CAPTION
Collaboration Among
Pharmacists and Physicians
To Improve Outcomes Now

The University of Iowa

The CAPTION Trial

MANUAL OF PROCEDURES

ASTHMA INTERVENTION ARM

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I. INTRODUCTION

Despite increased understanding of asthma and improved medications and information on the treatment of asthma, the morbidity and mortality of the disease is increasing. Many causes for these increases have been postulated, including poverty, noncompliance, poor follow-up, improper metered-dose inhaler technique by both patients and providers, and inadequate use of corticosteroid therapy.

The main goal of this study is to determine if a physician-pharmacist collaborative approach to managing care for persons with asthma can achieve better asthma control. We will conduct a prospective train in 11 clinics across the United States. The clinics all employ clinical pharmacists, and many have large populations of under-represented minorities.

A Study Coordinator in each clinic will enroll 15 subjects with persistent asthma. All enrolled subjects will receive Physician-Pharmacist Collaborative Management (PPCM) of their asthma for 9 months. Subjects will be followed for a total of 18 months. Measures of asthma control at two time points after enrollment in the study will be compared to the 9 month time period prior to enrollment in the study

A projected timetable for study activities is provided in APPENDIX I.

A. Protocol Synopsis

Primary Endpoint

The primary aim of this study is to determine if patients 12 years or older with a diagnosis of persistent asthma who receive Physician-Pharmacist Collaborative Management (PPCM) of asthma can achieve improved asthma control. The primary endpoint used to evaluate this aim will be the number of emergency department visits during the 9-month study period and also at 18 months from the initiation of the intervention compared to the 9-month time period prior to enrollment into the study.

Secondary Endpoints

Secondary aims and their associated endpoints are designed to:

1) Determine whether the PPCM intervention leads to improved quality of life. The secondary endpoint used to measure this aim will be scores on the Asthma Quality of Life Questionnaire at 9 and 18 months compared to baseline.
2) Determine whether the PPCM intervention leads to improved asthma control. The secondary endpoint used to measure this aim will be the Asthma Control Test scores at 9 and 18 months compared to baseline.

B. Inclusion and Exclusion Criteria

Inclusion Criteria

1) English or Spanish speaking males or females
2) At least 12 years of age
3) Diagnosis of persistent asthma (can be mild, moderate, or severe as long as patients don't meet any exclusion criteria)

Exclusion Criteria

1) Hypertension which would qualify them for the BP control group
2) History of severe, life-threatening asthma evidenced by a history of loss of consciousness, ICU admissions or mechanical ventilation due to asthma
3) Diagnosis of chronic obstructive pulmonary disease
4) Previous involvement in a multidisciplinary asthma management clinic
5) Pregnancy
6) Poor prognosis with a life expectancy estimated less than 2 years
7) Residence in a nursing home or diagnosis of dementia
8) Inability to give informed consent
9) Impaired cognitive function (>2 errors on the Short Portable Mental Status Questionnaire)
10) Asthma medications are EXCLUSIVELY prescribed and adjusted by a pulmonologist, not by the patient's primary care physician

C. Study Organization

Two teams of investigators at the University of Iowa are jointly conducting this study. Contact information is given for key members of each team.

The **Clinical Coordinating Center (CCC)** within the College of Pharmacy at the University of Iowa is responsible for the following key aspects of the trial:

1) Selection of participating sites
2) Assisting sites in obtaining approval for the study from their local Institutional Review Board
3) Negotiating with sites the work that is to be completed and the compensation that sites will receive
4) Training of site staff

Clinical Coordinating Center		
Barry L. Carter, Principal Investigator	barry-carter@uiowa.edu	319-335-8456
Gail Ardery, Clinical Site Director	gail-ardery@uiowa.edu	319-384-4128
Rosemary Tiwari, Project Manager	rosemary-tiwari@uiowa.edu	319-384-4651
CAPTION Fax Number		319-335-9511

The **Data Management Center (DMC)** within the Clinical Trials Statistical and Data Management Center in the College of Public Health at the University of Iowa is responsible for the following key aspects of the trial:

1) Creation of the trial's database
2) Creation of procedures for online submission of research data from sites.
3) Monitoring procedures at research sites.

Data Management Center		
Chris Coffey, Director, DMC	christopher-coffey@uiowa.edu	319-384-4197
Dixie Ecklund, Assoc. Director, DMC	dixie-ecklund@uiowa.edu	319-335-8446
Sushma Gampa, Protocol Coordinator/Monitor	sushma-gampa@uiowa.edu	319-384-4763
Jill Kuennen, Lead Data Manager	jill-kuennen@uiowa.edu	319-353-3041
Michele Costigan, Lead Protocol Coordinator	michele-costigan@uiowa.edu	319-384-4183
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Elizabeth Cozzie, Data Manager	elizabeth-cozzie@uiowa.edu	319-384-2751
Ankita Singhal, Data Manager	ankita-singhal@uiowa.edu	319-384-2750

D. Regulatory Requirements and Clinical Study Document Collection

Each site will be required to complete the following study-related tasks and to store and transmit to the University of Iowa CCC the relevant documents listed for each task.

1) IRB Approval

   Each site must obtain approval for the study from its local Institutional Review Board, including approval of study procedures and approval of informed consent documents. Required documents include:

   - The Institutional Review Board's letter of approval for the study.
   - All stamped informed consent documents approved and dated by the local IRB.

2) Site Signature Log

   Each site must submit a Site Signature Log to the CCC. The website will include a template for the log which each site can download (see APPENDIX II). The Physician Leader and the Study Coordinator must print his/her name, indicate all of the responsibility codes that describe their role(s) on the study and sign the document.

3) Subaward Agreement with the University of Iowa

   Administrative personnel at each site must also negotiate and sign a Subaward document created by the University of Iowa Department of Sponsored Programs. The agreement describes the terms and conditions for reimbursing sites for study-related costs.

   Dr. Ardery at the CCC will serve as the lead contact for questions regarding the subaward process.

Each of these study documents should be stored in a central, secure location where they can be easily found by site personnel who are working on the project.

In addition, a copy of each document will also need to be sent to the University of Iowa CCC by one of the following methods:

Scan and email to the CCC at gail-ardery@uiowa.edu

Fax to 319-335-9511

I. SITE TRAINING AND MONITORING

A. Initial Training Sessions

Regional conference training sessions for physician and pharmacist clinical leaders

We will use a "train the trainer" approach for the pharmacist and physician leader before patient enrollment begins. The session will be held live and led by Dr. Barry Carter, the study's Principal Investigator. The session will focus on:

- Strategies to effectively implement PPCM
- Strategies found to be most effective in overcoming clinical inertia, adverse drug reactions and poor medication adherence.
- Organizational strategies to operationalize PPCM, including identifying patients, alerting providers, creating referral structures and improving communication.
- Ways to establish a billing structure using the newly approved CPT codes to bill for pharmacist management services.
- A refresher for asthma management based on EPR-3 guidelines.
- The University of Iowa College of Medicine and the Collaborative Education Initiative (CEI) will provide continuing education credit for physicians and pharmacists respectively.

Local training of clinic physicians and pharmacists

Within one month of the regional training session, each physician-pharmacist pair will deliver the same intervention training program in their own clinic for all providers in the office during an expanded version of their noon conferences or in two separate conferences. The pharmacist will provide teambuilding and training sessions with their physicians twice a year for two years.

Follow-up contacts with University of Iowa Researchers

Following the initial local training sessions, Drs. Carter and Ardery will conduct a telephone conference with each physician-pharmacist pair to discuss any questions or issues that the providers were not able to answer regarding the training.

If there are organizational or financial barriers being encountered, Dr. Ardery will work with the clinic administrator to improve staffing, billing or other barriers. Drs. Carter and Ardery, in consultation with Dr. Vaughn, will continue to support these offices quarterly via telephone conference call during the first year and twice a year during year two.

Study Coordinator Training

The Study Coordinator will be required to obtain certification in human subjects protection education, either through a local educational institution or through a national certifying agency. This certification must meet criteria established by the site's governing Institutional Review Board.

Faculty and staff from the University of Iowa will hold a joint training session for Study Coordinators in Iowa City. Session content will include:

- Study design
- Ethical procedures for recruitment and informed consent
- Proper completion of case report forms
- Procedures for uploading data electronically to the DMC.

The CCC will email to all members of the site research team a weekly benchmark enrollment report comparing study sites.

B. Site Activation

Before each site can be fully activated and begin enrolling subjects the following tasks must be completed:

a. The letter of approval from the site's local IRB must be emailed to the CCC.

b. The IRB-approved consent documents for each site must be reviewed and approved by the CCC.

c. Each site must generate a list of all patients who have a qualifying ICD9 code and inform the CCC of the total number of unique patients on the list. More detailed instructions are provided in Section III.A Screening and Enrollment.

d. Each site must submit a Site Signature Log to the CCC. The website will include a template for the log which each site can download (see APPENDIX II). The study Physician Leader, Pharmacist Leader, all pharmacists who will be implementing the intervention and Study Coordinator should list their names, one or more responsibility code(s) to describe their role(s) on the study, and then sign the document. The site PI should sign and date at the bottom of the document after all personnel have completed their respective lines.

The completed Site Signature Log should either be faxed to 319-335-9511 or scanned and sent via email to gail-ardery@uiowa.edu.

C. Interim Monitoring Visits

The purpose of the monitoring visit is to ensure that the protocol is being followed, that subject's rights and safety are being protected, and to confirm data integrity and quality.

All centers will be monitored as scheduled by monitors from the Data Management Center. The first monitoring visit will occur after the first five subjects have been enrolled at a center or approximately three months after the first subject is enrolled, whichever comes first. All centers will have a close-out visit.

Study monitors will have access to medical records but will have NO contact with patient subjects.

Pre-Monitoring Procedures

1. The monitor will email the Study Coordinator with possible dates for the monitoring visit approximately 4-6 weeks ahead of these dates. Plan on at least two days for the visit. The Study Coordinator and PI should be available to meet with the monitor during the visit.

2. The monitor will send a letter to the center approximately 2 weeks ahead of the scheduled monitoring visit date explaining objectives of the visit and necessary materials. The monitor will need a reserved space in which to work and access to a photocopy machine and electronic records, if applicable. The following items should be available for review:
    - Screening Logs
    - Patient Clinic/Medical records
    - Paper copy CRFs and any other study-related source documents and records
    - Regulatory Documents
        - Site Signature log
        - IRB approvals
        - Approved informed consent documents
        - Approved recruitment materials
        - IRB correspondence
        - Certifications

On-site Monitoring

1) An initial meeting (approximately 30 minutes) will occur between the Study Coordinator and the monitor to orient the monitor to clinic/medical records, answer study questions, and review protocol procedures. The Study Coordinator should be available periodically throughout the visit to answer questions or to make data corrections, if necessary.
2) At the end of the monitoring visit, the monitor will meet briefly with the Study Coordinator and PI to discuss findings and a plan of action.

Post-Monitoring

1) The monitor will send the Study Center a formal report containing feedback and a detailed listing of all findings within 4 weeks of concluding the monitoring visit.
2) The monitor will contact the Study Coordinator to discuss pending items until all items are resolved. The Study Coordinator will respond to pending items in a timely manner and inform the monitor of any issues delaying resolution of the item.

D. Protocol Review Calls

Following the local training sessions for physicians, Drs. Carter and Ardery will conduct a telephone conference with each Physician Leader to discuss any questions or issues that the site leaders were not able to answer.

Drs. Carter and Ardery will continue to support these offices through teleconferences to be held:

- Quarterly during the first year
- Twice during the second year

During these calls, Drs. Carter and Ardery will review the protocol and individual site performance.

E. Close-Out Visits

A study monitor from the University of Iowa will visit each site at the end of the study to close-out that site's participation in the study.

F. Organizing and Maintaining Study Files

1. Each patient should have a study file containing signed informed consent document, completed case report forms and other source documentation.
2. Arrange patient files in order of study visits.
3. Complete paper copy CRFs before entering data on the website.
4. If corrections to paper copies are needed, draw a single line through the incorrect response, write the correct response, and initial and date the correction. White-Out or other similar products that obscure the original response may not be used on source documents.
5. Keep all Regulatory documents together in a binder.
    - IRB documents tab: All approval letters, modification/amendment submissions, approved and stamped copies of documents such as recruitment materials and ICFs, any correspondence with the IRB.
    - IRB reports tab: Some IRBs have separate templates for sites to report serious adverse events and protocol deviations. If your IRB requires such reporting please include these reports under this tab.
    - CAPTION Study tab: monitoring pre-visit letters, monitoring post-visit letters, site signature logs and study related certifications such as protocol training, data entry training for all staff members (past and present) who work on CAPTION should be filed here.

II. PROCEDURES FOR STUDY COORDINATORS

A. PATIENT SCREENING AND ENROLLMENT

The Study Coordinator will obtain informed consent from up to 30 patients with persistent asthma. **Your enrollment target is 15 qualifying subjects** who meet all inclusion criteria, sign informed consent and pass mental status screening. If you do not succeed in enrolling 15 qualified patients before 30 have signed informed consent, you must submit a modification to your IRB before consenting ANY additional subjects.

One focus of the study is management of asthma in minority populations. Our goal across sites is for 40% of enrolled patients to represent a minority population. The enrollment numbers displayed in APPENDIX III serve as individual site targets for minority enrollment. Not all sites have a sufficiently large minority population to achieve this level of minority enrollment. Other sites are likely to achieve far greater minority enrollment. The randomization methodology described below should never be violated in order to increase minority enrollment. And minority patients should not be pressured to join the study. However, Study Coordinators can promote minority subject retention by working diligently to accommodate subjects' schedules and assisting with transportation costs when possible.

Enrollment of subjects involves the following steps:

1) Identifying Patients Who Might Qualify for the Study

   - Request from your Information Technology staff a list of all patients who were seen in the clinic during the past 24 months and who carry a diagnosis of asthma (ICD9 code 493). Asthma does not need to have been the primary reason for any visit. The list may be in any order, whether alphabetical, by medical record number, date or random. (See APPENDIX X for details on requesting the list.)
   - If the list is not numbered, insert a Patient Number next to each patient's name on the list you receive, assigning the first patient name on the list Patient Number 1, the second patient on the list Patient Number 2, etc. Continue numbering throughout the entire list.
   - Ask the lead physician on the study to review the list for accuracy in numbering.
   - Communicate the total number of patients on your list to the CCC via email to gail-ardery@uiowa.edu.
   - NEVER send to the CCC a list that contains patient identifiers.
   - If you can de-identify the list (by deleting columns with names, birthdates or medical record numbers) and have anything except the numbering remaining, make a copy of the first 3 pages of your numbered list. Fax the first three pages of the resulting de-identified numbered list to 319-335-9511. The CCC will let you know of any concerns with the list or with the numbers assigned to the list.
   - If de-identifying the list leaves only the numbering visible, the CCC will review via telephone the critical indicators of an accurate list.

- Once the numbered list is finalized, you will receive Random Screening Numbers within 2 weeks. Do NOT begin screening until you receive Random Screening Numbers for patients on your list.

