phlegm/Mucus (1090)							
NIGHT-TIME EVALUATION (Between 8 PM and 1 AM)								
10. Time of PM Peak Flow (between 8 PM and 1 AM) (1100)		__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __	__ __ : __ __
11. PM Peak Flow (liters/min)** (1110) / (1115)		___ ___ ___	___ ___ ___	___ ___ ___	___ ___ ___	___ ___ ___	___ ___ ___	___ ___ ___
12. Total number of puff(s) from QVAR Inhaler **(PM)** (1120)		___	___	___	___	___	___	___
Symptoms++ since you woke	13. Shortness of Breath (1130)							
	14. Chest Tightness (1140)							
	15. Wheezing (1150)							
	16. Cough (1160)							
	17. Phlegm/Mucus (1170)							
24 HOUR EVALUATION								
18. Total number of puffs from albuterol (RESCUE) inhaler during past 24 hours. *(Do not record preventive use.)* (1190)		___ ___	___ ___	___ ___	___ ___	___ ___	___ ___	___ ___
19. Do you have a cold today? (Check only **one** response for each day.) *** Please contact a Study Coordinator as soon as possible.** (1200)		❑ Yes* ❑ No	❑ Yes* ❑ No	❑ Yes* ❑ No	❑ Yes* ❑ No	❑ Yes* ❑ No	❑ Yes* ❑ No	❑ Yes* ❑ No

** 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.

Asthma Clinical Research Network
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LARGE DIARY CARD

Subject's Initials: _ _ _
Date: _ _ / _ _ / _ _ _ _

Subject ID: 1 4 - _ _ - _ _ _
Subject Initials: _ _ _
Return Visit Number: _ _
Return Visit Date: _ _ / _ _ / _ _ (Month / Day / Year)

To the subject: If your peak flow is below ___ ___ (1000) liters/minute, use your RESCUE inhalers as instructed in the handout "If Your Asthma Gets Worse." Contact study personnel if your peak flow does not increase to this value after 2 hours 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 RESCUE1 and RESCUE2 inhalers (combined, total puffs), 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 QVAR Inhaler **(AM)** (1040)		___	___	___	___	___	___	___
5. Total number of puff(s) from Scheduled Diskus® **(AM)** (1045)		___	___	___	___	___	___	___
Symptoms++ during the night	6. Shortness of Breath (1050)							
	7. Chest Tightness (1060)							
	8. Wheezing (1070)							
	9. Cough (1080)							
	10. Phlegm/Mucus (1090)							
NIGHT-TIME EVALUATION (Between 8 PM and 1 AM)								
11. Time of PM Peak Flow (between 8 PM and 1 AM) (1100)		_ _ : _ _	_ _ : _ _	_ _ : _ _	_ _ : _ _	_ _ : _ _	_ _ : _ _	_ _ : _ _
12. PM Peak Flow (liters/min)** (1110) / (1115)		___ ___ ___	___ ___ ___	___ ___ ___	___ ___ ___	___ ___ ___	___ ___ ___	___ ___ ___
13. Total number of puff(s) from QVAR Inhaler **(PM)** (1120)		___	___	___	___	___	___	___
14. Total number of puff(s) from Scheduled Diskus® **(PM)** (1125)		___	___	___	___	___	___	___
Symptoms++ since you woke	15. Shortness of Breath (1130)							
	16. Chest Tightness (1140)							
	17. Wheezing (1150)							
	18. Cough (1160)							
	19. Phlegm/Mucus (1170)							
24 HOUR EVALUATION								
20. Total number of puffs from RESCUE1 inhaler during past 24 hours. *(Do not record preventive use.)* (1180)		___ ___	___ ___	___ ___	___ ___	___ ___	___ ___	___ ___
21. Total number of puffs from RESCUE2 inhaler during past 24 hours. *(Do not record preventive use.)* (1190)		___ ___	___ ___	___ ___	___ ___	___ ___	___ ___	___ ___
22. Do you have a cold today? (Check only **one** response for each day.) *** Please contact a Study Coordinator as soon as possible.** (1200)		❑ Yes* ❑ No	❑ Yes* ❑ No	❑ Yes* ❑ No	❑ Yes* ❑ No	❑ Yes* ❑ No	❑ Yes* ❑ No	❑ Yes* ❑ No

****** Record the best of three attempts. Circle the value if you have taken any medication from your RESCUE inhaler(s) 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.

Asthma Clinical Research Network
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LARGE ELIGIBILITY CHECKLIST 1

Subject ID: 1 4 - __ __ - __ __ __
Subject Initials: __ __ __
Visit Number: 1
Visit Date: __ __ / __ __ / __ __ (Month / Day / Year)
Interviewer ID: __ __ __ __ __ __

(Subject Interview completed)

1. ***Did the subject sign the LARGE main study (Visits 1-21) Informed Consent?*** ☐ 1 Yes ☐ 0 No **(1000)**

   If ***YES***, record the date the form was signed. __ __ / __ __ / __ __ __ __ (month / day / year) **(1010)**

2. Did the clinic receive confirmation via the Subject Status Report that the subject is eligible for enrollment at Visit 1? ☐ 1 Yes ☐ 0 No **(1020)**

3. Are you planning to move away from this clinical center in the <u>next 15 months</u> such that your ability to complete the study will be jeopardized? ☐ 1 Yes ☐ 0 No **(1030)**

4. Have you had a respiratory tract infection in the past 6 weeks? ☐ 1 Yes ☐ 0 No **(1040)**

5. Have you experienced a significant asthma attack in the past 6 weeks? ☐ 1 Yes ☐ 0 No **(1050)**

6. Do you work the night shift or have an altered day/night cycle for other reasons? ☐ 1 Yes ☐ 0 No **(1060)**

7. Is the subject eligible to proceed? ☐ 1 Yes ☐ 0 No **(1070)**

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

- ➔ ***If NO, complete the LARGE Termination of Study Participation (P14_TERM) form.***
- ➔ ***If YES, proceed with remaining Visit 1 procedures.***

Subject Source Documentation
Subject Initials: __ __ __ **(1080)**
Date: __ __ / __ __ / __ __ __ __ **(1090)**

Asthma Clinical Research Network
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LARGE ELIGIBILITY CHECKLIST 2

Subject ID: 1 4 - ___ ___ - ___ ___ ___
Subject Initials: ___ ___ ___
Visit Number: 1
Visit Date: ___ ___ / ___ ___ / ___ ___ (Month / Day / Year)
Coordinator ID: ___ ___ ___ ___ ___ ___

(Clinic Coordinator completed)

1. Does the subject have current evidence of any of the conditions listed on the Exclusionary Medical Conditions reference card (P14_EXCLMED)?
   If ***YES***, describe _____
   ☐ 1 Yes ☐ 0 No **(1000)**

2. Has the subject taken any medications listed on the Exclusionary Drugs reference card (P14_EXCLDRUG) within the specified time periods?
   If ***YES***, describe _____
   ☐ 1 Yes ☐ 0 No **(1010)**

3. Is the subject currently taking prescription or over-the-counter medication(s) other than those listed on the Allowed Medications reference card (P14_MEDALLOW)?
   If ***YES***, describe _____
   ☐ 1 Yes ☐ 0 No **(1020)**

4. Based on input from the subject and the study physician, will the subject need to use intranasal steroids at any time during the study?
   ☐ 1 Yes ☐ 0 No **(1030)**

   4a. If ***YES***, is the subject willing to use a single intranasal steroid at a stable dose continuously for the duration of the study?
   ☐ 1 Yes ☐ 0 No **(1040)**

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 **(1050)**

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 **(1060)**

7. During the last **2 weeks** of the pre-match phase, did the subject take his or her study QVAR on schedule (AM and PM doses of 3 puffs BID as reflected on subject's Pre-Match Diary Cards) at least 80% of the time? ☐ 1 Yes ☐ 0 No **(1070)**

8. Is the subject's prebronchodilator $FEV_1 \geq 50\%$ of predicted? ☐ 1 Yes ☐ 0 No **(1080)**

9. Is the subject eligible to proceed? ☐ 1 Yes ☐ 0 No **(1090)**

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

➔ ***If NO, complete the LARGE Termination of Study Participation (P14_TERM) form.***

➔ ***If YES, proceed with remaining Visit 1 procedures.***

Subject Source Documentation

Subject Initials: __ __ __ **(1100)**

Date: __ __ / __ __ / __ __ __ __ **(1110)**

Asthma Clinical Research Network
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LARGE ELIGIBILITY CHECKLIST 3

Subject ID: 1 4 - ___ ___ - ___ ___ ___
Subject Initials: ___ ___ ___
Visit Number: 4
Visit Date: ___ ___ / ___ ___ / ___ ___ (Month / Day / Year)
Coordinator ID: ___ ___ ___ ___ ___

(Clinic Coordinator completed)

1.	Since Visit 1, has the subject experienced a significant asthma exacerbation as defined in the protocol?	☐ 1 Yes	☐ 0 No	**(1000)**
2.	Since Visit 1, has the subject received treatment with any excluded medications (P14_EXCLDRUG)?	☐ 1 Yes	☐ 0 No	**(1010)**
3.	Have any of the subject's biological first degree relatives (i.e., parents, siblings, children) been randomized in the LARGE study?	☐ 1 Yes	☐ 0 No	**(1020)**
4.	Using the history stored in the Doser™, did the subject take at least 80% of the required puffs from his or her QVAR inhaler during the last **2 weeks** of the run-in period (i.e., interval between Visits 3 and 4)? ➔ Use Question #1c from P14_COMPLY to answer this question	☐ 1 Yes	☐ 0 No	**(1030)**
5.	Using the history stored in the Doser™, did the subject take 6 puffs per day (correct daily dose) on at least 70% of the days during the last **2 weeks** of the run-in period (i.e., interval between Visits 3 and 4)? ➔ Use Question #1f from P14_COMPLY to answer this question	☐ 1 Yes	☐ 0 No	**(1040)**
6.	Did the subject record <u>both</u> AM and PM peak flow measurements <u>and</u> symptoms on his or her Diary Cards (P14_DIARYR) on at least 75% of the days during the last **2 weeks** of the run-in period (i.e., interval between Visits 3 and 4)?	☐ 1 Yes	☐ 0 No	**(1050)**
7.	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 (P14_DIARYR) on at least 75% of the days during the last **2 weeks** of the run-in period (i.e., interval between Visits 3 and 4)?	☐ 1 Yes	☐ 0 No	**(1060)**
8.	During the **last week** of the run-in period, did the subject use an average of $\geq$16 puffs/24 hours from his or her RESCUE (albuterol) inhaler?	☐ 1 Yes	☐ 0 No	**(1070)**
9.	Is the subject able to use a Diskus® properly, as evidenced by achieving a score of 8 on two consecutive, separate inhalations using the Diskus Inhalation Technique Checklist (TECH_DISKUS)?	☐ 1 Yes	☐ 0 No	**(1080)**
10.	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	**(1090)**

11. Is the subject's prebronchodilator $FEV_1 \geq 50\%$ of predicted? ☐ 1 Yes ☐ 0 No **(1100)**

12. Does the subject wish to withdraw consent from the study? ☐ 1 Yes ☐ 0 No **(1110)**

☐ 0 No **(1120)**

13. Is there any new information that makes the subject ineligible according to the eligibility criteria? ☐ 1 Yes
If ***YES,*** describe: _____

14. Is there any other reason why this subject should not be included in the study? ☐ 1 Yes ☐ 0 No **(1130)**
If ***YES,*** describe: _____

15. Is the subject eligible? ☐ 1 Yes ☐ 0 No **(1140)**

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

➔ ***If the subject is eligible and will participate in LARGE, randomize the subject. Otherwise, please complete the LARGE Termination of Study Participation (P14_TERM) form.***

16. Drug Packet Number **(record on P14_LOG)**

1 4 ___ ___ - ___ ___ - ___ ___
(1150) (1160) (1170)

Asthma Clinical Research Network
NIH/NHLBI

LARGE SCHEDULED MEDICATIONS

(Visits 4 - 20 and 11A-11H)

Subject ID: 1 4 - __ __ - __ __ __
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 QVAR MDIs dispensed

- ❑ 0 None
- ❑ 1 One
- ❑ 2 Two
- ❑ 3 Three **(1010)**

3. Number of Scheduled Diskus(es)® dispensed

- ❑ 0 None
- ❑ 1 One
- ❑ 2 Two **(1020)**

If this is a dispensation at Visits 4-20, affix the new drug label below.

Note: No drug label will be available for dispensations at Visits 11A-11H.

Copy the drug label number below.

1 4 - __ __ - __ __
(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 dates of use for QVAR MDIs and Diskus(es)® have been calculated correctly and accurately transcribed onto the inhaler labels.
4) confirming that the correct medications were distributed at this visit.

Asthma Clinical Research Network
NIH/NHLBI

LARGE MEDICAL HISTORY

Subject ID: 1 4 - ___ ___ - ___ ___ ___
Subject Initials: ___ ___ ___
Visit Number: 1
Visit Date: ___ ___ / ___ ___ / ___ ___ (Month / Day / Year)
Coordinator ID: ___ ___ ___ ___ ___ ___

(Subject Interview completed)

PRIOR ASTHMA TREATMENT

I will read a list of medications. Indicate if you have <u>ever used</u> 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
1.	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)**	❑1 Yes ❑0 No ❑8 Unknown **(1000)**	___ ___ / ___ ___ / ___ ___ ___ ___ **(1010) (1020) (1030)**
1a.	If ***YES***, indicate average daily puffs in the past month. (Enter '00' if none used.)	___ ___ puffs **(1040)**	
1b.	If ***YES***, indicate average daily puffs used prior to screening for LARGE. (Enter '00' if none used.)	___ ___ puffs **(1050)**	
2.	Long-acting Inhaled Beta-Agonists (**Serevent, Foradil, Advair Diskus**)	❑1 Yes ❑0 No ❑8 Unknown **(1060)**	___ ___ / ___ ___ / ___ ___ ___ ___ **(1070) (1080) (1090)**
3.	Asthma medication via a Nebulizer Machine	❑1 Yes ❑0 No ❑8 Unknown **(1100)**	___ ___ / ___ ___ / ___ ___ ___ ___ **(1110) (1120) (1130)**
4.	Oral Beta-Agonists (**Alupent, Brethine, Bricanyl, Metaprel, Proventil, Ventolin, Repetabs, Volmax and others**)	❑1 Yes ❑0 No ❑8 Unknown **(1140)**	___ ___ / ___ ___ / ___ ___ ___ ___ **(1150) (1160) (1170)**
5.	Short-acting Oral Theophylline (**Aminophylline, Slo-Phyllin and others**)	❑1 Yes ❑0 No ❑8 Unknown **(1180)**	___ ___ / ___ ___ / ___ ___ ___ ___ **(1190) (1200) (1210)**
6.	Sustained release Oral Theophylline (**Slo-bid, Theo-Dur, Uniphyl and others**)	❑1 Yes ❑0 No ❑8 Unknown **(1220)**	___ ___ / ___ ___ / ___ ___ ___ ___ **(1230) (1240) (1250)**
7.	Inhaled Anticholinergic (**Atrovent, Combivent, Spiriva**)	❑1 Yes ❑0 No ❑8 Unknown **(1260)**	___ ___ / ___ ___ / ___ ___ ___ ___ **(1270) (1280) (1290)**