2) Determining the Order In Which Patient Records Are Screened

- You will receive from the CCC a Screening Log with multiple columns. A template for the log and a sample log are provided in APPENDIX IV.
- Use the screening log to track your screening and enrollment efforts. You may complete the log either on paper or electronically. Retain the ENTIRE log for the duration of the study. A sample screening log may be found in APPENDIX IV.
- Two columns of the Screening Log will be filled in:

  Column B: Random Screening Numbers, which indicate the order in which you should screen each patient

  Column C: Patient Numbers, which represent the numbers you assigned to your patient list from IT

ALWAYS SCREEN PATIENTS IN ORDER ACCORDING TO THE RANDOM SCREENING NUMBERS.

3) Logging the Screening and Enrollment Process

- **RETAIN THE SCREENING LOG FOR THE DURATION OF THE STUDY.** You will be asked to fax or email a de-identified copy of the log to the CCC monthly.
- The Study Coordinator will review the medical records in the order supplied by the DMC to determine if each patient meets study inclusion criteria and does not meet any of the study's exclusion criteria.
- Begin screening with the patient who has been assigned Random Screening Number 1 in Column B of the log. Use the paired Patient Number given in Column C of the log to easily find the patient on your IT list. Write the patient's name into Column A of your log.
- Consider the following information from each patient's medical record:
  - Diagnoses: Patient has a diagnosis of persistent asthma
  - Exclusion Criteria: Review Problem List and clinical notes to identify medical conditions that disqualify the patient. Try to determine if the patient's medications are prescribed and adjusted only by a pulmonologist, not by the patient's primary care physician.
  - Active in the Clinic: Determine that the patient remains in the practice.

- Complete columns D, E, F and G as follows:

  Column D: Enter Y if the subject was disqualified due to having severe, life-threatening asthma or COPD.

  Column E: Enter Y if the patient has other exclusion criteria that are disqualifying; otherwise, enter N.

  Column F: Enter Y if the patient has left the practice; otherwise, enter N.

  Column G: Enter Y if the patient seemed to meet screening criteria based on medical record review; otherwise, enter N.

YOU DO NOT NEED TO COMPLETE REMAINING COLUMNS FOR ANY PATIENTS FOR WHOM YOU WROTE "N" INTO COLUMN G.

Patients who appear to meet all of the inclusion criteria and none of the exclusion criteria will be invited to participate in the study. If they agree to participate, they will be scheduled for a baseline visit, sign informed consent and be enrolled if they continue to meet the inclusion criteria.

4) Mailing out IRB-approved letters of invitation to potential active observation patients

Your IRB has approved (and possibly stamped) a letter of invitation about the study. This letter should be mailed to each patient who seems to meet all of the medical record screening criteria, that is, those for whom you entered Y into column G of the log. The mailing will include:

- An invitational letter that provides a brief description of the study. The letter will be written in Spanish if the patient only speaks Spanish. You should enroll Spanish-only speakers only if you have an IRB-approved Spanish invitation letter and consent form and your clinic has a staff member who can interpret during study visits.
- A response card and the date by which the card should be returned. The letter will include a statement that the patient will be called if the card is not returned by this date. The letter will include an explanation of how the patient can avoid the call by returning the card or calling the staff to decline participation.

Please mail out letters on your clinic letterhead according to the following procedures:

- Your first mailing can include the first 30 pre-screened patients designated by the random order list from the DMC.
- The size of subsequent mailings should be determined by the number of patients that you still need to enroll. Your target for total number of patients who sign consent AND pass all screening requirements = **15**.

Some sample situations for how to handle subsequent mailings are described below. The goal is to not send out letters that will substantially exceed the number of patients you need to enroll. Therefore, the size of each subsequent mailing should again be determined by the number of patients you still need to enroll.

- Once you enroll 5 patients and have exhausted most patients remaining in the initial mailing, you could mail out letters to the next 30 patients designated by the random order list.
- Once you have enrolled 10 patients and have exhausted all patients to whom you have mailed the letter of invitation, you could mail out letters to the next 5 patients designated by the random order list.

Although patients must be invited in the order specified on the random list, ***baseline visits may be scheduled per the patient's preference***. In other words, it is not necessary to have the 15th patient on the list be fully enrolled before you can schedule a visit with the 16th patient on the list.

If you have a patient contact you after you have categorized the patient as "Unable to Contact" (see Column R below) and the patient is interested in participating, you may include that patient, even if your total number enrolled exceeds 15. However, due to limited funding and staff resources, please keep enrollments > 15 to a minimum.

5) Continue Logging the Screening and Enrollment Process

In columns H-K of the log, fill in the outcomes of your attempts to reach each patient by mail:

Column H: Enter the date on which the invitation letter was mailed.

Column I: Enter the date on which you received the return postcard. Enter N if the postcard is never returned.

Column J: Enter Y if the patient declined on the postcard and shred the postcard. Enter N if the postcard is never returned or if the patient expressed interest in hearing more about the study.

Column K: Enter Y if the patient expressed interest in hearing more about the study on the postcard. Enter N if the card is never returned or the patient declined on the card.

In columns L-V, log your attempts to reach the patient by phone. Review your IRB's determination regarding the timing and number of calls. If your IRB has approved a phone script, be sure to follow the script during these calls.

Columns L-Q: Enter each date on which you called the patient or the patient returned your call. Although the spreadsheet gives you room to log 6 calls, THE TIMING AND THE NUMBER OF CALLS THAT YOU MAKE SHOULD FOLLOW THE TIMING AND NUMBER OF CALLS APPROVED BY YOUR IRB AND SPECIFIED IN YOUR SITE'S LETTER OF INVITATION. Leave blank any columns M-Q that you do not use to log calls.

Column R: Enter Y if you were never able to reach the patient by phone. You do not need to attempt further contacts if you have exhausted the number of calls that your IRB has authorized. Enter N if you were able to reach the patient by phone.

Column S: Enter Y if the patient declined over the phone to participate. Otherwise, enter N.

Column T: Enter Y if the patient reported a disqualifying health condition over the phone. Otherwise, enter N.

Column U: Enter Y if the patient indicated over the phone that s/he was interested in learning more about the study. Otherwise, enter N.

Column V: Enter Y if the patient was interested but you were not able to negotiate a date for the baseline study visit. Otherwise, enter N.

In columns W-AB, log the results of your efforts to schedule/complete the patient's baseline visit:

Column W: Enter Y if the patient declined to sign consent during the baseline visit. Otherwise, enter N.

Column X: Enter Y if the patient signed informed consent. Otherwise, enter N.

Column Y: Enter Y if the patient scored 3 or more incorrect responses on the Short Portable Mental Status Questionnaire. Otherwise, enter N.

Column Z: Enter Y if an exclusion criterion was discovered after the patient signed consent. Otherwise, enter N.

Column AA: Enter Y if the patient was fully enrolled in the study. Otherwise, enter N.

Exhausting the List of Patients

If the list of patients is exhausted before you enroll 15 patients who fully qualify for the study, a new patient list can be run. However, the CCC should be notified before a second list is run.

Newly Diagnosed Patients

Patients who develop asthma after the initial patient list is generated cannot be included in the study. Once the original list is exhausted, let the CCC know that you need to generate a new list of patients. Patients with newly diagnosed asthma can be added at that time.

Patient Referrals to the Study

Patients cannot refer themselves to the study. Physicians or other clinic personnel cannot refer patients to the study. The only way a patient can be considered for the study is if the Study Coordinator considers the patient in the randomized order specified by the DMC.

Procedures for an Incorrect Count on the Patient List

If you determine that you provided an incorrect total number of patients on your screening list, inform the CCC as quickly as possible.

Incorrect Patient Enrollment/Protocol Deviation

If you determine that you enrolled a patient who does not qualify for the study, you must complete CRF#24. Protocol Deviation form. For more information, see section VIII SERIOUS ADVERSE EVENTS AND PROTOCOL COMPLIANCE.

B. Standard Operating Procedures for Obtaining Informed Consent

Only the Study Coordinator may obtain informed consent from patients. Other clinic staff may not refer patients to the study or review the consent document with patients. Staff members are welcome to take patient questions regarding the study and refer them to the Study Coordinator as needed.

The Study Coordinator MUST obtain signed consent from the patient on all consent documents before undertaking any other research procedures, including mental status screening.

1) Before meeting with the patient on the Baseline visit, make sure that your IRB-approved consent documents are still valid.
    - Each consent form is valid for a maximum of 12 months from the date of approval and often for less time when the approval process is long.
    - If your IRB dates your approved consent documents, make sure that the date the patient is being enrolled falls within the dates specified on the consent. You should NEVER have a patient sign a consent that has expired.
2) When your IRB provides a new consent, be sure to email all approved and dated/stamped documents and the IRB approval letter to gail-ardery@uiowa.edu.
3) The Study Coordinator will give the subject a consent document to read and review.
4) The Study Coordinator will specifically explain the following aspects of the study:
    - Purpose of the research study, duration of study participation, and the number of research visits or study contacts (e.g. telephone calls) required.
    - Which parts of the study are investigational (in this case the pharmacy intervention).
    - The study procedures/requirements.
    - The risks of the study.
    - The voluntary nature of the study – that the subject may stop the study at any time.
    - When a subject's participation in the study may be stopped (safety, compliance, sponsor stops the study).
    - HIPAA section – the clinic investigators must be allowed to have access to the participant's medical information and to create medical information in order for the subject to be in the study.
    - Contact information in case of a research-related Injury.
5) The Study Coordinator asks the subject what questions they have and provides answers.
6) For subjects whose capacity to consent, understand the study procedures, or read the consent form is in question, we recommend that the Study Coordinator provides some documentation of the patient's ability to sign consent. A template titled "Evaluation to Sign Informed Consent Document for Research" is provided in APPENDIX V. However, it is imperative that sites follow pertinent procedures specified by the local IRB. The

evaluation document should be stored in the subject's study file. It cannot be entered into the database. If you doubt that a patient is not able to sign informed consent, explain that you are choosing not to have the patient continue in the study.

7) If after reading the consent document and having their questions answered a patient agrees to participate in the study, the patient will sign and date the consent document.
8) The Study Coordinator then signs and dates the consent document.
9) The Study Coordinator will then make two COMPLETE copies of the consent document. One copy will be placed in the chart or medical record, unless the clinic does not permit this. The patient will be given a copy, and the original will be placed in the study case report binder. If clinic policy explicitly prohibits placing a copy of the signed consent in the patient's medical record AND the local IRB does not require placing a copy in the medical record, then clinic policy should be followed.
10) The signed consent forms will be reviewed by study monitors from the University of Iowa during interim monitoring visits to ensure compliance with the informed consent process.

1. Procedures for Spanish-Only Speakers

Either the University of Iowa Clinical Coordinating Center will translate your IRB-approved consent form into Spanish, or your clinic can arrange for translation.

Utilize bilingual Study Coordinators or interpreters within the office to explain the study and assist with obtaining informed consent.

When needed, have an interpreter present during clinic visits and telephone calls with the Study Coordinator.

The interpreter reads each question and obtains the responses from the patient.

The Study Coordinator remains present at these sessions to assist with any questions and to record data.

2. Procedures for Patients Who Cannot Read or Whose Ability to Give Informed Consent Is Not Clear

For subjects whose capacity to consent, understand the study procedures, or read the consent form is in question, we recommend that the Study Coordinator provides some documentation of the patient's ability to sign consent. A template titled "Evaluation to Sign Informed Consent Document for Research" is provided in APPENDIX V. However, it is imperative that sites follow pertinent procedures specified by the local IRB. The evaluation document should be stored in the subject's study file. It cannot be entered into the database. If you determine that a patient is not able to sign informed consent, explain that you are choosing not to have the patient continue in the study.

If the Study Coordinator suspects that a patient has difficulty with reading comprehension, s/he may read the consent form to the patient, if the patient is willing and this procedure is permitted by the local IRB.

The pharmacists can use diagrams of clocks and numbers of pills including the color and shape drawn next to the clock to show when each is used. Family members will be asked to assist if they are able to do so.

C. *Scheduled Visits for Subjects Enrolled in the Asthma Intervention Group*

INITIAL VISIT (BASELINE) – *After obtaining informed consent*, the Study Coordinator will:

1) Administer the Short Portable Mental Status Exam
   a. Adjust the patient's score for patient education level and race;
   b. If the patient's adjusted score is 3 or higher, explain that s/he cannot remain in the study. Do not continue with other activities; document screen failure in the tracking log.
   c. If the patient's adjusted score is 2 or lower, proceed with the remaining baseline activities.
   d. Complete the subject's final adjusted score on CRF#1. Informed Consent.
2) Verify that the subject meets all inclusion criteria and does not meet any of the exclusion criteria. On the Source Document for Verification of Inclusion and Exclusion Criteria (APPENDIX VI) is a list of each inclusion and exclusion criterion. Check the box associated with each criterion to verify that the subject meets each inclusion criterion and does NOT meet any of the exclusion criteria. If the subject fails to meet any one of the inclusion criteria or if the subject meets one or more exclusion criteria, explain to the subject that s/he does not qualify and will not have further study visits. Do NOT collect additional data.

   When completed, file the Source Document for Verification of Inclusion and Exclusion Criteria in the subject's study file. The document is NOT entered into the study database.
3) Administer patient surveys using the following forms:

   CRF#11. Asthma Demographic

   CRF#12 Asthma Control Test

   CRF#15. Asthma Medications

   CRF#14. Asthma Medication Adherence – complete Part A only

   CRF#17. Asthma Patient Self-Report: Oral corticosteroid courses prescribed during the 9 months prior to enrollment

   CRF# 18. Asthma Quality of Life Questionnaire

4) REFER ALL QUALIFYING, ENROLLED SUBJECTS TO THE INTERVENTION PHARMACIST.