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

8. Anti-allergic Inhaled Medications (**Intal, Tilade and others**) ❑1 Yes ❑0 No ❑8 Unknown (1300) __ __ / __ __ / __ __ __ __ (1310) (1320) (1330)

9. Anti-allergic Nasal Medications (**Nasalcrom, Astelin and others**) ❑1 Yes ❑0 No ❑8 Unknown (1340) __ __ / __ __ / __ __ __ __ (1350) (1360) (1370)

10. Anti-allergic Oral Medications (**Allegra, Claritin, Zyrtec, Chlor-Trimeton and others**) ❑1 Yes ❑0 No ❑8 Unknown (1380) __ __ / __ __ / __ __ __ __ (1390) (1400) (1410)

11. Leukotriene Antagonist / 5LO Inhibitors (**Accolate, Zyflo, Singulair**) ❑1 Yes ❑0 No ❑8 Unknown (1420) __ __ / __ __ / __ __ __ __ (1430) (1440) (1450)

12. IgE Blocker (**Xolair**) ❑1 Yes ❑0 No ❑8 Unknown (1460) __ __ / __ __ / __ __ __ __ (1470) (1480) (1490)

13. Topical Steroids - Prescription (**Synalar, Lidex, Dermacin, Fluocinonide and others**) ❑1 Yes ❑0 No ❑8 Unknown (1500) __ __ / __ __ / __ __ __ __ (1510) (1520) (1530)

14. Topical Steroids - OTC (**Hydrocortisone - multiple strengths and products)** ❑1 Yes ❑0 No ❑8 Unknown (1540) __ __ / __ __ / __ __ __ __ (1550) (1560) (1570)

15. Nasal Steroids (**Beconase, Vancenase, Flonase, Nasacort, Nasalide, Nasarel, Rhinocort, Nasonex and others)** ❑1 Yes ❑0 No ❑8 Unknown (1580) __ __ / __ __ / __ __ __ __ (1590) (1600) (1610)

16. Oral Steroids (**Prednisone, Medrol and others**) ❑1 Yes ❑0 No ❑8 Unknown (1620) __ __ / __ __ / __ __ __ __ (1630) (1640) (1650)

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 LARGE study. If you did, please indicate, to the best of your knowledge, the date last taken.

17. Inhaled Steroids (prior to LARGE study) ❑1 Yes ❑0 No ❑8 Unknown __ __ / __ __ / __ __ __ __
(**Azmacort, Beclovent, Vanceril, AeroBid, QVAR, Flovent, Pulmicort, Advair Diskus and others**) **(1660)** **(1670)** **(1680)** **(1690)**

➔ ***If NO or unknown, skip to Question #18.***

➔ ***If YES, complete Questions #17a - 17c.***

17a. Indicate most recent type of inhaled steroid taken prior to screening for LARGE

- ❑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 _____ **(1700)**

17b. Indicate number of daily inhaled steroid puffs used prior to screening for LARGE

__ __ puffs **(1710)**

17c. Indicate how long you had used the inhaled steroid prior to screening for LARGE

- ❑1 less than 1 month
- ❑2 1 - 6 months
- ❑3 greater than 6 months **(1720)**

PRIOR DISEASES, ILLNESSES AND SURGERIES

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

				If Yes, Comment
18.	Skin	❑1 Yes	❑0 No	_____ (1730)
19.	Blood, Lymph, or Immune Systems	❑1 Yes	❑0 No	_____ (1740)
20.	Eyes	❑1 Yes	❑0 No	_____ (1750)
21.	Ears, Nose, or Throat	❑1 Yes	❑0 No	_____ (1760)
22.	Breasts	❑1 Yes	❑0 No	_____ (1770)
23.	Endocrine Systems	❑1 Yes	❑0 No	_____ (1780)
24.	Lung - other than asthma	❑1 Yes	❑0 No	_____ (1790)
25.	Heart and Blood Vessels	❑1 Yes	❑0 No	_____ (1800)
26.	Liver or Pancreas	❑1 Yes	❑0 No	_____ (1810)
27.	Kidneys or Urinary Tract System	❑1 Yes	❑0 No	_____ (1820)
28.	Reproductive System	❑1 Yes	❑0 No	_____ (1830)
29.	Stomach or Intestines	❑1 Yes	❑0 No	_____ (1840)
30.	Muscles or Bones	❑1 Yes	❑0 No	_____ (1850)
31.	Nervous System	❑1 Yes	❑0 No	_____ (1860)
32.	Psychiatric	❑1 Yes	❑0 No	_____ (1870)
33.	Other _____	❑1 Yes	❑0 No	_____ (1880)

SUBJECT'S WEIGHT

(Clinic Coordinator completed)

34. Weight (*without shoes or heavy clothing*) ___ ___ ___ . ___ kg **(1890)**

Subject Source Documentation

Subject's Initials: __ __ __ **(1900)**

Date: __ __ / __ __ / __ __ __ __ **(1910)**

(Subject Interview completed)

Please reference the Drug Classifications list for a complete list of examples for the questions below. If any medications <u>other</u> <u>than</u> study drugs or study rescue medications were used, record the medication(s) on the Screening Concomitant Medications for Asthma/Allergies and Adverse Events (P14_SCREEN_MED) form or Concomitant Medications for Asthma/Allergies and Adverse Events (CMED) form, as appropriate.

1. Have you consumed caffeine in the past **6 hours**? ☐ 1 Yes ☐ 0 No **(1000)**
   ***Examples**: Pepsi, Coke, Coffee, Mountain Dew, Tea, Rootbeer, Red Bull*

2. Have you used medications with caffeine in the past **6 hours**? ☐ 1 Yes ☐ 0 No **(1010)**
   ***Examples**: Anacin, Darvon compound, Esgic, Excedrin, Fiorinal, Fioricet, No Doz, Norgesic, Vivarin*

3. Have you used any weight loss medications in the past **6 hours**? ☐ 1 Yes ☐ 0 No **(1020)**
   ***Examples**: bitter orange, Xenadrine EFX, Thermorexin*

4. Have you consumed any food containing alcohol or beverages containing alcohol in the past **6 hours**? ☐ 1 Yes ☐ 0 No **(1030)**

5. Have you used chlorpheniramine, diphenhydramine, fexofenadine, desloratadine, or loratadine in the past **48 hours**? ☐ 1 Yes ☐ 0 No **(1040)**
   ***Examples**: Chlor-Trimeton, Benadryl, Allegra, Clarinex, Claritin*

6. Have you used any antihistamines **other than** chlorpheniramine (Chlor-Trimeton and others), diphenhydramine (Benadryl), fexofenadine (Allegra), desloratadine (Clarinex), or loratadine (Claritin) in the past **72 hours**? ☐ 1 Yes ☐ 0 No **(1045)**

7. Have you used any decongestants or cold remedies in the past **48 hours**? ☐ 1 Yes ☐ 0 No **(1050)**
   ***Examples**: pseudoephedrine (Sudafed), oxymetazoline (Afrin)*

8. Have you used any cough medicines, anti-tussives, or expectorants in the past **48 hours**? ☐ 1 Yes ☐ 0 No **(1060)**
   Examples: *guaifenesin, dextromethorphan, Duratuss, Benylin, Triaminic expectorant, Dayquil Anti-Cough*

   ➔ ***Please check preparation for antihistamines and decongestants. Record use in Questions #5 - #7, as appropriate.***

9. Have you used a rescue intermediate-acting inhaled beta-agonist in the past **6 hours**? ☐ 1 Yes ☐ 0 No **(1070)**
   Example: *albuterol (RESCUE, RESCUE2, Ventolin or Proventil)*