5) Review the patient's medical record for the following information and supplement subject responses as needed on the following forms:

   CRF#11. Demographic Information: The duration of the patient's asthma

   CRF#13. Asthma Medical Record Abstraction: Healthcare utilization in past 9 months

   CRF#17. Asthma Patient Self-Report: Oral corticosteroid courses prescribed in the 9 months prior to enrollment

   CRF#15. Asthma Medications: Record current asthma medications, doses and frequency of administration as listed in the medical record; complete patient report on adherence (item 2.f)

9 MONTH VISIT (scheduled 8-10 months after enrollment) – At this visit, the Study Coordinator will:

1) CRF#15. Asthma Medications: Record current asthma medications, doses and frequency of administration as listed in the medical record; complete patient report on adherence (item 2.f)
2) Administer patient surveys using the following forms:
    a. CRF#12. Asthma Control Test
    b. CRF#14. Asthma Medication Adherence
    c. CRF#17. Asthma Patient Self-Report: Oral corticosteroid courses prescribed since the baseline visit with the Study Coordinator
    d. CRF# 18. Asthma Quality of Life Questionnaire
3) CRF#2. Serious Adverse Event: Assess for a serious adverse event; only enter data electronically on events that qualify as SAEs.
4) Collect the following information from the medical record:
    a. CRF#13. Asthma Medical Record Abstraction: Healthcare utilization in past 9 months

18 MONTH VISIT (FINAL CONTACT) (scheduled 17-19 months after enrollment) – This visit may be conducted via telephone. During this visit, the Study Coordinator will:

1) CRF#15. Asthma Medications: Record current asthma medications, doses and frequency of administration as listed in the medical record; complete patient report on adherence (item 2.f)
2) Administer patient surveys using the following forms:
    a. CRF#12. Asthma Control Test
    b. CRF#14. Asthma Medication Adherence
    c. CRF#17. Asthma Patient Self-Report: Oral corticosteroid courses prescribed since the 9 month visit with the Study Coordinator
    d. CRF# 18. Asthma Quality of Life Questionnaire
3) CRF#2. Serious Adverse Event: Assess for a serious adverse event; only enter data electronically on events that qualify as SAEs.
4) Collect the following information from the medical record:
    a. CRF#13. Asthma Medical Record Abstraction: Healthcare utilization in past 9 months

IV. PROCEDURES FOR CLINCAL PHARMACISTS AND CLINIC PHYSICIANS

A. Clinical Pharmacist Procedures

Scheduled Patient Visits

The clinical pharmacist will follow each subject for approximately 9 months following enrollment in the study. Recommended visit activities and frequencies are outlined below:

1) Initial Visit

   The pharmacist will conduct the following activities at the initial visit, requiring 30-45 minutes:

   a. Review the subject's medical record and perform a structured interview, including:
      - A detailed medication history of all prescription, nonprescription, and herbal therapies
      - An assessment of subject knowledge of asthma medications, purpose of each medication, goals of therapy, medication dosages and timing, and potential medication side effects
      - Administer and review the results of the Asthma Control Test
      - Evaluate subject's inhaler technique by reviewing the technique, then actually watching the patient utilize an MDI
      - Potential contraindications to specific pharmacologic agents
      - Expectations that there will be future dosage changes and monitoring and the pharmacist will discuss issues that might become future barriers to asthma control (e.g., side effects, non-adherence, environmental/situational factors)

   b. Direct subjects to pertinent written educational materials.

   c. Supply aids (medication logs or spacers), a wallet card listing all medications and doses, contact phone numbers for the pharmacist and asthma goals for patients with memory problems or unintentional non-adherence.

   d. Create a care plan with treatment recommendations for the physician. The care plan will make specific recommendations to improve medication management to achieve asthma control. All recommendations will begin with NHLBI EPR-3 guidelines and be individualized from there.

   e. Document all visits, recommendations made to the physician and recommendations accepted by the physician in the medical record or the pharmacy record, depending on the policies and procedures in the office, and on the study's Pharmacist Encounter Form.

   f. Present the care plan directly to the physician unless the physician prefers written or electronic communication.

g. Implement the care plan after obtaining physician agreement or physician modifications.

h. Pharmacists may choose to electronically enter the Pharmacist Encounter Form for each visit into the study database themselves. However, pharmacists who choose to enter these forms must initially complete the form on paper. Moreover, they must complete website data entry training with the DMC via a brief phone call. To enter the form, the pharmacist **MUST** enter a code for each drug referenced on the form. Alternately, the pharmacist can write in the drug name and dose and give the hard copy form to the Study Coordinator, who will fill in drug codes. A copy of the drug codes may be found in APPENDIX VII.

2) Follow-Up Visits

The PPCM model *recommends* structured face-to-face follow-up visits with the subject at the following time points after the baseline visit. However, the pharmacist may tailor subject visit schedules to meet the individual subject's needs. If a subject's asthma is well-controlled, perhaps telephone follow-up may be appropriate for *some* of the later visits.

- 2 months
- 4 months
- 6 months
- 8 months

Each follow-up visit is estimated to take 10-15 minutes and will include assessment and documentation of the following on CRF#16. Asthma Pharmacist Encounter:

- Current asthma medications
- Medication adherence
- Modification of the care plan as needed, with changes also documented in the subject's medical record
- Communication with the subject's physician as needed

In addition, the pharmacist should assess for:

- Serious adverse events (submission of CRF#2. Serious Adverse Event is only required if the pharmacist identifies a serious adverse event that occurred since the last pharmacist visit.)
- CRF#12. Asthma Control Test

The PPCM model also recommends additional visits if asthma remains poorly-controlled.

Documentation

The pharmacist should complete CRF #16 Asthma Pharmacist Encounter Form after every contact with a study patient including phone follow ups.

The pharmacist should also complete CRF # 12 Asthma Control Test at every visit. It can also be administered during a pharmacist phone call with a subject but is not required.

Sites may choose to have the Study Coordinator enter the Pharmacist Encounter Forms into the study database or to have the clinic pharmacist enter the data from this form into the database. The form includes a name field, which should be completed if the pharmacist intends for the Study Coordinator to enter these data. The database will not include the name field.

Billing

Part B of the Pharmacist Encounter Form asks for detailed information on the time the pharmacist spends on various activities related to study visits. It is important for pharmacists to complete Part B even if the clinic is not billing payers for pharmacist study visits.

The Data Management Center (DMC) will automatically code each visit as either a 'new patient' visit or an 'established patient' visit and assign the codes for 99605 and 99606, respectively.

The DMC will also automatically account for the first 15 minutes of each visit using either code 99605 or 99606.

The pharmacist will need to calculate the number of CPT units that could be billed based on visit time beyond the first 15 minutes of each visit.

The pharmacist should follow the detailed instructions provided in APPENDIX XI DOCUMENTATION OF PHARMACIST TIME in order to complete Part B of the Pharmacist Encounter Form.

B. Clinic Physician Procedures

The Study Coordinator will notify both the clinic physician and the pharmacist of patients who are enrolled into the asthma study.

For each subject, the clinic pharmacist will create a care plan with treatment recommendations, including steps for improving medication management to achieve improved asthma control

The pharmacist care plan will be documented in the subject's medical record or pharmacy record.

The pharmacist will communicate the care plan directly to the subject's physician at the time of the patient's initial visit with the pharmacist. Communication may be either face-to-face or electronic.

The clinic physician will either agree with the care plan or modify the care plan.

The pharmacist will document care plan modifications made by the physician, if any.

The physician will collaborate with the pharmacist to achieve improved asthma control throughout the subject's time in the study.

The physician may delegate medication and dosage changes to the pharmacist without direct consultation each time, if the physician prefers this approach.

V. INSTRUCTIONS FOR COMPLETING CASE REPORT FORMS

All case report forms (CRFs) excepting physician and pharmacist surveys will be stored on the website for downloading. Sample hard copy forms are provided in APPENDIX VIII.

All case report forms should be completed on paper. Paper forms are considered to be source documents and should be securely stored in the subject's research file in a locked file cabinet in a locked office.

Paper forms must carry each subject's study ID, not their name. The only permitted exception is the Pharmacist Encounter Form.

Study Coordinators should electronically enter data from the paper CRF to the electronic case report form (eCRF).

FORMS SCHEDULE: ASTHMA INTERVENTION GROUP

Scheduled visits should be completed during the 60 day period surrounding the due date, that is, 30 days before the due date – 30 days after the due date.

Time Points (Study Visit)	Baseline	9 months	18 months	Event Driven
Visit Window	NA	+/- 1 mo	+/- 1 mo	
CRF#1. Informed Consent	X			X
CRF#2. Asthma Serious Adverse Event		X	X	X
CRF#3. Study Termination				X
CRF#11. Asthma Demographic	X			
CRF#12. Asthma Control Test	X	X	X	X
CRF#13. Asthma Med Record Abstraction	X	X	X	
CRF#14. Asthma Medication Adherence	X	X	X	
CRF#15. Asthma Medications	X	X	X	
CRF#16. Asthma Pharmacist Encounter				X
CRF#17. Asthma Patient Self Report	X	X	X	
CRF#18. Asthma Quality of Life Questionnaire	X	X	X	
CRF#24. Protocol Deviation Form				X

Some CRFs will require medications to be entered into a table. The medications are identified by a code on the list of Drug Codes for Asthma Medications. The eCRF will not accept medications that are not on the list. If you need to enter such a medication, contact the CCC and provide the name of the medication. They will assign a code and inform the DMC that a new medication needs to be added to the list of medications. After this has occurred, the CCC will notify you that it is now possible to enter your data.

CRF#1.Informed Consent

This form must be completed for all subjects consented into the study. A subject ID will be generated when the form is submitted. Record this number on all paper CRFs completed for the subject.

Item 1: Select 'Alternative asthma intervention' as the type of consent.

Item 2: A version number and/or version date must be entered to identify the version of the inform consent document used.

> Item 2.a: Enter the version number available on the footer of the consent document. If no version number is available, select the N/A check box. If the N/A check box is selected, any value entered in the version number field will be cleared.
>
> Item 2.b: Enter the version date or date of approval of the consent document or select the N/A check box. This information is typically available on page 1 of the informed consent document. If the N/A check box is selected, any value entered in the version date field will be cleared.

Item 3: Enter the date on which the subject signed the informed consent document referenced in Item 2.

Item 4: Enter the subject's final adjusted score on the Short Portable Mental Status Questionnaire used to screen subjects for mental deficiencies. If the score is >2, a subject ID will be generated but no additional eCRFs will become available for the subject.

Item 5: Do NOT complete this item for patients designated for the alternative asthma intervention.

Item 6: Indicate if the subject is ineligible for another reason not included in item 4 or 5. If yes is selected, enter an explanation in the text field (Item 6.a); a subject ID will be generated but no additional eCRFs will become available for the subject.

CRF#2. Serious Adverse Event

Complete Sections A and B on the hard copy form at the time of each Study Coordinator follow-up visit with subjects. These items will not be entered into the database. However, a copy of the completed paper form should be retained in the subject's file for monitoring.

Part A

> Visit Date: Enter the date of the study visit.
>
> Item A.1: Ask the subject the question as written on the CRF and select either the 'Yes' or 'No' option.
>
> Item A.2: Ask the subject the question as written on the CRF and select either the 'Yes' or 'No' option.

Part B

> Item B.1: Review the medical record for the time period since the last study visit. Select 'Yes' for this item if an SAE is found documented in the medical record.
>
> Item B.2: If an SAE occurs during the study visit select 'Yes' for this item.

If your answer to all of the items in Sections A and B is No, **STOP HERE** and **FILE the hard copy form** in the subject's folder. Do **NOT** complete Section C on the hard copy form. Do **NOT** submit the form electronically.

If your answer to one or more items in Sections A and B is Yes OR if you become aware of an SAE through another means, **skip to item C.9** and determine which of the listed outcome(s) occurred.

Part C, item C.9. Check/select any or all options a – g OR option h ('None of the above') to indicate the outcomes that are attributed to the event as documented in the subject's medical record (check all that apply):

- ☐ a. Death

  Item C.9a.1: If death was an outcome of the SAE, enter the date of death in this field.
- ☐ b. Life-threatening
- ☐ c. Hospitalization – initial or prolonged
- ☐ d. Disability
- ☐ e. Congenital anomaly
- ☐ f. Required intervention to prevent permanent impairment/damage

  Option 9.f should be used for an event that does not result in death, a life-threatening condition, hospitalization, disability or congenital deformity but that did jeopardize the subject and required a specific medical intervention to prevent one or more of outcomes C.9.a – C.9.e from occurring.
- ☐ g. Important medical event as determined by the site PI or designee

  Option 9.g should only be chosen when the site judges the event to represent significant hazard or harm to the research subject.
- ☐ h. None of the above

If the outcome of the identified event is C.9.h. (None of the above), **STOP HERE** and **FILE the hard copy form** in the subject's folder. The event represents a non-serious adverse event. Do **NOT** complete items C.1-C.8 in Section C on the hard copy form. Do **NOT** submit the form electronically.

If the outcome of the identified event is one or more of the outcomes in C.9.a. – C.9.g., the event represents a SERIOUS adverse event. **Complete all items in Section C on the hard copy form, ENTER PART C ELECTRONICALLY**, and file the hard copy form in the subject's folder.

Item C.1: If the date of the SAE is documented in the medical record, enter that date here. If the date is not in the medical record, enter the event date reported by the patient.

Item C.2: Enter the date on which the Study Coordinator became aware of the SAE.

Item C.3: Select an option from the list of possible SAE descriptors in APPENDIX IX.

If none of the descriptors appear to match the SAE, click on the link below the drop down box on the electronic eCRF to view a more detailed explanation of each descriptor.

If you still cannot identify a descriptor from the list, contact the CCC for assistance before selecting 'Other'.

If you are instructed to select the 'Other' option, write in a descriptor in the space provided on the paper CRF. On the electronic CRF, select 'Other' from the drop down list. A text field will become available where you can enter the descriptor text recorded on the paper form.

Item C.4: Indicate if the SAE is an exacerbation of a condition existing prior to enrollment.

Item C.5: Indicate if the SAE was associated with one of the medications on the list of Drug Codes for Antihypertensive Medications. If 'Yes' is selected for this item, complete items C.5.a and C.5.b.

Item C.5.a: Write in/select the name and code of the medication.

Item C.5.b: Indicate if the medication was stopped because of the adverse event.

Item C.6, C.7, and C.8: Enter text describing the details of the SAE as requested.

CRF#3.Study Termination

This eCRF will be completed when a subject is terminated early from the study or when a subject has completed all follow-up study visits. If the subject was terminated due to an adverse event, also complete eCRF #2 Serious Adverse Event.

Item 1: Indicate if the subject has completed all research study visits or if the subject is being terminated early.

Item 1.a: If 'Yes' is selected for Item 1, enter the date of the subject's final study contact (i.e. the 18 month phone call).

Item 1.b: If 'No' is selected for Item 1, enter the date on which the subject was terminated.

Item 1.c: If 'No' is selected for Item 1, enter the date of the subject's last research study contact with either the Study Coordinator or pharmacist.

Item 2: If 'No' is selected for Item 1, select the reason the subject was terminated early. Some options also require a text description if the option is selected. If the subject died due to an AE, selected 'Subject withdrew/terminated due to Adverse Event'; do *not* select 'Subject death'.

Item 3: Enter a comment (optional)

CRF11.Asthma Demographic

Item 1: Enter the date of the baseline study visit.

Item 2: Enter the subject's birth date.

Item 3: Select the subject's gender (male, female)

Item 4: Select any or all of options a – e or option f ('Declined to answer') according to the subject's response.

Item 5: Select the ethnicity the subject chose.

Item 6, 7, 8, 9, 10, and 12: For each item, indicate the options selected by the subject.

Item 11: Select the smoking status the subject chose. If the subject selected 'Currently smokes', complete items 11.a and 11.b. If the subject selected 'Former smoker', complete items 11.a, 11.b, and 11.c. If the subject selected 'Never smoked', do *not* complete item 11.a, 11.b, or 11.c.

Item 11.a: Enter the number of years the subject says s/he smoked.

Item 11.b: Enter the number of cigarettes the subject says s/he smoked each day.

Item 11.c: Select the time since quitting the subject chose.

Item 13: Select the option that best describes the duration of the subject's asthma diagnosis.

CRF#12. Asthma Control Test

This eCRF should be completed at each Study Coordinator visit and at each pharmacist encounter.

Part A: Check/enter the date of the study visit at which the questionnaire was administered.

Part B: Check/select the option that indicates the subject's response to the question.

Part C: Calculate and enter the total score by adding the numbers associated with each of the subject's responses.

CRF#13. Asthma Medical Record Abstraction

Visit: Check/indicate the study visit for which the form is being completed. This information will not be entered in the eCRF but should be recorded for your records.

Item 1: Enter the date of the study visit for which the form is being completed.

Table 2: Enter each clinic visit documented in the medical record that occurred since the last scheduled study visit with the Study Coordinator (including visits unrelated to asthma).

Item 2.a: Enter the date that the subject was seen in the clinic, hospital, or emergency room.

Item 2.b: Check/select to indicate if the clinic visit was related to asthma or some other condition.

Item 2.c: Check/select to indicate the location of the clinic visit.

Item 2.d: Check/select to indicate if corticosteroids were prescribed at the clinic visit.

Item 2.e: If 'Yes' is selected for Item 2.d, indicate the duration (in days) of steroid use.

CRF#14.Asthma Medication Adherence

Visit: Indicate the study visit for which the form is being completed. This information will not be entered in the eCRF but should be recorded for your records.

Part A: Enter the date of the study visit at which the questionnaire was administered.

Part B

Item B.1: Check the subject's medical record to determine if there is at least one active prescription for an asthma medication. This should be done prior to the study visit if possible.

Items B.2: If the answer to B.1 is Yes, further check the subject's medical record to determine if a rescue asthma medication is the only prescribed asthma medication.

B.3, B.4, B.5, B.6, B.7, and B.8: If the subject has at least one active prescription (Item B.1 = Yes, and Item B.2 = No), that is NOT a rescue inhaler, read each item to the subject and record his/her responses. Otherwise, do not complete Items B.2, B.3, B.4, B,5, B.6, B.7 or B.8.

CRF#15.Asthma Medications

Visit: Check the study visit for which the form is being completed. This information will not be entered in the eCRF but should be recorded for your records.

Item A.1: Enter the date of the study visit for which the information is being collected.

Table A.2: Write in/enter the subject's current medications at the time of the study visit into the table. Include all medications that are currently prescribed according to the medical record.

Item A.2.a: Write in the medication/enter the medication code in the text field.

Item A.2.b: Write in/select the strength of the medication from the list of options.

Item A.2.c: Write in/select the dose (i.e. number of tabs) from the list of options.

Item A.2.d: Write in/ select the frequency from the list of options.

Item A.2.e: Check the box to indicate if the medication is prescribed on an "as needed" basis.

Item A.2.f: Check/select one option to indicate how the patient is taking each medication.

CRF#16.Asthma Pharmacist Encounter

This eCRF will be completed as needed each time the subject meets with the pharmacist. The subject's name should be entered on the paper form only; it will not be entered into the data base.

Item A.1: Enter the date of the pharmacist encounter.

Item A.2: Select the type of visit the subject had with the pharmacist

Item A.3: Select the pharmacist code from the list of options.

Table A.4: Write in on the hard copy form the name, unit strength, dose and frequency of the subject's current asthma medications at the time of the pharmacist encounter; check the box to indicate PRN status (if applicable) and select an option to indicate adherence status. When entering electronically, select from the available options. Include all medications that are currently prescribed according to the medical record.

Item A. 4.a: Write in the medication name/enter the medication code in the text field.

Item A.4.b: Write in the medication strength/select the strength of the medication from the list of options.

Item A.4.c: Write in the dose/select the dose (i.e. number of tabs) from the list of options.

Item A.4.d: Write in the frequency/select the frequency from the list of options.

Item A.4.e: Check the box to indicate if the medication is prescribed on an "as needed" basis.

Item A.4.f: Check/select one option to indicate how the patient is taking each medication.

Item A.5: Check/select any or all of options a – g or option h ('No lifestyle changes recommended') to indicate the lifestyle changes that were recommended to the subject. If option g is selected, specify the change in the space provided (Item 5.d.1).

Item A.6: Indicate if increased medication compliance was recommended to the subject.

Item A.7: Indicate if the pharmacist recommended continuation of the current regimen or a change to the subject's prescription plan.

Table A.8: If a change to the plan was recommended, enter *only the medications that the pharmacist wished to change* in the table.

Item A. 8.a: Write in the medication name. On the paper form, the Study Coordinator should fill in the medication code. On the electronic form, enter the medication code in the text field.

Item A. 8.b: Write in/enter the change type relative to the same medication as it is listed in Table A.4. If a new drug is recommended, select "Start New Drug" for that medication.

Item A. 8.c: Write in the medication strength/select the strength of the medication from the list of options.

Item A. 8.d: Write in the dose/select the dose (i.e. number of tabs) from the list of options.

Item A.8.e: Write in the frequency/select the frequency from the list of options.

Item A.8.f: Check the box to indicate if the medication is prescribed on an "as needed" basis.

Item A.8.g: Write in/enter electronically any comments the pharmacist may have made with respect to that medication (optional).

Item A.8.h: Check/enter the physician's decision for each medication change recommended by the pharmacist.

Item A.9: Check/select any or all options a – g, option h ('Patient declined to re-schedule'), or option i ('Pharmacist intervention completed') to indicate when the pharmacist plans to follow-up with the subject. If option g is selected, specify the other time frame in the space provided (Item 9g.1).

Table A.10: Enter ALL medications prescribed after pharmacist recommendation and physician review. Complete this table (on paper and electronically) ONLY if the physician modifies any of

the medication recommendations listed in Table A.12. If the physician does not modify the recommended medications, the table should not be completed.

Item A.10.a: Write in the medication name. On the paper form, the Study Coordinator should fill in the medication code. On the electronic form, enter the medication code in the text field.

Item A.10.b: Check/enter the change type relative to the same medication as it is listed in Table A.4. If a new drug is being added, check/select "Start New Drug" for that medication.

Item A.10.c: Write in the medication strength/select the strength of the medication from the list of options.

Item A.10.d: Write in the dose/select the dose (i.e. number of tabs) from the list of options.
Item A.10.e: Write in the frequency/select the frequency from the list of options.

Item A.10.f: Check the box to indicate if the medication is prescribed on an "as needed" basis.

Item B.1 and B. 2: Enter the start and end times of the pharmacist encounter using military time. If the encounter occurred in the morning, enter the hours and minutes as usual. If the encounter occurred in the afternoon, add 12 to the hours and enter the minutes as usual.

Item B.3: Circle/select the number of minutes the pharmacist spent on each of the activities listed. Circle/select NA for an item that is not applicable to the patient or teaching situation.

Item B.4: Check/select the CPT code for the initial 15 minutes of the encounter.

Item B.5: Write in/enter the number of 15 minute units of CPT code 99607.

CRF#17.Asthma Patient Self-Report

Visit: Check on paper the study visit for which the form is being completed. This information will not be entered in the eCRF but should be recorded for your records.

Part A: Enter the date of the study visit at which the questionnaire was administered.

Part B: Circle/select the option that indicates the subject's response to each question in (1)–(6).

CRF#17.Asthma Quality of Life Questionnaire

Visit: Check on paper the study visit for which the form is being completed. This information will not be entered in the eCRF but should be recorded for your records.

Part A: Enter the date of the study visit at which the questionnaire was administered.

Part B: Circle/select the option that indicates the subject's response to each question in B.1-B.20.

CRF#24.Protocol Deviation

Item 1: Enter the date of the deviation.

Item 2: Enter the date the Study Coordinator became aware of the deviation.

Item 3: Select any or all options 3.a – 3.h to indicate the type of deviation. If you select option 3.a, enter a description of the unmet inclusion criteria in the space provided. If you select option 3.b, enter a description of the exclusion criteria in the space provided. If you select option 3.g, enter the date of the SAE in Item 3.g.1 and provide a description in Item 3.g.2. If you select option 3.h, enter a description of the "Other" protocol deviation in the space provided.

Complete the Corrective Action Plan on hard copy. This is for your center's use only and will not be entered into the database.

VI. PROVIDER, PATIENT AND CLINIC SURVEYS

Physician and Pharmacist Surveys (overseen by the University of Iowa IRB)

- Web-Based Training Conference Session Implementation Survey

  The Physician Leader and Pharmacist Leader will be mailed a survey prior to the web-based training session asking about a recent change in the clinic, problems encountered and successes obtained when implementing the change. They should confer to select the change and jointly respond to the survey. Survey responses will be discussed during the training session.

The following surveys will be mailed to sites and distributed to the appropriate personnel. These surveys should be completed prior the beginning of patient enrollment.

- Physician Leader Implementation Survey

  This survey asks the physician leader questions on physician-pharmacist collaboration in the clinic.

- Physician Mail Implementation Survey

  This survey asks each physician in the clinic questions on physician-pharmacist collaboration.

- Pharmacist Mail Implementation Survey

  This survey asks each pharmacist in the clinic questions on physician-pharmacist collaboration.

- Barriers and Enablers of the PPCM Intervention

  All physicians and pharmacists in the clinic will be invited to complete a survey prior to patient enrollment that measures participant attitudes, intentions to implement PPCM, enablers and barriers to implementation of PPCM. Physicians and pharmacists will be invited to take the same survey at the end of the study.

  Surveys will be mailed to providers along with a letter detailing the elements of consent. Providers who choose to participate should return the survey to the Study Coordinator sealed in the envelope provided.

Study Coordinator and Office Administrator Surveys (overseen by the University of Iowa IRB)

A study investigator will conduct telephone interviews with the Study Coordinator and the office administrator to evaluate problems with logistical issues, patient flow, patient acceptance and quality improvement that they observed. These interviews will be conducted at the completion of the intervention.

A study investigator (Dr. Ardery) will fax or email a consent letter to the Study Coordinator and the Office Administrator, asking them to return a postage-paid postcard if they wish to participate in the interview. The investigator will answer questions in a follow-up phone call. Receipt of the postcard and completion of the interview will indicate consent.

VII. PROTECTION OF HUMAN SUBJECTS

This project involves human subjects research that meets the definition of "clinical research" and also meets the NIH definition of a Phase III Clinical Trial.

A. OVERSIGHT BY LOCAL INSTITUTIONAL REVIEW BOARD

Each site must obtain approval for the study from its local Institutional Review Board. Study Coordinators and clinic investigators will need to obtain training and approval as specified by their local Institutional Review Board. Information pertinent to the IRB application is provided below.

Once IRB approval is obtained, each site should email their approval letter and a copy of each approved informed consent document to the CCC.

B. POTENTIAL RISKS AND PROTECTIONS AGAINST RISK

Risk to subjects is minimal since they will continue to receive at least their usual and customary medical care from their physician. We know of no study that has found that the type of PPCM care proposed here leads to worse asthma control. The treatments that will be recommended are all supported by current national guidelines.

No patient will be coerced to participate or continue in the study. Patients will be informed that their decision about participation will have no effect on their relationship with their physician or their care and that they can withdraw from the study at any time if they choose. Each patient will also be informed that the investigators will obtain prescription, medical record, and billing data during the course of their participation in the study.

Each subject will sign informed consent. The subject will receive a copy of the signed consent document, and a copy will be placed in the subject's medical record per clinic and IRB protocol.

All subjects will be provided contact information for the Study Coordinator or clinic physician PI in the event the subject would like to discuss a study-related issue or adverse event that arises. All participating subjects will be provided contact information for the local IRB and instructed to contact the IRB with questions about the rights of research subjects or research related injury.

There is the possibility that adverse reactions could occur, but the close follow-up will minimize the potential for adverse outcomes. Subjects will be encouraged to contact their providers immediately if adverse events do occur. In addition, the study's Data and Safety Monitoring Board will evaluate the differences between groups and any adverse events at least twice a year or more frequently if adverse outcomes occur. It is possible that some of the pharmacists' recommendations might not be appropriate for the patient. However, the physician will always be free to accept or reject the recommendations, so this should not increase the risk to the subject.

All data concerning serious adverse events will be reviewed by the Data Safety Monitoring Board at least twice a year. Serious events will be evaluated immediately via email and/or conference call. Any serious adverse effects will be reported to the local IRB. If any adverse outcomes might influence the continued participation of patient subjects, all active observation patients will be informed.

The Study Coordinator will attempt to telephone or personally speak with each subject who drops from the study to identify their reason(s) for withdrawing and whether anything could have been done to retain them in the study.

Provider Subjects (overseen by the University of Iowa IRB)

The physician and pharmacist leader at each site will be asked to attend a teleconference team training session. Investigators from the University of Iowa will lead a discussion of a prior collaborative intervention at each clinic. This discussion could potentially be sensitive and carry the potential for social embarrassment. However, physicians and pharmacists will be told that they do not have to answer any questions that they do not wish to answer.

Clinic physicians, pharmacists, the Study Coordinator and the Office Administrator will be invited to participate as survey subjects in the trial. This portion of the study will be overseen by the University of Iowa IRB These individuals will receive a letter approved and stamped by the University of Iowa IRB containing elements of consent and be informed that they can decline to answer any questions that they do not wish to answer. Risk to provider subjects is minimal, since these individuals will only provide survey and/or interview data.

C. LINKAGES TO SUBJECTS AND ACCESS TO PATIENT IDENTITIES

Original data information that contains patient subject identifiers will be stored in locked cabinets and offices at participating sites and will only be accessible to the members of the site research team and, under their supervision, the University of Iowa study monitors. To help protect subject confidentiality, we will use identification code numbers rather than names on study forms. Data will be maintained in locked offices and storage areas, and sites will use password-protected computer files. The list linking the subjects' study identification codes and their names will be stored in a separate location that is accessible only to the Study Coordinator and, under site supervision, to University of Iowa study monitors.

The only personnel who will have direct contact with patient subjects will be the Study Coordinator, pharmacists and physicians employed at the clinic. The study monitors from the Data Management Center will need full access to the subjects' medical records in the course of the monitoring visits. Monitors will have no contact with clinic patients. The Study Coordinator will record data on worksheets that serve as case report forms. The only identifiers that will be collected are the subject's birth date and the dates of clinic visits. The only persons with access to link the code number to the subject will be the Study Coordinator and the research study monitors.

Patient subject data will be electronically uploaded by the site Study Coordinator to a database located on a secure server at the University of Iowa Clinical Trials Statistical & Data Management Center. Access to the database is strictly password-protected.

Survey and interview data provided by the clinic pharmacists, physicians, Study Coordinator and Office Administrator will be completed by telephone or mailed survey. Providers will be assigned unique study codes, and only these codes will be placed onto data collection instruments. Links between provider codes and provider names will be stored electronically on secure, password-protected files at the University of Iowa. University of Iowa researchers will enter provider data into password-protected databases located on secure servers within the Clinical Trials Statistical & Data Management Center and the Clinical Coordinating Center. Hard copy data collection forms will be filed in locked cabinets in locked offices in the University of Iowa Clinical Coordinating Center. Provider data will be analyzed without links to provider names.