10. **(Complete at Visits 0A1, 0C2, 0PA only)**
    Have you used a long-acting inhaled beta-agonist in the past **24 hours**? ☐ 1 Yes ☐ 0 No **(1080)**
    Examples: *Serevent, Foradil, Advair*

11. **(Complete at Visits 0A2 and 0C1 only)**
    Have you used a long-acting inhaled beta-agonist in the past **48 hours**? ☐ 1 Yes ☐ 0 No **(1084)**
    Examples: *Serevent, Foradil, Advair*

12. **(Complete at Visits 5-9 and 13-17 only)**
    Have you used your Scheduled Diskus in the past **24 hours**? ☐ 1 Yes ☐ 0 No **(1087)**

13. **(Complete at spirometry-only visits: 0A1, 0C2, 0PA-0PZ, 1, 2, 3, 5, 6, 7, 8, 10, 11, 11A-11H, 13, 14, 15, 16, 18, 19, 21 only)**
    Have you used a rescue short-acting inhaled anticholinergic in the past **6 hours**? ☐ 1 Yes ☐ 0 No **(1090)**
    Examples: *Atrovent (RESCUE1), Combivent, Duoneb*

14. **(Complete at methacholine visits: 0A2, 0C1, 4, 9, 12, 17, 20 only)**
    Have you used a rescue short-acting inhaled anticholinergic in the past **24 hours**? ☐ 1 Yes ☐ 0 No **(1095)**
    Examples: *Atrovent (RESCUE1), Combivent, Duoneb*

15. **(Complete at Visits 0A1, 0A2, 0C1, 0C2, 0PA only)**
    Have you used any oral corticosteroids in the past **6 weeks**? ☐ 1 Yes ☐ 0 No **(1125)**
    Example: *Prednisone, Medrol*

16. Have you used any nasal steroids in the past **48 hours**? ☐ 1 Yes ☐ 0 No **(1130)**
    Examples: *Flonase, Rhinocort, Nasonex*

17. At this time, is your asthma worse because of recent exposure to triggers? ☐ 1 Yes ☐ 0 No **(1160)**
    Examples: *cold air, smoke, allergens, recent exercise, a recent respiratory tract infection, or other pulmonary infection*

18. **(Complete at Visits 0A2 and 0C1 only)**
Have you had a respiratory tract infection in the past **6 weeks**? ☐ 1 Yes ☐ 0 No **(1165)**

19. **(Complete at Visit 0PA only)**
Have you had a respiratory tract infection in the past **4 weeks**? ☐ 1 Yes ☐ 0 No **(1167)**

20. Is there any other reason you should not proceed with spirometry testing? ☐ 1 Yes ☐ 0 No **(1170)**

If ***YES***, explain _____

_____

21. Is the subject eligible to proceed with the spirometry testing? ☐ 1 Yes ☐ 0 No **(1180)**

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

➔ ***If YES, proceed to Question #21 or the next form/procedure listed on the visit procedure checklist.***

22. ***Complete for all subjects at Visit 0A1 or 0A2.***
If subject is less than 21 years old, complete Question #21 at each visit.

Height (*without shoes*) ___ ___ ___ cm **(1190)**

Asthma Clinical Research Network
NIH/NHLBI

LARGE SCREENING ELIGIBILITY CHECKLIST 1

Subject ID: 1 4 - __ __ - __ __ __
Subject Initials: __ __ __
Visit Number: 0 A __
Visit Date: __ __ / __ __ / __ __ (Month / Day / Year)
Coordinator ID: __ __ __ __ __ __

(Clinic Coordinator completed)

1. ***Did the subject sign the LARGE/Genetics Informed Consent?*** ❑ 1 Yes ❑ 0 No **(1000)**

   1a. If ***YES***, record the date the form was signed. __ __ / __ __ / __ __ __ __ (month / day / year) **(1010)**

   ➔ ***Consent should be reviewed and signed on the day Visit 0A1 or 0A2 is performed.***

2. Is the subject willing to give a blood sample for DNA isolation and genotyping? ❑ 1 Yes ❑ 0 No **(1020)**

3. Did the subject participate in the BAGS (1), BARGE (8), SOCS (3) or SLIC (3) trials? ❑ 1 Yes ❑ 0 No **(1030)**

   ➔ ***Verify aliases through ACRN Registry Module.***

4. Is the subject 18 years of age or older? ❑ 1 Yes ❑ 0 No **(1040)**

5. Does the subject have current evidence of any of the conditions listed on the Exclusionary Medical Conditions reference card (P14_EXCLMED)? ❑ 1 Yes ❑ 0 No **(1050)**
   If ***YES***, describe _____

6. Has the subject taken any medications listed on the Exclusionary Drugs reference card (P14_EXCLDRUG) within the specified time periods? ❑ 1 Yes ❑ 0 No **(1060)**
   If ***YES***, describe _____

7. Is the subject currently taking prescription or over-the-counter medication(s) other than those listed on the Allowed Medications reference card (P14_MEDALLOW)? ❑ 1 Yes ❑ 0 No **(1070)**
   If ***YES***, describe _____

8. Based on input from the subject and the study physician, will the subject need to use intranasal steroids at any time during the study? ❑ 1 Yes ❑ 0 No **(1080)**

   8a. If ***YES***, is the subject willing to use a single intranasal steroid at a stable dose continuously for the duration of the study? ❑ 1 Yes ❑ 0 No **(1090)**

9. 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 **(1100)**

10. Has the subject experienced a significant asthma exacerbation in the past **6** weeks? ☐ 1 Yes ☐ 0 No **(1110)**

11. Has the subject experienced a life-threatening asthma exacerbation requiring treatment with intubation and mechanical ventilation in the past **10** years? ☐ 1 Yes ☐ 0 No **(1120)**

12. How many times has the subject smoked cigarettes, a pipe, cigar, marijuana, or any other substance **OR** used any smokeless tobacco products (e.g., chew, snuff)...

12a. in the past **12** months? ___ ___ ___ times **(1130)**

Is Question #12a > 5? ☐ 1 Yes ☐ 0 No **(1140)**

12b. in the past **30** days? ___ ___ ___ times **(1150)**

Is Question #12b > 0? ☐ 1 Yes ☐ 0 No **(1160)**

13. Record smoking history in pack-years. (Enter 00.0 if subject never smoked.) ___ ___ . ___ **(1170)**

Is Question #13 ≥ 10? ☐ 1 Yes ☐ 0 No **(1180)**

14. Is the subject potentially able to bear children? ☐ 1 Yes ☐ 0 No ☐ 9 N/A **(1190)**
(If subject is male, check N/A and go to Question #15.)

14a. If ***YES***, is the subject using one of the approved methods indicated on the Birth Control (BIRCTRL) reference card ? ☐ 1 Yes ☐ 0 No **(1200)**

14b. If ***YES***, is the subject currently pregnant or lactating? ☐ 1 Yes ☐ 0 No **(1210)**

15. Is the subject eligible to proceed? ☐ 1 Yes ☐ 0 No **(1220)**
If any of the shaded boxes are completed, the subject is ineligible.

➔ ***If YES, proceed with remaining Visit 0A1 or 0A2 procedures.***

Screening Source Documentation

Subject Initials: __ __ __ **(1230)**

Date: __ __ / __ __ / __ __ __ __ **(1240)**

Asthma Clinical Research Network
NIH/NHLBI

LARGE SCREENING ELIGIBILITY CHECKLIST 2

Subject ID: 1 4 - __ __ - __ __ __
Subject Initials: __ __ __
Visit Number: 0 A __
Visit Date: __ __ / __ __ / __ __ (Month / Day / Year)
Coordinator ID: __ __ __ __ __ __

(Clinic Coordinator completed)

1. Is the subject regularly using inhaled corticosteroids? ☐ 1 Yes ☐ 0 No **(1000)**

   ➔ If ***NO***, answer Question #1a and skip to Question #2.