D. THE FEDERAL HEALTH INSURANCE PORTABILITY AND ACCOUNTABILITY ACT (HIPAA)

We will keep the patients' participation in this research study confidential to the extent permitted by law. They will be informed that it is possible that certain individuals may become aware of their participation in this study including the study monitor, federal government regulatory agencies, auditing departments and the local Institutional Review Board.

The Federal Health Insurance Portability and Accountability Act (HIPAA) requires that the patient's health care system obtains permission from all subjects in the active observation group so that the research team may access or create "protected health information." Sites should request IRB permission to waive consent on passive observation patients in which only chart review is performed by the Study Coordinator employed in the patient's clinic so long as the abstracted information is completely de-identified.

All data will be transmitted electronically via a secured website in an encrypted format and saved to the database at the University of Iowa Clinical Trials Statistical & Data Management Center. All data are backed up daily on an independent server and also backed up weekly and stored offsite. The servers are located in secured offices at the Clinical Trials & Statistical Data Management Coordinating Center. There are multiple security measures in place to ensure data protection. Subjects will be informed that we may share their health information related to this study with other parties including federal government regulatory agencies, the Department of Health and Human Services, the subject's health system Institutional Review Board and the University of Iowa Institutional Review Boards and study monitors. They will be informed that they cannot participate in this study unless they permit us to use their protected health information. If they choose not to allow us to use their protected health information, we will discuss non-research alternatives available to them. The subjects will be informed that their decision will not affect their right to medical care that is not research-related. They will also be informed that their signature on the Consent Document authorizes their health care facility to give us permission to use or create health information about them.

Subjects will be informed that they may not be allowed to see study information until after this study is over, but that they may be given access to their health care records by contacting their health care provider. They will also be informed that permission for us to access or create protected health information about them for purposes of this study has no expiration date. They will also be informed that if we have sent their health information to a third party, such as the study sponsor, or we have removed their identifying information, it may not be possible to prevent its future use.

E. POTENTIAL BENEFITS OF THE PROPOSED RESEARCH TO THE SUBJECTS OR OTHERS

Potential benefits to physicians include an increase in knowledge about their patient's drug therapy and improved asthma management for their patients. We expect that subjects who receive the PPCM intervention will have improved asthma control and fewer hospitalizations and emergency department visits. If the intervention is effective, it might be used on a broader scale for a wide variety of health systems.

F. IMPORTANCE OF THE KNOWLEDGE TO BE GAINED

Few studies have examined PPCM for asthma, and most have been conducted in community pharmacies. The few studies that used the PPCM model for asthma within a clinic setting have yielded mixed results in outcomes. However, one researcher found that a PPCM program for asthma management resulted in significantly fewer emergency department visits during the study period compared to two similar time periods prior to study initiation. The true benefit derived from PPCM for asthma is unknown.

G. INCLUSION OF WOMEN AND MINORITIES

This application will include both men and women. We expect 50% of patients will be women.

Patients from minority groups will be eligible for this study, and no patient will be excluded based on race or ethnic group. The goal of the study nationally will be to recruit at least 40% of patients from under-represented minority groups.

H. DATA AND SAFETY MONITORING

The Clinical Trials & Statistical Data Management Center's DMC will be responsible for receiving and processing submitted reports of Serious Adverse Events (SAEs) and Unanticipated Problems (UPs) and for forwarding such reports to one of two Medical Monitors. The Medical Monitors perform the following functions: 1) ongoing, real-time reviews of all individual SAE reports to determine if events are unanticipated, related and serious, and suggestive of greater risk; 2) monthly reviews of cumulative SAE data to judge whether there are concerning trends in the occurrence of events, and the possible relationship of those trends to the trial; 3) review any reports of UPs identified by the DMC or CCC that meet the NHLBI criteria for reporting. When needed, a Medical Monitor may ask the CCC to communicate with a site in order to obtain additional chart information pertinent to a submitted report.

The study's Data and Safety Monitoring Board (DSMB) is responsible for safeguarding the interests of study participants by assessing the safety and efficacy of study procedures, and by periodic monitoring of safety data and the overall conduct of the study. The DSMB will develop an operational plan during the first six months of the study. The operational plan will be consistent with NHLBI's Policy on Human Subjects Research: Data and Safety Monitoring Plans dated May 2005. The plan will include conflict of interest disclosure statements for each member, frequency and location of meetings, policies and procedures and dissemination of meeting materials, notification of NHLBI staff, data to be reviewed and procedures for evaluating data and reporting findings.

The DMC will provide the Data and Safety Monitoring Board data on numbers of patients recruited into the study, patient outcomes, and serious adverse events. The DSMB reviews the following types of safety data provided by the DMC: 1) quarterly reports; 2) bi-annual reports for DSMB meetings; and 3) individual concerns identified by the Medical Monitors. After reviewing pertinent reports, the DSMB determines whether any trend that may be identified is related to the trial, whether the study's informed consent form and process needs to be modified, whether the study's procedures need to be modified and whether the study should be discontinued due to serious adverse events or adverse outcomes in either the control group or those related to the intervention. The DMC application describes methods for interim analyses and how data will be supplied to the DSMB.

The DSMB consists of the following members:

- Barry Davis, MD, PhD, The University of Texas School of Public Health – Chair and statistician
- Keith Ferdinand, MD, The Morehouse School of Medicine
- Michael D. (Mick) Murray, PharmD, MPH, The University of North Carolina School of Pharmacy,
- Katherine Gloer, PhD, The University of Iowa – Executive Secretary

VIII. SERIOUS ADVERSE EVENTS AND PROTOCOL COMPLIANCE

Serious Adverse Event Assessment and Reporting

Study Coordinators should assess subjects for the occurrence of a serious adverse event. ***A serious adverse event does NOT need to be related to the study in order to be reported.***

As specified by NHLBI policy, serious adverse events (SAEs) are considered to be those events that result in at least one of the following outcomes:

a. Death

a.1 Date: __ __/__ __/__ __ __ __ (mm/dd/yyyy)

b. Life-threatening

c. Inpatient hospitalization or prolongation of an existing hospitalization

d. Persistent or significant disability/incapacity

e. A congenital anomaly/birth defect

f. Other events that might jeopardize the subject and may require medical or surgical intervention to prevent one of the outcomes listed above

Option 9.f should be used for an event that does not result in death, a life-threatening condition, hospitalization, disability or congenital deformity but that did jeopardize the subject and required a specific medical intervention to prevent one of these outcomes from occurring.

g. Important medical event as determined by the site PI or designee

Option 9.g should only be chosen when a site judges the event to represent significant hazard or harm to research subjects.

If there is any question about whether an event should be classified as an SAE, please contact the CCC for further direction.

ALL SERIOUS ADVERSE EVENTS SHOULD BE REPORTED WITHIN 24 HOURS OF THE TIME THAT A RESEARCH TEAM MEMBER BECOMES AWARE OF THE EVENT.

If the Study Coordinator is not available to submit eCRF #2 within the 24 hour timeframe, a member of the study team may complete the hard copy version of the SAE form and either FAX the hard copy form to the DCC Protocol Coordinator or scan the form into an electronic file and email the fill to the DCC Coordinator. The DCC will then enter the information into the electronic data system.

Study Coordinators collect serious adverse event data on CRF#2. Serious Adverse Event at all visits AFTER the baseline visit:

Part A. Administer screening questions (1) and (2) at every visit AFTER the baseline visit.

Question 1: Have you had any changes in your health since the last study visit?

Question 2: Have you been hospitalized or received care in an Emergency Room since your last study visit

Part B. Complete questions (1) and (2) for events that are documented in the medical record but that are not reported by the subject

COMPLETE PARTS A and B ON HARD COPY ONLY, NOT IN THE DATABASE.

Part C. Complete item C.9 if 1) Yes is selected for any question in Part A or Part B or a serious adverse event is identified in the medical record or through any other means AND 2) one or more of the items in 9.a – 9.g is/are checked. Part C should NOT be completed if item 9.h is checked.

If the outcome of the event is identified to be C.9.h (None of the above) **STOP** and **FILE** the hard copy in the subject's folder. The event represents a non-serious adverse event. Do **NOT** complete items C.1-C.8 in Section C on the hard copy form. Do **NOT** submit the form electronically.

If the outcome of the identified event is one or more of the outcomes in C.9.a. – C.9.g., the event represents a SERIOUS adverse event. **Complete all items in Section C on the hard copy form, ENTER PART C ELECTRONICALLY**, and file the hard copy form in the subject's folder.

See Section V. INSTRUCTIONS FOR COMPLETING CASE REPORT FORMS for more details on completion of CRF#2. Serious Adverse Event.

A list of serious adverse event descriptors is provided in APPENDIX IX. Please use these descriptors to complete Item 3 in Part C of the form.

ENTER PART C INTO THE STUDY DATABASE.

Protocol Compliance

All providers participating in the study should make all efforts to comply with the study protocol. Deviations from the specified protocol should be submitted on paper and electronic CRF #24. Protocol Deviation.

Critical areas of compliance for Study Coordinators include:

1. Ensuring that all enrolled subjects meet the study's inclusion and exclusion criteria.
2. Ensuring that all enrolled subjects sign informed consent.
3. Having subjects complete their 9 month and 18 month visits.
4. Screening for and promptly reporting adverse events.

Pharmacists implementing the study's intervention have been provided with a recommended schedule for subject visits. However, pharmacists will not be expected to follow the recommended schedule for all subjects. Rather, they may tailor the timing and frequency of visits to meet each subject's needs and to maximize outcomes.

APPENDIX I: PROJECTED STUDY TIMETABLE

Activity	Months						Responsible Staff
	0- 9	*10- 12*	*13- 16*	*17- 21*	*22-45*	*46-52*	
Train nurses in enrollment, data collection							Ecklund (DMC), Ardery, Carter
Train physician leaders/clinical pharmacists							Carter, James, Joyce, Rosenkrans, Buys
Onsite team building sessions							Physician and pharmacist leader
Physician surveys							Study Coordinator, clinic physicians, Ardery
Recruit asthma patients		**9 enrolled**	**6 enrolled**				Study Coordinators, DMC
PPCM intervention with asthma patients							Clinic Pharmacists
Follow each asthma subject x 18 months							Study Coordinators
Formative evaluation – acceptance of intervention							Vander Weg, James, Ardery
Organizational support and evaluation							Vaughn, Carter, Ardery
Safety and monitoring evaluations by DSMB							DMC, DSMB
Final asthma data analysis							DMC, Coffey
Study close out							Study Coordinators, DMC

APPENDIX II: SITE SIGNATURE LOG TEMPLATE

Investigator Name		***Site Name and Location***		***Page Number***	___ ***of*** ___

Name and Title of Site Staff Use Block Capitals	**Signature**	**Initials**	**Responsibilities*** (See below)							**Involved From** DD-MMM-YY	**Involved To** DD-MMM-YY

****DELEGATION OF RESPONSIBILITIES CODES***	***NOTES FOR COMPLETING THIS FORM***
A. Study Coordinator *B. Study Pharmacist* *C. Study Lead Physician* *D. Study PI*	• *Please PRINT CLEARLY when completing this form* • *Please enter all dates in the MM-DD-YYYY format (e.g., 01-21-2005)* • *Use 'Involved From' and 'Involved To' to record staff changes during the study* • *Enter a new line and applicable dates when responsibilities change*

Principal Investigator Signature:_____ Date Initially Completed:_____

Principal Investigator Signature:_____ Date Updated:_____

Principal Investigator Signature:_____ Date Updated:_____

FAX COMPLETED FORM TO GAIL ARDERY AT 319-335-9511

APPENDIX II: SITE SIGNATURE LOG TEMPLATE

Investigator Name		***Site Location***		***Page Number***	***___ of ___***

Principal Investigator Signature:______________________ Date Updated:______________________

Principal Investigator Signature:______________________ Date Updated:______________________

Principal Investigator Signature:______________________ Date Updated:______________________

Principal Investigator Signature:______________________ Date Updated:______________________

Principal Investigator Signature:______________________ Date Updated:______________________

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Principal Investigator Signature:______________________ Date Updated:______________________

Principal Investigator Signature:______________________ Date Updated:______________________

Principal Investigator Signature:______________________ Date Updated:______________________

APPENDIX III: INDIVIDUAL SITE ENROLLMENT TARGETS FOR ASTHMA SUBJECTS

TARGETED/PLANNED ENROLLMENT FOR ASTHMA SUBJECTS:			
Ethnic Category	**Sex/Gender**		
	Females	**Males**	**Total**
Hispanic or Latino	2	1	3
Not Hispanic or Latino	6	6	12
Ethnic Category: Total of All Subjects *	**8**	**7**	**15**
Racial Categories			
American Indian/Alaska Native	1	0	1
Asian	0	1	1
Native Hawaiian or Other Pacific Islander	0	1	1
Black or African American	1	1	2
White	6	4	10
Racial Categories: Total of All Subjects *	**8**	**7**	**15**

			Medical Record Screening Process				Attempted contacts by mail			
Column A Patient Name	Column B Random Screening Number	Column C Patient Number	Column D Disqualified d/t/ Severe Asthma or COPD	Column E Disqualified by Other Exclusion Criteria	Column F Patient Left Practice	Column G Meets Med Record Screening Criteria	Column H Date Letter Mailed	Column I Date Postcard Received	Column J Declined on Postcard	Column K Expressed Interest on Postcard in Hearing More About the Study

Attempted contacts by phone										
Column L Date Phone Call 1	Column M Date Phone Call 2	Column N Date Phone Call 3	Column O Date Phone Call 4	Column P Date Phone Call 5	Column Q Date Phone Call 6	Column R Unable to contact	Column S Declined on Phone	Column T Exclusion Criterion Identified on Phone	Column U Indicated Interest on Phone in Hearing More About the Study	Column V Unable to Schedule Baseline Visit

Baseline Visit Outcomes				
Column W Declined Consent at Baseline Visit	Column X Signed Informed Consent	Column Y SPMSQ Scored Did Not Meet Criteria	Column Z Exclusion Criterion Discovered After Consent Signed	Column AA Fully Enrolled into Study

Column A Patient Name	Column B Random Screening Number	Column C Patient Number	Medical Record Screening Process				Attempted contacts by mail			
			Column D Disqualified d/t/ Severe Asthma or COPD	Column E Disqualified by Other Exclusion Criteria	Column F Patient Left Practice	Column G Meets Med Record Screening Criteria	Column H Date Letter Mailed	Column I Date Postcard Received	Column J Declined on Postcard	Column K Expressed Interest on Postcard in Hearing More About the Study
Andrea Adams	1	783	Y	N	N	N				
Bob Barker	2	1891	N	N	N	Y	1/13/2010	2/6/2010	Y	N
Carol Carter	3	38	Y	N	N	N				
David Dirksen	4	149	N	N	N	Y	1/13/2010			
Eric Evans	5	1057	N	Y	N	N				
Fred Flowers	6	588	Y	N	N	N				
Gail Gerber	7	1380	Y	N	N	N				
Henry Hill	8	875	Y	N	N	N				
Ingrid Iverson	9	68	N	N	N	Y	1/13/2010	1/18/2010	N	Y
Jenny Jackson	10	4	N	N	N	Y	1/13/2010	2/2/2010	Y	
Karl Karsen	11	1577	N	N	N	Y	1/13/2010	2/2/2010	Y	
Linda Levson	12	411	Y	N	N	N				
Mary Matson	13	349	Y	N	N	N				
Nancy Noyes	14	12	N	N	N	Y	1/13/2010			
Oliver Olson	15	1133	Y	N	N	N				
Peter Pan	16	624	N	N	N	Y	1/13/2010			
Quo Q'hai	17	217	N	N	N	Y	1/13/2010	1/22/2010	N	Y
Richard Robertson	18	99	N	N	N	Y	1/13/2010			
Steven Sampson	19	1492	Y	N	N	N				
Tim Taylor	20	255	N	N	N	Y	1/13/2010	1/12/2010	N	Y
Una Uberhaus	21	1776	Y	N	N	N				
Victoria Velasquez	22	401	Y	N	N	N				
Walter Winchel	23	1666	Y	N	N	N				
Xavier Xupha	24	52	N	N	N	Y	1/13/2010			
Yvonne Yogerst	25	596	N	N	Y	N				
Zia Zobert	26	44	Y	N	N	N				

Attempted contacts by phone										
Column L Date Phone Call 1	Column M Date Phone Call 2	Column N Date Phone Call 3	Column O Date Phone Call 4	Column P Date Phone Call 5	Column Q Date Phone Call 6	Column R Unable to contact	Column S Declined on Phone	Column T Exclusion Criterion Identified on Phone	Column U Indicated Interest on Phone in Hearing More About the Study	Column V Unable to Schedule Baseline Visit
1/30/2010	2/7/2010					N	N	N	Y	N
1/30/2010	2/7/2010	2/14/2010	2/21/2010	2/28/2010	3/3/2010	Y				
1/30/2010							Y			
1/30/2010	2/7/2010					N	N	N	Y	N
1/30/2010	2/7/2010					N	N	N	Y	N

Baseline Visit Outcomes				
Column W Declined Consent at Baseline Visit	Column X Signed Informed Consent	Column Z SPMSQ Score Qualified	Column AA Exclusion Criterion Discovered After Consent Signed	Column AB Fully Enrolled into Study
N	Y	Y	N	Y
N	Y	Y	N	Y
N	Y	Y	N	Y

APPENDIX V: EVALUATION TO SIGN INFORMED CONSENT DOCUMENT FOR RESEARCH

(Complete for each patient whose capacity to read or sign informed consent is in question and file in the patients study folder)

Check the following indicators of the patient's mental status:

	Yes	No
Subject is alert		
Subject is able to communicate without difficulty		

If you check "No" to EITHER statement above, explain to the patient that s/he cannot participate and check "No" in the Certification of Ability to Sign Informed Consent section below.

If you check "Yes" to BOTH statements above, ask the patient to undertake each task listed below and check to denote whether each response is appropriate.

	Patient Responds Appropriately	
	Yes	No
Please name at least two potential risks of participating in the study.		
Please name at least two things that you will be expected to do during the study.		
Please explain what you would do if you did not wish to continue participating in the study.		
Please explain what you would do if you experienced distress or discomfort during the study.		

If the patient does NOT respond appropriately to all four questions, explain to the patient that s/he cannot participate and check "No" in the certification section below

If the patient DOES respond appropriately to all four questions, check "Yes" in the certification section below.

CERTIFICATION OF ABILITY TO SIGN INFORMED CONSENT

	Yes	No
Patient meets the above criteria required to sign informed consent.		

_____ _____

Study Coordinator Signature Date

APPENDIX VI: SOURCE DOCUMENT FOR VERIFICATION OF INCLUSION AND EXCLUSION CRITERIA

Inclusion Criteria	Has Inclusion Criterion*	
English or Spanish speaking males or females	Yes	No
At least 12 years of age	Yes	No
Has a diagnosis of persistent asthma (can be mild, moderate or severe as long as they don't meet any of the exclusion criteria)	Yes	No
Exclusion Criteria	**Has Exclusion Criterion***	
Hypertension which would qualify them for the BP control group	Yes	No
History of severe, life-threatening asthma evidenced by a history of loss of consciousness, ICU admissions or mechanical ventilation due to asthma	Yes	No
Diagnosis of chronic obstructive pulmonary disease	Yes	No
Previous involvement in a multidisciplinary asthma management clinic	Yes	No
Pregnancy	Yes	No
Poor prognosis with a life expectancy estimated less than 2 years	Yes	No
Residence in a nursing home or diagnosis of dementia	Yes	No
Inability to give informed consent	Yes	No
Impaired cognitive function (>2 errors on the Short Portable Mental Status Questionnaire)	Yes	No
Pulmonologist EXCLUSIVELY prescribes and adjusts asthma medications	Yes	No

***SUBJECT MUST MEET ALL OF THE INCLUSION CRITERIA AND NONE OF THE EXCLUSION CRITERIA TO REMAIN IN THE STUDY.** Form is NOT available in the database.

APPENDIX VII: LIST OF ASTHMA DRUG CODES

Inhaled Corticosteroids – Class Code = A100

Code	Generic Name	Brand Name	Strengths Available
A101	Beclomethasone propionate HFA	QVAR	40 mcg, 80 mcg
A102	Budesonide	Pulmicort Flexhaler, Pulmicort Respules	90 mcg, 180 mcg, 0.25 mg, 0.5 mg, 1 mg
A103	Budesonide/Formoterol	Symbicort	80/4.5 mcg, 160/4.5 mcg
A104	Ciclesonidse	Alvesco	80 mcg, 160 mcg
A105	Flunisolide	Aerobid	250 mcg
A106	Fluticasone propionate	Flovent HFA, Flovent Diskus	HFA is 44 mcg, 110 mcg, 220 mcg, Diskus is 50 mcg, 100 mcg, 250 mcg
A107	Fluticasone/Salmeterol	Advair Diskus or Advair HFA	HFA is 45/21 mcg, 115/21 mcg, 230/21 mcg; Diskus is 100/50 mcg, 250/50 mcg, 500/50 mcg
A108	Mometasone furoate	Asmanex Twisthaler	110 mcg, 220 mcg
A109	Triamcinolone acetonide	Azmacort	75 mcg
A110	Mometasone/Formeterol	Dulera	100/5 mcg, 200/5 mcg

Long Acting Beta 2 Bronchodilators – Class Code = A200

Code	Generic Name	Brand Name	Strengths Available
A201	Formoterol fumarate	Foradil Aerolizer	12 mcg
A202	Salmeterol xinofoate	Serevent Diskus	50 mcg
A203	Arfomoterol tartrate	Brovana Inhalation solution	15 mcg
A204	Formeterol fumarate	Perforomist Inhalation solution	20 mcg

Mast Cell Stablilizers – Class Code = A300

Code	Generic Name	Brand Name	Strengths Available
A301	Cromolyn sodium	Intal	800 mcg Nebulizer: 20 mg
A302	Nedocromil	Tilade	1.75 mg

Leukotriene Modifiers – Class Code = A400

Code	Generic Name	Brand Name	Strengths Available
A401	Montelukast	Singulair	4 mg, 5 mg, 10 mg,
A402	Zafirlukast	Accolate	10 mg, 20 mg
A403	Zileuton	Zyflo CR	1200 mg

Immunomodulators – Class Code = A500

Code	Generic Name	Brand Name	Strengths Available
A501	Omalizumab	Xolair	150 mg
A502	C1 inhibitor (human)	Cinryze	500 units

Short Acting Beta Agonists – Class Code = A600

Code	Generic Name	Brand Name	Strengths Available
A601	Albuterol sulfate HFA	ProAir HFA, Proventil HFA, Ventolin HFA	90 mcg
A602	Albuterol sulfate nebulizer solution	AccuNeb Inhalation solution	0.021%, 0.042%, 0.083%, 0.5%
A603	Albuterol sulfate oral syrup or tablet		2 mg, 4 mg
A604	Albuterol sulfate extended-release tablets	VoSpire ER	4 mg, 8 mg
A605	Levalbuterol HCL	Xopenex	45 mcg, 0.31 mg, 0.63 mg, 1.25 mg
A606	Pirbuterol acetate	Maxair Autoinhaler	200 mcg
A607	Isoetarine Hydrochloride	Isoetharine	0.25%, 1%
A608	Isoproterenol hydrochloride	Isuprel	0.2 mg
A609	Metaproterenol sulfate	Alupent	0.4%, 0.6% Tablet: 10 mg and 20 mg
A610	Terbutaline sulfate		Solution: 1 mg Tablet: 2.5 mg, 5 mg

Anticholinergics –Class Code = A700

Code	Generic Name	Brand Name	Strengths Available
A701	Ipratropium bromide	Atrovent	17 mcg Nebulizer: 0.02%
A702	Ipratropium bromide/albuterol sulfate	Combivent, Duoneb	18/103 mcg, Nebulizer: 0.5/2.5 mg
A703	Tiotropium bromide	Spiriva	18 mcg

Oral Corticosteroid – Class Code = A800

Code	Generic Name	Brand Name	Strengths Available
A801	Cortisone acetate		25 mg
A802	Dexamethasone		Solutions: 0.5 mg, 0.75 mg, 1 mg, 1.5 mg, 2 mg, 3 mg, 4 mg, 5 mg, 6 mg, 9 mg,10 mg Tablet: 0.5 mg, 0.75 mg, 1 mg, 1.5 mg, 2 mg, 4 mg, 6 mg
A803	Hydrocortisone	Cortef	5 mg, 10 mg, 20 mg
A804	Prenisolone	Orapred, Prelone, Pediapred, Oraped	5 mg, 10 mg, 15 mg, 20 mg, 30 mg
A805	Prednisone		1 mg, 2.5 mg, 5 mg, 10 mg, 20 mg, 50 mg

Oral Methylxanthines – Class Code = A900

Code	Generic Name	Brand Name	Strengths Available
A901	Theophylline	Elixophyllin, Theo 24, Theochron, Uniphyl	80 mg/15 ml, 100 mg, 125 mg, 200 mg, 300 mg, 400 mg, 450 mg, 600 mg, 800 mg

APPENDIX VIII: HARD COPY CASE REPORT FORMS

Date Administered: _ _/_ _/_ _ _ _ (mm/dd/yyyy)

QUESTIONNAIRE

"I will now ask you some questions that require use of your memory. Please rely only on your memory." *(Do not allow the patient to look at a calendar, newspaper, or other memory aid.)*

	Subject Response	Instructions	Scoring Correct (0)	Scoring Incorrect (1)
1. What is the date today?	_____	Scored correctly only when the exact month, date, and year are given correctly (need all 3 parts).		_____
2. What day of the week is it?	_____			_____
3. What is the name of the place you are currently located?	_____	Scored correctly if any correct description of the location is given – my home or correct name of town of residence.		_____
4. What is your telephone number?	_____	Verify with number in Contact Information. Area code not necessary.		_____
5. How old are you?	_____	Scored correctly when stated age corresponds to date of birth.		_____
6. When were you born?	_____	Scored correctly only when the month, exact date, and year are all given (need all 3 parts).		_____
7. Who is the President of the U.S. now?	_____	Requires only the last name of the President.		_____
8. Who was President just before him?	_____	Requires only the last name of the President.		_____
9. What was your mother's maiden name?	_____	Does not need to be verified. Scored correct if a female 1st name plus a last name other than the subject's last name is given.		_____
10. Subtract 3 from 20 and keep subtracting 3 from each new number, all the way down. [20-17-14-11-8-5-2]	_____	Requires that the entire series must be performed correctly to be scored as correct. Any error in the series or unwillingness to attempt is scored as incorrect.		_____
		Total Number of Errors:		_____

ADJUSTED SCORING

a) Decrease total number of errors by 1 if the subject:
   - Only has a grade school education
     OR
   - Is African-American

b) Decrease total number of errors by 2 if the subject:
   - Only has a grade school education
     AND
   - Is African-American

c) Increase the total number of errors by 1 if the subject:
   - Has had education beyond high school

Adjusted Score: _____

If adjusted score is: 0-2 Errors – Keep in study
3-10 Errors – Exclude from study

1. Type of consent
    - ○ Hypertension active observation
    - ○ Alternative asthma intervention
    - ○ Hypertension passive observation

If 'Hypertension passive observation' is selected above, stop. Submit the form without answering any remaining questions.

2. Version of consent document

    The version number or version date should appear in either the header or footer of the informed consent document or on a stamp applied to that document. *Note: The informed consent form approved by your IRB may contain either a version number or a version date, but not necessarily both. If one of the items does not appear on the form, check the N/A box for that item.*

    a. Version number: _____ ☐ N/A
    b. Version date: __ __/__ __/__ __ __ __ (mm/dd/yyyy) ☐ N/A

3. Date informed consent signed: __ __/__ __/__ __ __ __ (mm/dd/yyyy)

SCREENING ELIGIBILITY

4. Short Portable Mental Status Questionnaire (SPMSQ) score: ____

    If the SPMSQ score is >2, the subject is NOT eligible.

5. Baseline blood pressure control (Complete only if 'Hypertension active observation' is selected for Item 1.)

    ○ Average systolic <130 mm Hg AND average diastolic <80 mm Hg AND subject IS currently diagnosed with diabetes OR chronic kidney disease

    Blood pressure is controlled; subject is NOT eligible.

    ○ Average systolic <140 mm Hg AND average diastolic <90 mm Hg AND subject IS NOT currently diagnosed with diabetes OR chronic kidney disease

    Blood pressure is controlled; subject is NOT eligible.

    ○ Average systolic blood pressure >200 mm Hg OR average diastolic blood pressure >115 mm Hg

    Refer to the Manual of Operations for instructions on handling hypertensive urgencies; subject is NOT eligible.

    ○ Uncontrolled

    If one of the following options is selected for Item 5, enter the subject's average research blood pressure in items 5.a and 5.b:

    Option 1 – 'Average systolic <130 mm Hg AND average diastolic <80 mm Hg AND subject IS currently diagnosed with diabetes OR chronic kidney disease'

    Option 2 – 'Average systolic <140 mm Hg AND average diastolic <90 mm Hg AND subject IS NOT currently diagnosed with diabetes OR chronic kidney disease'

    Option 3 – 'Average systolic blood pressure >200 mm Hg OR average diastolic blood pressure >115 mm Hg'

    a. Average Systolic: __ __ __
    b. Average Diastolic: __ __ __

(Continue to 'Item 6' on page 2.)