   ➔ If ***YES***, skip to Question #1b and complete rest of the form.

   1a. Is the subject's prebronchodilator $FEV_1 \geq 40\%$ of predicted? ☐ 1 Yes ☐ 0 No **(1010)**

   1b. Is the subject's prebronchodilator $FEV_1 \geq 50\%$ of predicted? ☐ 1 Yes ☐ 0 No **(1020)**

   1c. Has the subject been on a stable dose of inhaled corticosteroids for at least 2 weeks? ☐ 1 Yes ☐ 0 No **(1030)**

   1d. Has the subject been using greater than the equivalent of 1000 µg inhaled fluticasone daily? ☐ 1 Yes ☐ 0 No **(1040)**

   ➔ Refer to the ICS Equivalency (P14_ICS_EQUIV) reference card.

2. Is the subject eligible to proceed? ☐ 1 Yes ☐ 0 No **(1050)**
   If any of the shaded boxes are completed, the subject is ineligible.

   ➔ ***If YES, proceed with the remaining Visit 0A1 or 0A2 procedures.***

Asthma Clinical Research Network
NIH/NHLBI

LARGE SCREENING ELIGIBILITY CHECKLIST 3

Subject ID: 1 4 - __ __ - __ __ __
Subject Initials: __ __ __
Visit Number: 0 __ __
Visit Date: __ __ / __ __ / __ __ (Month / Day / Year)
Coordinator ID: __ __ __ __ __ __

(Clinic Coordinator completed)

1. Is the subject's prebronchodilator FEV_1 at this visit $\geq$ 55% of predicted? ❑ 1 Yes ❑ 0 No **(1000)**

   ➔ If ***YES***, complete Section 1.

   ➔ If ***NO***, complete Section 2.

Section 1

2. Is the subject regularly using ICS at this time? ❑ 1 Yes ❑ 0 No **(1010)**

   ➔ If ***YES***, complete Question #3 and skip to Question #5.

   ➔ If ***NO***, complete Question #4 and continue with the remainder of the form.

3. Does the subject have a methacholine $PC_{20} \leq 16$ mg/ml? ❑ 1 Yes ❑ 0 No **(1020)**

4. Does the subject have a methacholine $PC_{20} \leq 8$ mg/ml? ❑ 1 Yes ❑ 0 No **(1030)**

5. Is the subject eligible to proceed? ❑ 1 Yes ❑ 0 No **(1040)**

   If either shaded box in Section 1 is completed, the subject is ineligible at this point.

   ➔ ***If YES,* STOP *here and continue with remaining visit procedures.***

   ➔ ***If NO and the subject completed a methacholine challenge, the subject may return at a later date for a continuation visit to perform albuterol reversibility testing to qualify. Complete Question #6 and proceed accordingly.***

   ➔ ***If NO and the subject was not eligible to complete a methacholine challenge, the subject may complete albuterol reversibility testing today. Complete Question #6 and proceed accordingly.***

6. Will the subject complete reversibility testing? ❑ 1 Yes ❑ 0 No **(1050)**

   ➔ If ***NO***, STOP here and complete a P14_SCREEN_PM_TERM form (if Visit 0C1). Subject is ineligible for the study.

   ➔ If ***YES***, follow continuation visit procedures on the P14_VISITSA2 or P14_VISITSC1 checklist and complete Section 2 on the next page.

Section 2

7. Did the subject's FEV_1 improve $\geq$ 12% in response to two puffs of albuterol? ☐ 1 Yes ☐ 0 No **(1060)**

8. Did the subject's FEV_1 increase at least 200 ml in response to two puffs of albuterol? ☐ 1 Yes ☐ 0 No **(1070)**

9. Is the subject eligible to proceed? ☐ 1 Yes ☐ 0 No **(1080)**

If either shaded box in Section 2 is completed, the subject is ineligible.

➔ ***If YES, continue with remaining visit procedures.***

➔ ***If NO, complete a P14_SCREEN_PM_TERM form (if Visit 0C1). Subject is ineligible for the study.***

Asthma Clinical Research Network
NIH/NHLBI

LARGE SCREEN/PRE-MATCH TERMINATION (Prior to Visit 1)

Subject ID: 1 4 - __ __ - __ __ __
Subject Initials: __ __ __
Visit Number: 0 __ __
Visit Date: __ __ / __ __ / __ __ (Month / Day / Year)
Coordinator ID: __ __ __ __ __ __

(Clinic Coordinator completed)

Complete this form only for those subjects who have successfully completed the first screening visit (0A1 or 0A2) and have been terminated or deemed ineligible prior to Visit 1. After the form is completed, fax it immediately to the LARGE primary data manager at the DCC at (717) 531-4359.

1. Who initiated termination of the subject?
   - ❑1 Subject
   - ❑2 Clinical Staff **(1000)**

   ➔ ***If subject withdrew due to impending clinical staff termination, please indicate termination by clinical staff.***

   ➔ ***If Clinical Staff, skip to Question #3.***

2. Indicate the **primary** reason the subject has withdrawn from the study.
   - ❑1 no longer interested in participating *****
   - ❑2 no longer willing to follow pre-match 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 dissatisfied with asthma control during pre-match phase
   - ❑9 side effects of study medications during pre-match phase *****
   - ❑10 other ***** **(1010)**

   *** Additional explanation required:**

   _____

   _____

   _____

   ➔ ***Skip to the SIGNATURES section.*** **(1020)**

3. Is the subject being terminated from the study due to an ineligible genotype? ❑1 Yes ❑0 No **(1030)**

   3a. If ***YES***, was the subject given the standard ACRN notification letter? ❑1 Yes ❑0 No **(1040)**

   ➔ ***All genotype ineligible subjects must receive this letter.***

   ➔ ***Skip to the SIGNATURES section.***

4. Is the subject being terminated from the study due to closure of recruitment (i.e., subjects waiting for a match at recruitment close)? ❑ 1 Yes ❑ 0 No **(1050)**

   ➔ ***If YES, skip to the SIGNATURES section.***

5. Did clinical staff terminate the subject due to ...

   5a. pregnancy? *(Check N/A if the subject is male.)* ❑ 1 Yes ❑ 0 No ❑ 9 N/A **(1060)**

   5b. randomization of a first degree relative? ❑ 1 Yes ❑ 0 No **(1070)**

   5c. ineligibility for reasons other than ineligible genotype? ***** ❑ 1 Yes ❑ 0 No **(1080)**

   5d. loss to follow-up? ***** ❑ 1 Yes ❑ 0 No **(1090)**

   5e. an asthma-related adverse event? ***** ❑ 1 Yes ❑ 0 No **(1100)**

   5f. a medication-related adverse event? ***** ❑ 1 Yes ❑ 0 No **(1110)**

   5g. an adverse event not related to asthma or medications? ***** ❑ 1 Yes ❑ 0 No **(1120)**

   5h. non-compliance with QVAR dosing? ***** ❑ 1 Yes ❑ 0 No **(1130)**

   5i. non-compliance with diary completion? ***** ❑ 1 Yes ❑ 0 No **(1140)**

   5j. non-compliance with visit attendance? ***** ❑ 1 Yes ❑ 0 No **(1150)**

   5k. other reason? ***** ❑ 1 Yes ❑ 0 No **(1160)**

*** Additional explanation required:**

_____

_____

_____ **(1170)**

5l. Indicate the letter corresponding to the primary reason the subject was terminated. ____ **(1180)**

SIGNATURES

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

I verify that all information collected on the ACRN LARGE 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 LARGE Protocol.