6. Is the subject ineligible for another reason not listed above?
    - ○ Yes
    - ○ No

        a. If yes, specify: _____

SUBJECT MUST MEET ALL OF THE INCLUSION CRITERIA AND NONE OF THE EXCLUSION CRITERIA TO REMAIN IN THE STUDY

(Do not enter into database)

Inclusion Criteria	Has Inclusion Criterion	
English or Spanish speaking males or females	Yes	No
At least 12 years of age	Yes	No
Has a diagnosis of persistent asthma (can be mild, moderate or severe as long as they don't meet any of the exclusion criteria)	Yes	No
Exclusion Criteria	**Has Exclusion Criterion**	
Hypertension which would qualify them for the BP control group	Yes	No
History of severe, life-threatening asthma evidenced by a history of loss of consciousness, ICU admissions or mechanical ventilation due to asthma	Yes	No
Diagnosis of chronic obstructive pulmonary disease	Yes	No
Previous involvement in a multidisciplinary asthma management clinic	Yes	No
Pregnancy	Yes	No
Poor prognosis with a life expectancy estimated less than 2 years	Yes	No
Residence in a nursing home or diagnosis of dementia	Yes	No
Inability to give informed consent	Yes	No
Impaired cognitive function (>2 errors on the Short Portable Mental Status Questionnaire)	Yes	No

Complete Part A and Part B of the paper form at <u>EVERY study visit</u> (per protocol) after the baseline visit. These items (part A and B) <u>will not</u> be entered into the database. Retain a copy (of the completed paper form) in the subject's study file for monitoring.

A. Visit Date: __ __/__ __/__ __ __ __ (mm/dd/yyyy)

Screening Questions (to be read to the subject)

1. **"Have you had any changes in your health since your last study visit?"**
   ○ Yes ○ No

2. **"Have you been hospitalized or received care in the emergency department since your last study visit?"**
   ○ Yes ○ No

B. Serious adverse event not reported by the subject

1. Serious adverse event (SAE) found documented in medical record (Study Coordinator to review medical record for time period since last study visit):
   ○ Yes ○ No

2. SAE occurred at the time of the study visit:
   ○ Yes ○ No

*If your answer to one or more items in Sections A and B is Yes, skip to Section C, item 9 to verify that the event is an SAE. If the outcome of the identified event matches one or more of items C.9.a. – C.9.g., the event represents a SERIOUS adverse event (SAE). **Complete all items in Section C** on the hard copy form, **ENTER THE FORM ELECTRONICALLY**, and file the hard copy form in the subject's folder.*

*Also complete Section C and enter the form electronically **ANY** time an event is identified that matches one or more of the outcomes listed in C.9.a. – C.9.g (e.g., another clinic staff member or the study pharmacist becomes aware of a serious adverse event outside of a scheduled study visit).*

*If the outcome of the identified event is C.9.h. (None of the above), select C.9.h and **STOP HERE.** FILE the hard copy form in the subject's folder. The event represents a non-serious adverse event. Do NOT complete items C.1 – C.8 on the hard copy form. Do NOT submit the form electronically.*

Serious Adverse Event (SAE)

1. Date of SAE: __ __/__ __/__ __ __ __ (mm/dd/yyyy)

2. Date site became aware of SAE: __ __/__ __/__ __ __ __ (mm/dd/yyyy)

3. SAE descriptor: _____

4. Was the SAE an exacerbation of a pre-existing condition (i.e. existing prior to enrollment)?

   ○ Yes ○ No

5. Was the SAE related or might it have been related to a medication on CAPTION study list of drug codes?

   ○ Yes ○ No

a. Medication	b. Stopped because of Adverse Event?
_____ Code: __ __ __ __	○ Yes ○ No
_____ Code: __ __ __ __	○ Yes ○ No
_____ Code: __ __ __ __	○ Yes ○ No
_____ Code: __ __ __ __	○ Yes ○ No

6. Describe any details about the SAE that might help us determine whether it is drug-related.

_____

_____

_____

_____

_____

_____

7. Describe relevant scans/tests/laboratory data, including dates.

_____

_____

_____

_____

_____

_____

_____

_____

8. Describe other relevant history, including pre-existing medical conditions (e.g. allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction).

_____

_____

_____

_____

_____

_____

_____

9. Outcomes that are attributed to the SAE in the medical record or reported by the subject at the study visit (check all that apply) :

☐ a. Death

a.1 Date: __ __/__ __/__ __ __ __ (mm/dd/yyyy)

☐ b. Life-threatening

☐ c. Hospitalization – initial or prolonged

☐ d. Disability

☐ e. Congenital anomaly

☐ f. Required intervention to prevent permanent impairment/damage

Option 9.f should be used for an event that does not result in death, a life-threatening condition, hospitalization, disability or congenital deformity but that did jeopardize the subject and required a specific medical intervention to prevent one or more of outcomes C.9.a – C.9.e from occurring.

☐ g. Important medical event as determined by the site PI or designee

Option 9.g should only be chosen when a site judges the event to represent significant hazard or harm to a research subject.

☐ h. None of the above

*If there is **any** question about whether an event should be classified as an SAE, please **contact the CCC by phone or email for a recommendation on this decision**.*

1. Did the subject complete all study visits with the Study Coordinator?
   - ○ Yes
     a. Date of final visit: __ __ / __ __ / __ __ __ __ (mm/dd/yyyy)
   - ○ No
     b. Date of early termination: __ __ / __ __ / __ __ __ __ (mm/dd/yyyy)
     c. Date of last study visit with Study Coordinator or Pharmacist: __ __ / __ __ / __ __ __ __ (mm/dd/yyyy)

2. If the subject terminated the study early, please indicate the reason.
   - ○ Subject eligibility status changed
     a. Reason: _____
   - ○ Subject chose to withdraw
     b. Reason: _____
   - ○ Subject lost to follow-up (Unable/unwilling to travel/moved from area/unable to locate)
   - ○ Research team chose to discontinue subject
     c. Reason: _____
   - ○ Subject withdrew/terminated due to Adverse Event
     d. Specify: _____
   - ○ Subject death (enter death date for question 1.b)
   - ○ Other
     e. Specify: _____

3. Comments:

_____

_____

_____

_____

_____

_____

_____

_____

_____

1. Visit Date: _ _/_ _/_ _ _ _ (mm/dd/yyyy)

INSTRUCTIONS (to be read to the subject):

"The first questions ask for some basic information about you."

(Research nurse is to check the box corresponding to the subject's answers.)

2. Birth Date: _ _/_ _/_ _ _ _ (mm/dd/yyyy)

3. Gender
   - ○ Male
   - ○ Female

4. Race (check all that apply)
   - ☐ a. American Indian or Alaska Native
   - ☐ b. Asian
   - ☐ c. Native Hawaiian or other Pacific Islander
   - ☐ d. Black or African-American
   - ☐ e. White
   - ☐ f. Declined to answer

5. Ethnicity
   - ○ Hispanic or Latino
   - ○ Non-Hispanic or Non-Latino Origin
   - ○ Declined to Answer

6. Education (Select the highest grade completed or degree/certificate received.)
   - ○ 1 – 5 years
   - ○ 6 – 8 years
   - ○ 9 – 12 years
   - ○ Post-high school technical /associate degree or certificate
   - ○ 4-year BA or BS degree
   - ○ Master's degree
   - ○ Doctoral degree

7. Insurance Status (Select only the primary insurer.)
   - ○ Private insurance
   - ○ Medicare
   - ○ Medicaid
   - ○ Other insurer
   - ○ None/Self-pay
   - ○ Free care

8. Insurance Coverage for Prescriptions
   - ○ Yes
   - ○ No

9. Annual Household Income
   - ○ <$10,000
   - ○ $10, 000-$24, 999
   - ○ $25,000- $39,999
   - ○ $40,000-$54,999
   - ○ $55,000-$79,999
   - ○ $80,000-$99,999
   - ○ >$100,000
   - ○ Refused to answer

10. Marital Status
   - ○ Never married
   - ○ Married
   - ○ Living as married
   - ○ Divorced or separated
   - ○ Widowed

11. Smoking Status
   - ○ Currently smokes (If 'Currently smokes' is selected, skip question 11.c)
   - ○ Former smoker
   - ○ Never smoked (If 'Never smoked' is selected, skip questions 11.a – 11.c)

   a. Number of years smoked: __ __
   b. Number of cigarettes smoked per day: __ __
   c. Elapsed time since quitting
      - ○ < 5 years
      - ○ 5-14 years
      - ○ ≥ 15 years

12. Current Alcohol Intake
   - ○ None
   - ○ < 1 drink per day
   - ○ 1-2 drinks per day
   - ○ 3-4 drinks per day
   - ○ > 4 drinks per day

13. Duration of Asthma
   - ○ New diagnosis
   - ○ < 6 months
   - ○ 6 months - 1 year
   - ○ >1 - 3 years
   - ○ >3 - 5 years
   - ○ >5 - 10 years
   - ○ >10 years

14. Asthma Diagnosis
   - ○ Persistent asthma (not otherwise classified)
   - ○ Mild persistent asthma
   - ○ Moderate persistent asthma
   - ○ Severe persistent asthma

A. Date Administered: _ _/_ _/_ _ _ _ (mm/dd/yyyy)

B. Asthma Control Test

1. In the past 4 weeks, how much of the time did your asthma keep you from getting as much done at work, school, or at home?
   - ○ All of the time (1)
   - ○ Most of the time (2)
   - ○ Some of the time (3)
   - ○ A little of the time (4)
   - ○ None of the time (5)

2. During the past 4 weeks, how often have you had shortness of breath?
   - ○ More than once a day (1)
   - ○ Once a day (2)
   - ○ 3 to 6 times a week (3)
   - ○ Once or twice a week (4)
   - ○ Not at all (5)

3. During the past 4 weeks, how often did your asthma symptoms (wheezing, coughing, shortness of breath, chest tightness or pain) wake you up at night or earlier than usual in the morning?
   - ○ 4 or more nights a week (1)
   - ○ 2 to 3 nights a week (2)
   - ○ Once a week (3)
   - ○ Once or twice (4)
   - ○ Not at all (5)

4. During the past 4 weeks, how often have you used your rescue inhaler or nebulizer medication (such as Albuterol)?
   - ○ 3 or more times per day (1)
   - ○ 1 or 2 times per day (2)
   - ○ 2 or 3 times per week (3)
   - ○ Once a week or less (4)
   - ○ Not at all (5)

5. How would you rate your asthma control during the past 4 weeks?
   - ○ Not controlled at all (1)
   - ○ Poorly controlled (2)
   - ○ Somewhat controlled (3)
   - ○ Well controlled (4)
   - ○ Completely controlled (5)

C. Total Score _____

Visit: ○ Baseline
○ 9 months
○ 18 months

1. Date of Study Visit: _ _/_ _/_ _ _ _ (mm/dd/yyyy)

2. Clinic Visits Documented in the Medical Record in the Past 9 Months:

a. Clinic Date	b. Visit Type	c. Visit to (check all that apply)	d. Corticosteroids Prescribed?	e. Duration of steroid course (days)
_ _/_ _/_ _ _ _	O Asthma O Other	☐ Emergency Dept. ☐ Clinic Visit ☐ Hospitalization	O Yes O No	________
_ _/_ _/_ _ _ _	O Asthma O Other	☐ Emergency Dept. ☐ Clinic Visit ☐ Hospitalization	O Yes O No	________
_ _/_ _/_ _ _ _	O Asthma O Other	☐ Emergency Dept. ☐ Clinic Visit ☐ Hospitalization	O Yes O No	________
_ _/_ _/_ _ _ _	O Asthma O Other	☐ Emergency Dept. ☐ Clinic Visit ☐ Hospitalization	O Yes O No	________
_ _/_ _/_ _ _ _	O Asthma O Other	☐ Emergency Dept. ☐ Clinic Visit ☐ Hospitalization	O Yes O No	________
_ _/_ _/_ _ _ _	O Asthma O Other	☐ Emergency Dept. ☐ Clinic Visit ☐ Hospitalization	O Yes O No	________

Visit: ○ Baseline
○ 9 months
○ 18 months

A. Visit Date: _ _/_ _/_ _ _ _ (mm/dd/yyyy)

B. Medication Adherence

1. Check medical record prior to visit: Does the subject have at least one active prescription for an asthma medication? ○ Yes ○ No

   (If NO, stop here and do NOT ask remaining questions.)

2. Is the only prescribed asthma medication a rescue inhaler? ○ Yes ○ No

   (If YES, stop here and do NOT ask remaining questions.)

3. Some people have difficulty in taking asthma medication as prescribed. Do you have difficulty with this? ○ Yes ○ No

4. How many days in the past week did you forget to take your asthma medication?

   _____ days

5. How many days in the past week did you not take your medication on purpose?

   _____ days

6. How many days in the past week did you add an extra pill or puff other than your rescue inhaler (e.g. albuterol)?

   _____ days

7. In the last 6 months, did you ever take less medicine because you felt you needed less (other than your rescue inhaler)? ○ Yes ○ No

8. In the last 6 months, if you felt worse when you took the medicine, did you ever stop taking it? ○ Yes ○ No

Study Visit: ○ Baseline
○ 9 months
○ 18 months

1. Date of Study Visit: _ _/_ _/_ _ _ _ (mm/dd/yyyy)

2. <u>Asthma</u> Medications Currently Prescribed at the Time of the Study Visit (to be completed at each study visit):

<u>INSTRUCTIONS (to be read to the subject)</u>: "I have a list of the asthma medications that we think you are taking. Please tell me how much of each medication you are taking or if you are not taking the medication."

a. Medication	b. Unit Strength	c. Dose	d. Frequency	e. PRN	f. Patient Report on Adherence
______________ Code: ___ ___ ___ ___				☐	O Patient taking as prescribed O Patient taking but at a different dose or frequency O Patient not taking now
______________ Code: ___ ___ ___ ___				☐	O Patient taking as prescribed O Patient taking but at a different dose or frequency O Patient not taking now
______________ Code: ___ ___ ___ ___				☐	O Patient taking as prescribed O Patient taking but at a different dose or frequency O Patient not taking now
______________ Code: ___ ___ ___ ___				☐	O Patient taking as prescribed O Patient taking but at a different dose or frequency O Patient not taking now
______________ Code: ___ ___ ___ ___				☐	O Patient taking as prescribed O Patient taking but at a different dose or frequency O Patient not taking now

Subject Name: ____ (For site use only; do not enter into database.)

A. PHARMACIST ENCOUNTER

1. Encounter Date: _ _/_ _/_ _ _ _ (mm/dd/yyyy)

2. Contact Type:
   - ○ Initial
   - ○ Follow-up
   - ○ Phone Communication

3. Pharmacist Code: ______________

4. Asthma Medications (list ONLY asthma medications that are documented as current in the medical record):

a. Medication	b. Unit Strength	c. Dose	d. Frequency	e. PRN	f. Patient Report on Adherence
________________ Code: __ __ __ __				☐	O Patient taking as prescribed O Patient taking but at a different dose or frequency O Patient not taking now
________________ Code: __ __ __ __				☐	O Patient taking as prescribed O Patient taking but at a different dose or frequency O Patient not taking now
________________ Code: __ __ __ __				☐	O Patient taking as prescribed O Patient taking but at a different dose or frequency O Patient not taking now
________________ Code: __ __ __ __				☐	O Patient taking as prescribed O Patient taking but at a different dose or frequency O Patient not taking now
________________ Code: __ __ __ __				☐	O Patient taking as prescribed O Patient taking but at a different dose or frequency O Patient not taking now

5. Recommended lifestyle change options (check all that apply):

- ☐ a. ↓ weight
- ☐ b. ↓ smoking
- ☐ c. Avoid allergen(s)
- ☐ d. Other
  - d.1 Specify: ___________________________
- ☐ e. No lifestyle changes recommended

6. ↑ Asthma medication compliance recommended
   - ○ Yes
   - ○ No

7. New Plan/Recommendations
   - ○ Continue current regimen
   - ○ Recommend change to plan (List changes to plan in Item A.8)

8. Recommended Change to Plan:

a. Medication	b. Change Type	c. Unit Strength	d. Dose	e. Frequency	f. PRN	g. Comments	h. Physician Decision
______________ Code: __ __ __ __	O Start New Drug O Discontinue Drug O Increase Dose O Decrease Dose O Regimen Change (same dose)				☐		O Accept O Reject O Modify
______________ Code: __ __ __ __	O Start New Drug O Discontinue Drug O Increase Dose O Decrease Dose O Regimen Change (same dose)				☐		O Accept O Reject O Modify
______________ Code: __ __ __ __	O Start New Drug O Discontinue Drug O Increase Dose O Decrease Dose O Regimen Change (same dose)				☐		O Accept O Reject O Modify
______________ Code: __ __ __ __	O Start New Drug O Discontinue Drug O Increase Dose O Decrease Dose O Regimen Change (same dose)				☐		O Accept O Reject O Modify

9. Planned Follow-up with Pharmacist (check all that apply):

☐ a. 1 week ☐ b. 2 weeks ☐ c. 4 weeks ☐ d. 6 weeks ☐ e. 8 weeks ☐ f. 3 months

☐ g. Other time frame

g.1 Specify:________________________________

☐ h. Patient declined to re-schedule ☐ i. Pharmacist intervention completed

10. Final Plan (Complete only if changed from pharmacist recommended plan):

a. Medication	b. Change Type	c. Unit Strength	d. Dose	e. Frequency	f. PRN
______________________ Code: __ __ __ __	O Start New Drug O Discontinue Drug O Increase Dose O Decrease Dose O Regimen Change (same dose)				☐
______________________ Code: __ __ __ __	O Start New Drug O Discontinue Drug O Increase Dose O Decrease Dose O Regimen Change (same dose)				☐
______________________ Code: __ __ __ __	O Start New Drug O Discontinue Drug O Increase Dose O Decrease Dose O Regimen Change (same dose)				☐
______________________ Code: __ __ __ __	O Start New Drug O Discontinue Drug O Increase Dose O Decrease Dose O Regimen Change (same dose)				☐

B. PHARMACIST TIME DOCUMENTATION

1. Start time: __ __ __ __ (use military time, e.g. 1645)

2. End time: __ __ __ __ (use military time, e.g. 1645)

Please complete the following by estimating the number of minutes you spent doing each activity.

3. Activity	**Minutes to complete activity** (circle one)
a. Medical record review prior to patient visit	0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 >30 NA
b. Consultation with other provider or family	0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 >30 NA
c. Patient assessment/medication history	0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 >30 NA
d. Medical record review during patient visit	0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 >30 NA
e. Order laboratory	0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 >30 NA
f. Order medications/write prescriptions	0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 >30 NA
g. Medical education	0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 >30 NA
h. Lifestyle modification education	0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 >30 NA
i. Education on inhaler technique or peak flow measurement	0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 >30 NA
j. Recommendations to MD	0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 >30 NA
k. Documentation in medical record	0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 >30 NA

Please use the following CPT codes to code medication therapy management service(s) provided during the visit by a pharmacist, individual, face-to-face with patient, with assessment and intervention if provided:

99605 Initial 15 minutes, ***new*** patient

99606 Initial 15 minutes, ***established*** patient

99607 Each ***additional*** 15 minutes (Use 99607 in conjunction with 99605, 99606; code separately in addition to code for primary service.)

CPT code for initial 15 minutes:

Baseline encounter = 99605 (new patient)

Encounters after Baseline = 99606 (established patient)

4. Number of 15 minute units of CPT code 99607 (1=15 additional minutes, 2=30 additional minutes, 3=45 additional minutes, etc.): _____

Visit: ○ Baseline
○ 9 months
○ 18 months

A. Visit Date: _ _/_ _/_ _ _ _ (mm/dd/yyyy)

B. Self Report

1. Courses of oral corticosteroids (e.g. prednisone) in past 9 months: _____

2. Number of days on oral corticosteroids (e.g. prednisone) in past 9 months: _____

3. Number of hospitalizations due to asthma in the past 9 months: _____

4. Number of emergency room visits due to asthma in the past 9 months: _____

5. Number of doctor's office visits due to asthma in the past 9 months: _____

6. Number of days of school or work missed due to asthma in the past 9 months: _____
For subjects not currently working or attending school, this question should be "Number of days that asthma was severe enough that you would have missed work or school in the past 9 months: _____"

Visit: ○ Baseline
○ 9 months
○ 18 months

A. Visit Date: _ _/_ _/_ _ _ _ (mm/dd/yyyy)

INSTRUCTIONS (to be read to the subject):

The following questions ask about how asthma may be affecting your daily life. Each question begins, "In the past 4 weeks, how much have you _____" and is followed by a situation or feeling. Please select a number from 0 to 3 that reflects **how much the situation or feeling has happened to you in the past 4 weeks,** where 0 indicates that the situation or feeling has not happened at all, 1 indicates that it has happened a little, 2 indicates it has happened somewhat, and 3 indicates it has happened a great deal in the past 4 weeks.

B. QUESTIONNAIRE

In the past 4 weeks how much have you….	Not at All [0]	A Little [1]	Somewhat [2]	A Great Deal [3]
1. Been troubled by episodes of shortness of breath	0	1	2	3
2. Been troubled by wheezing attacks	0	1	2	3
3. Been troubled by tightness in the chest	0	1	2	3
4. Been restricted in walking down the street on level ground or doing light housework because of asthma	0	1	2	3
5. Been restricted in walking up hills or doing heavy housework because of asthma	0	1	2	3
6. Felt tired or a general lack of energy	0	1	2	3
7. Been unable to sleep at night	0	1	2	3
8. Felt sad or depressed	0	1	2	3
9. Felt frustrated with myself	0	1	2	3

In the past 4 weeks how much have you….	Not at All [0]	A Little [1]	Somewhat [2]	A Great Deal [3]
10. Felt anxious, under tension, or stressed	0	1	2	3
11. Felt that asthma is preventing me from achieving what I want from life	0	1	2	3
12. Felt that asthma has interfered with my social life	0	1	2	3
13. Been limited in going certain places because they are bad for my asthma	0	1	2	3
14. Been limited in going to certain places because I have been afraid of having an asthma attack and not being able to get help	0	1	2	3
15. Felt generally restricted	0	1	2	3
16. Been restricted in the sports, hobbies, or other recreations I can engage in because of my asthma	0	1	2	3
17. Felt that asthma is controlling my life	0	1	2	3
18. Been worried about my present or future life because of asthma	0	1	2	3
19. Been worried about asthma shortening my life	0	1	2	3
20. Felt dependent on my asthma inhalers	0	1	2	3

SUBMIT THIS FORM ELECTRONICALLY WITHIN 24 HOURS OF BECOMING AWARE OF A PROTOCOL DEVIATION

1. Date of Deviation: __ __ / __ __ / __ __ __ __ (mm/dd/yyyy)

2. Date Site became Aware of Deviation: __ __ / __ __ / __ __ __ __ (mm/dd/yyyy)

3. Type of Deviation (check all that apply)

☐ a. Subject did not meet all inclusion criteria
a.1 Describe unmet criterion or criteria: _____

☐ b. Subject met one or more exclusion criteria
b.1 Describe criterion or criteria: _____

☐ c. Subject did not sign informed consent or consent information was not provided to the subject according to IRB-approved procedure

☐ d. A fourth blood pressure measurement was not taken when the second and third measurements differed by greater than 4 mm Hg.

☐ e. Subject missed window for 9 month study visit

☐ f. Subject missed window for final visit (18 month Asthma or 24 month BP)

☐ g. Serious adverse event was not reported within 24 hours
g.1 Event Date: __ __ / __ __ / __ __ __ __ (mm/dd/yyyy)
g.2 Describe Event: _____
_____
_____
_____

☐ h. Other
h.1 Specify: _____
_____
_____
_____

Corrective Action Plan (For site use only; do not enter into database.):
_____
_____
_____
_____
_____
_____
_____
_____

APPENDIX IX: SERIOUS ADVERSE EVENT DESCRIPTORS

Following is a list of Serious Adverse Event descriptors that will be used to populate a drop-down box for Item C.3. on CRF # 2 Serious Adverse Event.

If you wish to report a specific symptom that is not on the list below, please check with the CCC before using the 'Other' descriptor.

SAE Descriptor	Instructions for Use
Fever	Do not report if fever is related to a cold or viral infection.
Rash/itching	Covers rash, itching, hives, flushing or similar change in skin. Do not report if symptoms are related to contact with an allergen such as poison ivy or oak.
Angioedema	Covers swelling of the lips, face or tongue.
Rhythm disorder	Covers any new rhythm disorder such as tachycardia or a racing heartbeat that is not typical for the subject.
Chest pain	Covers any new development or worsening of chest pain that does not reflect stable angina.
Headache	Do not report if subject has a history of frequent headaches.
Other pain	Other pain that is not related to an injury or chronic condition.
Shortness of breath	Covers shortness of breath, wheezes, stridor, and gasping for breath that is not typical for the subject.
Cough	Use only for a new cough that is not related to a cold, other infection or seasonal allergy and that follows initiation of a new medication.
Weight gain	Use for new and unintended weight gain with sudden onset, e.g., related to CHF.
Lower extremity edema	Swollen legs or lower extremity edema that is new in onset or substantially worse than usual for the subject.
Kidney problem	Covers a new or worsening kidney problem such as acute renal failure or a 20% increase in creatinine level; do not report a kidney infection.
Liver problem	Covers a new or worsening liver problem such as an increase in one or more liver function tests to > 2 times normal.
Nausea or vomiting	Do not report instances related to influenza, other infection or food poisoning.
Other GI problem	Use only for a new GI problem such as diarrhea, constipation, cramping or abdominal pain that is not related to influenza, other infection or food poisoning; do not use to report nausea or vomiting
Neurological change	Use only for a new or worsening neurological change, e.g. tingling in hands or feet
Trouble walking or falls	Trouble walking or falls
Lightheadedness or passing out	Lightheadedness, dizziness, passing out, or loss of consciousness
Orthostatic hypotension	Orthostatic hypotension (that is not chronic)
Urinary problem	Urinary problem such as urgency or frequency that is not related to infection

SAE Descriptor	Instructions for Use
Blood disorder	Bleeding that is not related to a blood dyscrasia such as leucopenia or thrombocytopenia
Change in lab values	Change in lab values related to a drug side effect such as a marked drop in potassium or sodium or a marked increase in serum creatinine.
Mood change	A marked change in mood, such as new or recurrent depression, anxiety or agitation; not intended to cover chronic conditions
Problem with sexual activity	Development of a new problem with sexual activity
Weakness	Covers new onset or worsening of weakness, fatigue, lethargy or other marked decrease in strength
Other	CHECK WITH CCC BEFORE USING THE 'Other' DESCRIPTOR

APPENDIX X: PROCEDURES FOR GENERATING PATIENT LISTS

1) Ask your IT staff to run a list of all patients who have been seen in the clinic within the last 24 months and who have an ICD9 code of 493 (indicating a diagnosis of asthma).

2) IT should eliminate duplicates from the list if at all possible. Ideally, you would receive the list in Excel so that you could sort to double-check for duplicates.

3) If possible, have your IT staff number each unique patient on each list sequentially starting with "1." Otherwise, manually write in sequential numbers until every unique patient has been assigned a number. You may simply write in the numbers adjacent to the names.

4) Once you have the list numbered, discuss with the CCC whether or not de-identifying the first 2-3 pages would leave remaining any indication of visits. If we determine that it would, make a copy of the first 3 pages of the list. Write in your clinic name at the top of this list. Take a black magic marker and cross out the patient names on these copied pages. Then fax those 3 pages to 319-335-9511.

5) Please make sure that the clinic name is at the top of the first page and that your numbering shows.

6) If de-identifying the list leaves only the numbering visible, the CCC will review via telephone the critical indicators of an accurate list.

7) Also let the CCC know via email the total number of patients on the complete list that you received from IT.

8) We will review the list and let you know if the number of patients on the list seems reasonable and if your numbering appears accurate.

9) If your de-identified list of patients only shows the list of numbers, the CCC will review with you the checks we want you to perform on the list.

10) We will then reach consensus on the total number of patients that we should randomize for the study.

11) The CCC will send the total number of unique patients to the DMC, and they will randomize patients.

12) The CCC will return to you a log that has your patients randomized. You should use the log for tracking patients who are screened for the study.

APPENDIX XI: DOCUMENTATION OF PHARMACIST TIME

Part B of the Pharmacist Encounter Form asks for the time the pharmacist spends on various activities related to study visits.

1. Items 1 and 2: These items ask for the "Door to Door" times for each subject visit:
   - Item 1: The time when the pharmacist and the subject begin their visit
   - Item 2: The time when the subject completes the visit

   This time span documented in Items 1 and 2 can be SHORTER than the total amount of time documented in the grid in Item 3.

2. Item 3: Provide an estimated duration for each activity 3.a – 3.k, being as precise as you can.
   - Items 3.c through 3.i: The total time spent for these activities should correspond with the in and out times documented in Items 1 and 2.

   Ordering labs or reviewing other records might occur in a different location. However, if they occur during the time of the subject visit, they still constitute "Door to Door" time.

3. The Data Management Center (DMC) will automatically code each visit as either a 'new patient' visit or an 'established patient' visit and assign the codes for 99605 and 99606, respectively.

4. The DMC will also automatically account for the first 15 minutes of each visit using either assigned code 99605 or assigned code 99606.

5. Item 4: Calculate the number of CPT units billable *after* the initial 15 minutes are accounted for automatically:
   - Sum the amounts of time documented for activity items 3.c through 3.i to calculate the total amount of the visit time that is billable
   - Subtract 15 minutes from the resulting total, since the initial 15 units will be accounted for by the DMC
   - Round the resulting value up to the next 15 minute increment

     EXAMPLE:

     Item 1: 0930 Item 2: 10:03

     Total "Door to Door" time = 33 minutes

     Subtract initial 15 minutes = 33 – 15 = 18 minutes

     Round up 18 minutes to the next 15 minute increment = 30 minutes

     Final value for Item 4 = 30 ÷ 15 = 2

6. Items 3.a, 3.b, 3.j and 3.k are NOT captured in the CPT codes used for billing:
   - Item 3.a reflects "pre-service" time
   - Item 3.b probably occurs outside of the subject's study visit
   - Items 3.j and 3.k are considered to be "post-service"