_____ **(1190)** ___ ___ /___ ___ /___ ___ ___ ___ **(1200)**

Clinic Coordinator Signature month day year

Asthma Clinical Research Network
NIH/NHLBI

LARGE SIGNIFICANT ASTHMA EXACERBATION (Visits 1-21 and 11A-11H)

Subject ID: 1 4 - ___ ___ - ___ ___ ___
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. This form applies only to exacerbations occurring after enrollment at Visit 1.

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 use (ipratropium and albuterol combined) of ≥ 8 puffs per 24 hours over baseline use for a period of 48 hours? ☐1 Yes ☐0 No **(1000)**

1b. Use of rescue inhaler(s) (ipratropium and albuterol combined) ≥ 16 total puffs per 24 hours for a period of 48 hours? ☐1 Yes ☐0 No **(1010)**

1c. A PEFR that did not increase to ≥ 65% of baseline despite 60 minutes of rescue treatment (albuterol or ipratropium, as applicable)? ☐1 Yes ☐0 No **(1020)**

1ci. If **YES**, record the subject's postbronchodilator PEFR value after 60 minutes of rescue (RESCUE, RESCUE1, or RESCUE2) use. ___ ___ ___ L/min **(1025)**

1d. Symptoms persisting after 60 minutes of rescue treatment (albuterol or ipratropium, as applicable)? ☐1 Yes ☐0 No **(1028)**

1e. Treatment with oral, inhaled, or intravenous corticosteroids as a result of rescue intervention or by the opinion of the treating physician? ☐1 Yes ☐0 No **(1030)**

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

2. Did the subject experience a significant asthma exacerbation? ☐1 Yes ☐0 No **(1040)**
If any of the shaded boxes are completed, the subject experienced a SIGEX.

➔ ***If YES, but the subject has not yet been randomized, complete this form, then STOP. The subject is ineligible for the study. Please complete the P14_TERM form.***

➔ ***If NO, STOP HERE. DO NOT SUBMIT THIS FORM TO THE DCC.***

3. Date significant asthma exacerbation occurred ___ ___ / ___ ___ / ___ ___ ___ ___ (1050)
month day year

4. Did the subject seek care for the asthma exacerbation? ☐1 Yes ☐0 No (1060)
➔ ***If NO, skip to Question #7.***

5. What type of care was sought?

5a. Study Investigator? ☐1 Yes ☐0 No (1070)

If ***YES***, indicate type of contact.
☐1 Scheduled clinic visit
☐2 Unscheduled clinic visit
☐3 Phone contact (1080)

5b. Primary Care or Other Physician? ☐1 Yes ☐0 No (1090)
If ***YES***, name of physician: _____

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

5c. Emergency Room visit? ☐1 Yes ☐0 No (1110)
If ***YES,*** name of hospital: _____

6. Was the subject hospitalized? ☐1 Yes ☐0 No (1120)
➔ ***If YES, please complete the Serious Adverse Event Reporting Form (SERIOUS).***

If ***YES***,

6a. Duration of hospital stay? ___ ___ . ___ days (1130)

6b. Was intubation or ventilation assistance required? ☐1 Yes ☐0 No (1140)

6c. Name of hospital: _____

7. Please indicate whether the following medications were used to treat the asthma exacerbation:

7a.	Ipratropium rescue inhaler (RESCUE 1)	☐ 1 Yes	☐ 0 No **(1150)**
7b.	Albuterol rescue inhaler (RESCUE, RESCUE 2)	☐ 1 Yes	☐ 0 No **(1160)**
7c.	Nebulized beta-agonist ➔ ***If YES, please complete the CMED form.***	☐ 1 Yes	☐ 0 No **(1170)**
7d.	Inhaled corticosteroids ➔ ***If YES, please complete the CMED form.***	☐ 1 Yes	☐ 0 No **(1180)**
7e.	Oral corticosteroids ➔ ***If YES, please complete the CMED form.***	☐ 1 Yes	☐ 0 No **(1190)**
7f.	Intravenous corticosteroids ➔ ***If YES, please complete the CMED form.***	☐ 1 Yes	☐ 0 No **(1200)**

8. Was the asthma exacerbation treated as outlined in the protocol? ☐ 1 Yes ☐ 0 No **(1210)**

If ***NO***, explain_____

_____

_____

9. Was the asthma exacerbation related to 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 **(1220)**

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

☐ 1 Definitely related
☐ 2 Probably related
☐ 3 Relationship undetermined
☐ 4 Probably not related
☐ 5 Definitely not related **(1230)**

11. Was the asthma exacerbation related to the collection of exhaled breath condensates? *(Check one box only)*

☐ 1 Definitely related
☐ 2 Probably related
☐ 3 Relationship undetermined
☐ 4 Probably not related
☐ 5 Definitely not related **(1240)**

12. Has the subject experienced more than two asthma exacerbations during a given treatment phase (run-out or blinded treatment period)? ☐ 1 Yes ☐ 0 No **(1250)**

➔ ***If YES, the subject must be terminated from the study. Please complete the P14_TERM form.***

Asthma Clinical Research Network
NIH/NHLBI

LARGE SUBJECT STUDY TREATMENT QUESTIONNAIRE (Visits 4-9 and 12-17)

Subject ID: 1 4 - ___ ___ - ___ ___ ___
Subject Initials: ___ ___ ___
Visit Number: ___ ___
Visit Date: ___ ___ / ___ ___ / ___ ___ (Month / Day / Year)
Coordinator ID: ___ ___ ___ ___ ___ ___

(Subject completed)

This questionnaire is to be completed by the LARGE subject at the end of Visits 9 and 17. If a randomized subject terminates prior to Visit 17, please ask him or her to complete this form during the termination visit. This form should <u>not</u> be completed if a subject terminates between visits 9 and 12.

1. **Scheduled Diskus**

As a LARGE study participant you were randomized to receive either a real (i.e., active) salmeterol Diskus or a look-alike placebo (i.e., inactive) Diskus. Please check the box that most closely represents your feelings about the **scheduled Diskus** you used **over the past 18 weeks.**

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

2. Please comment with respect to the **taste** of the medication you received from your **scheduled Diskus over the past 18 weeks.**

- ☐ 1 Tasted good **(1040)**
  (*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 Diskus over the past 18 weeks.**

- ☐ 1 Smelled good **(1050)**
  (*Describe*) _____
- ☐ 2 No noticeable smell
- ☐ 3 Smelled bad
  (*Describe*) _____

4. Please comment with respect to any **physical sensations** produced by the medication you you received from your **scheduled Diskus over the past 18 weeks.**

☐ 1 Pleasant sensations **(1060)**

(*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 Diskus**.

☐ 1 I have no further comments **(1070)**

☐ 2 I observed the following: (*Describe below*)

_____

_____

_____

_____

Subject Source Documentation

Subject's Initials: __ __ __ **(1020)**

Date: __ __ / __ __ / __ __ __ __ **(1030)**

Asthma Clinical Research Network
NIH/NHLBI

LARGE TERMINATION OF STUDY PARTICIPATION

(Visits 1-21 and 11A-11H)

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

(Clinic Coordinator completed)

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

(Visit 21 only)

1. Has the subject completed the study through Visit 21? ❑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:**

_____

_____

_____ **(1030)**

➔ ***Skip to the SIGNATURES section.***

4. Did clinical staff terminate the subject due to ...

4a.	pregnancy? *(Check N/A if the subject is male.)*	❑ 1 Yes	❑ 0 No	❑ 9 N/A **(1040)**
4b.	randomization of a first degree relative?	❑ 1 Yes	❑ 0 No **(1050)**	
4c.	ineligibility during the run-in period (Visits 1-4) *****	❑ 1 Yes	❑ 0 No **(1060)**	
4d.	loss to follow-up? *****	❑ 1 Yes	❑ 0 No **(1070)**	
4e.	an asthma-related adverse event? *****	❑ 1 Yes	❑ 0 No **(1080)**	
4f.	a medication-related adverse event? *****	❑ 1 Yes	❑ 0 No **(1090)**	
4g.	an adverse event not related to asthma or medications? *****	❑ 1 Yes	❑ 0 No **(1100)**	
4h.	non-compliance with QVAR dosing? *****	❑ 1 Yes	❑ 0 No **(1110)**	
4i.	non-compliance with scheduled Diskus® dosing? *****	❑ 1 Yes	❑ 0 No **(1120)**	
4j.	non-compliance with diary completion? *****	❑ 1 Yes	❑ 0 No **(1130)**	
4k.	non-compliance with visit attendance? *****	❑ 1 Yes	❑ 0 No **(1140)**	
4l.	non-compliance with peak flow monitoring? *	❑ 1 Yes	❑ 0 No **(1150)**	
4m.	subject experienced more than two asthma exacerbations during a given treatment phase (run-out or blinded treatment period)?	❑ 1 Yes	❑ 0 No **(1155)**	
4n.	other reason? *****	❑ 1 Yes	❑ 0 No **(1160)**	

*** Additional explanation required:**

_____

_____

_____ **(1170)**

4o. Indicate the letter corresponding to the primary reason the subject was terminated. ____ **(1180)**

SIGNATURES

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

I verify that all information collected on the ACRN LARGE 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 LARGE Protocol.

_____ **(1190)** ___ ___ /___ ___ /___ ___ ___ ___ **(1200)**

Clinic Coordinator Signature — month day year

_____ **(1210)** ___ ___ /___ ___ /___ ___ ___ ___ **(1220)**

Principal Investigator Signature — month day year

Asthma Clinical Research Network
NIH/NHLBI

LARGE
VISIT 12 SCHEDULING CHECKLIST 1

Subject ID: 1 4 - ___ ___ - ___ ___ ___
Subject Initials: ___ ___ ___
Visit Number: 1 1
Visit Date: ___ ___ / ___ ___ / ___ ___ (Month / Day / Year)
Coordinator ID: ___ ___ ___ ___ ___ ___

(Clinic Coordinator completed)

1. Has the subject experienced a significant asthma exacerbation during the LARGE trial? ☐ 1 Yes ☐ 0 No **(1000)**

   1a. If **YES**, record the date of the subject's *latest* significant asthma exacerbation from Question #3 on the LARGE Significant Asthma Exacerbation (P14_SIGEX) form: ___ ___ / ___ ___ / ___ ___ ___ ___ (month / day / year) **(1010)**

   1b. If **YES**, did the subject experience his/her last significant asthma exacerbation at least **6 weeks** prior to today's date? ☐ 1 Yes ☐ 0 No **(1020)**

2. Has the subject taken prednisone (for any reason) during the LARGE trial? ☐ 1 Yes ☐ 0 No **(1030)**

   2a. 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: ___ ___ / ___ ___ / ___ ___ ___ ___ (month / day / year) **(1040)**

   2b. If **YES**, was the subject's last dose of prednisone taken at least **4 weeks** prior to today's date? ☐ 1 Yes ☐ 0 No **(1050)**

3. Has the subject taken open-label inhaled corticosteroids (ICS) (any dose, any brand, for any reason) in excess of the scheduled study dose of 3 puffs BID of QVAR during the LARGE trial? ☐ 1 Yes ☐ 0 No **(1060)**

   3a. If **YES**, record the date of the subject's last dose of open-label ICS from the Concomitant Medications for Asthma/Allergy and Adverse Events (CMED) form: ___ ___ / ___ ___ / ___ ___ ___ ___ (month / day / year) **(1070)**

   3b. If **YES**, was the subject's last dose of open-label ICS taken at least **4 weeks** prior to today's date? ☐ 1 Yes ☐ 0 No **(1080)**

4. Is the subject prepared to schedule Visit 12 at this time? ☐ 1 Yes ☐ 0 No **(1090)**
   If any of the shaded boxes are completed, the subject is NOT prepared to schedule Visit 12.

   ➔ ***If YES, schedule Visit 12.***
   ➔ ***If NO, schedule the subject for Visit 11A to occur 2 weeks from today.***

Asthma Clinical Research Network
NIH/NHLBI

LARGE
VISIT 12 SCHEDULING CHECKLIST 2

Subject ID: 1 4 - ___ ___ - ___ ___ ___
Subject Initials: ___ ___ ___
Visit Number: 1 1 ___
Visit Date: ___ ___ / ___ ___ / ___ ___ (Month / Day / Year)
Coordinator ID: ___ ___ ___ ___ ___ ___

(Clinic Coordinator completed)

1. Has the subject experienced a significant asthma exacerbation during the LARGE trial? ❑1 Yes ❑0 No **(1000)**

   1a. If **YES**, record the date of the subject's *latest* significant asthma exacerbation from Question #3 on the LARGE Significant Asthma Exacerbation (P14_SIGEX) form: ___ ___ / ___ ___ / ___ ___ ___ ___ (month / day / year) **(1010)**

   1b. If **YES**, did the subject experience his/her last significant asthma exacerbation at least **6 weeks** prior to today's date? ❑1 Yes ❑0 No **(1020)**

2. Has the subject taken prednisone (for any reason) during the LARGE trial? ❑1 Yes ❑0 No **(1030)**

   2a. 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: ___ ___ / ___ ___ / ___ ___ ___ ___ (month / day / year) **(1040)**

   2b. If **YES**, was the subject's last dose of prednisone taken at least **4 weeks** prior to today's date? ❑1 Yes ❑0 No **(1050)**

3. Has the subject taken open-label inhaled corticosteroids (ICS) (any dose, any brand, for any reason) in excess of the scheduled study dose of 3 puffs BID of QVAR during the LARGE trial? ❑1 Yes ❑0 No **(1060)**

   3a. If **YES**, record the date of the subject's last dose of open-label ICS from the Concomitant Medications for Asthma/Allergy and Adverse Events (CMED) form: ___ ___ / ___ ___ / ___ ___ ___ ___ (month / day / year) **(1070)**

   3b. If **YES**, was the subject's last dose of open-label ICS taken at least **4 weeks** prior to today's date? ❑1 Yes ❑0 No **(1080)**

4. Has a study investigator assessed the subject at this visit? ❑1 Yes ❑0 No **(1090)**

   4b. If **YES**, does the study investigator allow the subject to schedule Visit 12 at this time? ❑1 Yes ❑0 No **(1100)**

5. Is the subject prepared to schedule Visit 12 at this time? ❑1 Yes ❑0 No **(1110)**
   If any of the shaded boxes are completed, the subject is NOT prepared to schedule Visit 12.

   ➔ ***If YES, schedule the subject for Visit 12 to occur 2 weeks from today.***

   ➔ ***If NO, schedule the subject for another intermediate visit (e.g., 11b, 11c, etc.) to occur 2 weeks from today.***

Asthma Clinical Research Network
NIH/NHLBI

LARGE
VISIT 12 SCHEDULING CHECKLIST 3

Subject ID: 1 4 - ___ ___ - ___ ___ ___
Subject Initials: ___ ___ ___
Visit Number: 1 2
Visit Date: ___ ___ / ___ ___ / ___ ___ (Month / Day / Year)
Coordinator ID: ___ ___ ___ ___ ___ ___

(Clinic Coordinator completed)

1. Has the subject experienced a significant asthma exacerbation during the LARGE trial? ❑ 1 Yes ❑ 0 No **(1000)**

   1a. If **YES**, record the date of the subject's *latest* significant asthma exacerbation from Question #3 on the LARGE Significant Asthma Exacerbation (P14_SIGEX) form: ___ ___ / ___ ___ / ___ ___ ___ ___ (month / day / year) **(1010)**

   1b. If **YES**, did the subject experience his/her last significant asthma exacerbation at least **8 weeks** prior to today's date? ❑ 1 Yes ❑ 0 No **(1020)**

2. Has the subject taken prednisone (for any reason) during the LARGE trial? ❑ 1 Yes ❑ 0 No **(1030)**

   2a. 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: ___ ___ / ___ ___ / ___ ___ ___ ___ (month / day / year) **(1040)**

   2b. If **YES**, was the subject's last dose of prednisone taken at least **6 weeks** prior to today's date? ❑ 1 Yes ❑ 0 No **(1050)**

3. Has the subject taken open-label inhaled corticosteroids (ICS) (any dose, any brand, for any reason) in excess of the scheduled study dose of 3 puffs BID of QVAR during the LARGE trial? ❑ 1 Yes ❑ 0 No **(1060)**

   3a. If **YES**, record the date of the subject's last dose of open-label ICS from the Concomitant Medications for Asthma/Allergy and Adverse Events (CMED) form: ___ ___ / ___ ___ / ___ ___ ___ ___ (month / day / year) **(1070)**

   3b. If **YES**, was the subject's last dose of open-label ICS taken at least **6 weeks** prior to today's date? ❑ 1 Yes ❑ 0 No **(1080)**

4. Is the subject prepared to complete Visit 12 at this time? ❑ 1 Yes ❑ 0 No **(1090)**
   If any of the shaded boxes are completed, the subject is NOT prepared to complete Visit 12.

   ➔ ***If YES, complete Visit 12 today.***
   ➔ ***If NO, complete an intermediate visit (e.g., 11a, 11b, 11c, etc.) today.***

Asthma Clinical Research Network
NIH/NHLBI

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 *(based on 24-hour clock)* ___ ___ ___ ___ **(1010)**

The best effort reflects the trial where the sum of FEV_1 and FVC is maximized.

3. Results of best effort post-albuterol:

   3a. FVC ___ . ___ ___ L **(1020)**

   3b. FEV_1 ___ . ___ ___ L **(1030)**

   3c. FEV_1 (% predicted) ___ ___ ___ % predicted **(1040)**

   3d. PEFR ___ ___ . ___ ___ L/S **(1050)**

   3e. FEF_{25-75} ___ . ___ ___ 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)**

Asthma Clinical Research Network
NIH/NHLBI

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 *(based on 24-hour clock)* ___ ___ ___ ___ **(1010)**

The best effort reflects the trial where the sum of FEV_1 and FVC is maximized.

3. Results of best effort post-albuterol:

   3a. FVC ___ . ___ ___ L **(1020)**

   3b. FEV_1 ___ . ___ ___ L **(1030)**

   3c. FEV_1 (% predicted) ___ ___ ___ % predicted **(1040)**

   3d. PEFR ___ ___ . ___ ___ L/S **(1050)**

   3e. FEF_{25-75} ___ . ___ ___ 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)**

Asthma Clinical Research Network
NIH/NHLBI

POST-IPRATROPIUM (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).

Note: Ipratropium should NOT be administered to subjects who have a hypersensitivity/allergy to soy or peanuts.

➔ ***Administer 4 puffs of ipratropium and wait 30 minutes, then perform spirometry.***

1. Time ipratropium administered *(based on 24-hour clock)* ___ ___ ___ ___ **(1000)**

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

The best effort reflects the trial where the sum of FEV_1 and FVC is maximized.

3. Results of best effort post-ipratropium:

   3a. FVC ___ . ___ ___ L **(1020)**

   3b. FEV_1 ___ . ___ ___ L **(1030)**

   3c. FEV_1 (% predicted) ___ ___ ___ % predicted **(1040)**

   3d. PEFR ___ ___ . ___ ___ L/S **(1050)**

   3e. FEF_{25-75} ___ . ___ ___ 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)**

Asthma Clinical Research Network
NIH/NHLBI

URINE PREGNANCY TEST

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

(Clinic Coordinator Completed)

Complete this form for female subjects only.

1. Is the subject unable to bear children due to any of the following reasons?

1a. Post-menopausal (at least one year since last menses)	☐ 1 Yes	☐ 0 No **(1000)**
1b. Hysterectomy	☐ 1 Yes	☐ 0 No **(1010)**
1c. Tubal ligation	☐ 1 Yes	☐ 0 No **(1020)**

➔ ***If any of the shaded boxes are filled in, a pregnancy test is not required. Proceed to the source documentation box.***

2. Pregnancy test results
   - ☐ 1 Positive
   - ☐ 2 Negative **(1030)**

➔ ***If pregnancy test results are positive, the subject must be terminated from study participation. Complete the appropriate Termination of Study Participation form and follow study termination procedures.***

Subject Source Documentation
Subject's Initials: __ __ __ **(1040)**
Date: __ __ / __ __ / __ __ __ __ **(1050)**

"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 ___ ___ / ___ ___ / ___ ___ ___ ___ **(1020)**
   (Ask the subject his/her date of birth.) 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)**

* R E G I S T R Y *

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.

Asthma Clinical Research Network
NIH/NHLBI

SERIOUS ADVERSE EVENT REPORTING FORM

Subject ID: ___ ___ - ___ ___ - ___ ___ ___
Subject Initials: ___ ___ ___
Visit Number: ___ ___ ___
Current Date: ___ ___ / ___ ___ / ___ ___ (Month / Day / Year)
Coordinator ID: ___ ___ ___ ___ ___ ___

(Clinic Coordinator completed)

This form and a final resolution report (including relevant documents) written by the Principal Investigator should be faxed to the DCC at (717) 531-4359 within 72 hours of notification of a serious event. Also fax the Clinical Adverse Events form (AECLIN), the appropriate Concomitant Medications for Asthma and Allergies (CMED) form, and any relevant source documents.

1. Date of Adverse Event ___ ___ / ___ ___ / ___ ___ ___ ___ (Month / Day / Year) **(1000)**

2. Description of Adverse Event (ICD9 Code) ___ ___ ___ . ___ ___ **(1010)**

   Describe: _____

3. Time interval between taking the study drug (last dose before symptoms) and subsequent onset of symptoms. ___ ___ **(1020)**

4. Unit of time for above interval **(1030)**
   - ☐ 1 second(s)
   - ☐ 2 minute(s)
   - ☐ 3 hour(s)
   - ☐ 4 day(s)

5. Why was the event serious?

   5a. Fatal Event ☐ 1 Yes ☐ 0 No **(1040)**

   5b. Life-threatening event ☐ 1 Yes ☐ 0 No **(1050)**

   5c. Inpatient hospitalization required ☐ 1 Yes ☐ 0 No **(1060)**
   ➔ ***If NO, skip to Question #5d.***

   Admission date ___ ___ / ___ ___ / ___ ___ ___ ___ (Month / Day / Year) **(1070)**

   Discharge date ___ ___ / ___ ___ / ___ ___ ___ ___ (Month / Day / Year) **(1080)**

   5d. Hospitalization prolonged ☐ 1 Yes ☐ 0 No **(1090)**

   5e. Disabling or incapacitating ☐ 1 Yes ☐ 0 No **(1100)**

   5f. Overdose ☐ 1 Yes ☐ 0 No **(1110)**

   5g. Cancer ☐ 1 Yes ☐ 0 No **(1120)**

   5h. Congenital anomaly ☐ 1 Yes ☐ 0 No **(1130)**

   5i. Serious laboratory abnormality with clinical symptoms ☐ 1 Yes ☐ 0 No **(1140)**

   5j. Other *(specify)* _____ ☐ 1 Yes ☐ 0 No **(1150)**

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: __ __ / __ __ / __ __ __ __

Asthma Clinical Research Network
NIH/NHLBI

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 ___ ___ / ___ ___ / ___ ___ ___ ___ (month / day / year) **(1010)**

   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.

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)

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.***