

Flunisolide HFA in Children with Small Airway Disease

INFORMED CONSENT AND RESEARCH AUTHORIZATION

Flunisolide HFA in Children with Small Airway Disease

Industry Contracts number: OICB1500055

Sponsor(s) name & address: MEDA Pharmaceuticals, 1265 Davidson Ave, Sorensen, NJ 08873

Investigator(s) name, Degree, University Department, & address:

Scott Bickel, MD, and Nemr Eid, MD

Division of Pediatric Pulmonology

University of Louisville

571 S Floyd St., Suite 414

Louisville, KY 40202

Site(s) where study is to be conducted:

University of Louisville Pediatric Pulmonology Clinic

210 E. Gray St.

Suite 802

Louisville, Kentucky 40202

Phone number for subjects to call for questions: 502-588-4940

Introduction and Background Information

You/Your child (referred to as you in the rest of this document) are invited to take part in a research study because you have been diagnosed with asthma and have not been on inhaled medication for at least the past four weeks. The study is being conducted under the direction of Scott Bickel, MD, and Nemr Eid, MD, at the University of Louisville. About 50 local subjects will be invited to take part in this research.

Purpose

The purpose of this study is to see how Flunisolide HFA (an FDA approved inhaled medication to treat asthma) affects the lungs in asthma, especially the small airways deeper in the lungs as measured by tests that are commonly used in the day-to-day care of patients with asthma.

Procedures

To participate in this study, you must meet certain criteria that will be evaluated and determined by the study doctor and/or study staff. Your medical history and current medical condition will be reviewed. You will be asked for personal information, such as your date of birth and race/ethnicity. The study doctor in charge of this study or a member of the study doctor's staff will discuss with you all requirements for participation in this study.

Your participation in this study will last for up to 14 weeks. If you consent to participate, you will have the following procedures while you are in this study.

Flunisolide HFA in Children with Small Airway Disease

Visit 1: (1 hour)

At this visit you can expect us to do the following:

- Ask you to review and sign this informed consent and HIPAA document
- Obtain your past medical history and any medications you have taken in the past 4 weeks or are currently taking
- Ask you to fill out a simple questionnaire to help show how well your asthma has been controlled.
- Measure oxygen saturation on room air
- Perform a physical exam (weight, height, blood pressure, heart rate, temperature, etc)
- Collect urine to preform a pregnancy test if you are a female who could be pregnant
- Require that you have the following procedures:
 - Spirometry - a breathing test where you will be asked to take a very deep breath and blow out as hard and quick as you can into a mouthpiece connected to a computer
 - Impulse oscillometry - a test where you will be asked to sit up straight and breathe normally for about 30 seconds while you have a mouthpiece in place. You will hear a quiet “ticking” sound during the procedure but it is painless and does not require significant effort.

This visit will determine if you are eligible to be enrolled in the study. If you meet the study criteria, we will ask you to continue in the study and schedule a second visit.

Visit 2: (1 hour; 1 to 56 days after visit 1))

At this visit you can expect us to do the following:

- Ask you to fill out a simple questionnaire to help show how well your asthma has been controlled
- Review your health status/medical history
- Review any medications you are taking
- Obtain vital signs (heart rate, temperature, respiratory rate and blood pressure)
- Measure your oxygen saturation on room air
- Measure your height and weight
- Perform a short physical exam
- Perform pre-bronchodilator impulse oscillometry
- Perform pre-bronchodilator spirometry
- Receive bronchodilator (albuterol, 4 puffs via spacer, or ProAir if you are currently using it)
- Perform post-bronchodilator impulse oscillometry
- Perform post-bronchodilator spirometry
- Randomly assign you (a process like flipping a coin) to a one of two doses of flunisolide (either 80 mcg 1 puff twice a day or 80 mcg 2 puffs twice a day)
- Provide you with flunisolide and teach you how to use the study drug device, per manufacturer’s instructions
- Provide you with albuterol sulfate for breakthrough symptoms.

Visit 3: (1 hour; 6 weeks after visit 2)

At this visit you can expect us to do the following:

- Review your health status/medical history

Flunisolide HFA in Children with Small Airway Disease

- Review any medications you are taking
- Obtain vital signs (heart rate, temperature, respiratory rate and blood pressure)
- Measure your oxygen saturation on room air
- Measure your height and weight
- Perform a short physical exam
- Perform pre-bronchodilator impulse oscillometry
- Perform pre-bronchodilator spirometry
- Receive bronchodilator (albuterol, 4 puffs via spacer)
- Perform post-bronchodilator impulse oscillometry
- Perform post-bronchodilator spirometry
- Record any adverse events you may have experienced

Potential Risks

The following table details the known risks related to Flunisolide HFA and how often they may occur.

Very Common Greater than 10%	Common Between 1% and 10%	Uncommon Between 0.1% and 1%
<ul style="list-style-type: none"> • Sore throat • Runny nose • Headache 	<ul style="list-style-type: none"> • Fever • Allergic reaction • Infection • Back pain • Vomiting • Upset stomach • Cough • Sinus infection • Nose bleed • Rash 	<ul style="list-style-type: none"> • Urinary tract infection

The following table details the know risks related to albuterol and how often they occur.

Very Common Greater than 10%	Common Between 1% and 10%	Uncommon Between 0.1% and 1%
<ul style="list-style-type: none"> • Asthma worsening 	<ul style="list-style-type: none"> • Ear infection • Allergic reaction • Dry mouth and throat • Diarrhea • Cough, hoarseness, sore throat, runny or stuffy nose • Swollen lymph nodes • Muscle pain • Skin infection • Hives • Migraine headache • Chest pain • Bronchitis 	<ul style="list-style-type: none"> • Heart rhythm abnormality • Bronchospasm (wheezing, chest tightness, trouble breathing), especially after starting a new canister of this medicine • Chest pain and fast, pounding, or uneven heart beats • Tremor, nervousness • Low potassium (confusion, uneven

Flunisolide HFA in Children with Small Airway Disease

	<ul style="list-style-type: none"> • Nausea • Vomiting 	<p>heart rate, extreme thirst, increased urination, leg discomfort, muscle weakness or limp feeling)</p> <ul style="list-style-type: none"> • Dangerously high blood pressure (severe headache, blurred vision, buzzing in your ears, anxiety, confusion, chest pain, shortness of breath, uneven heartbeats, seizure)
--	--	---

There may also be other procedures required as part of the study. The risks associated with Impulse oscillometry and spirometry include becoming short of breath when asked to inhale and exhale deeply and quickly.

In addition, you may suffer harms that we have not seen before.

Possible Pregnancy Risks

You should discuss pregnancy risks with your doctor before signing this consent form. Women who are pregnant or breast feeding may not participate in this research study. If you are pregnant or become pregnant, your unborn child may suffer harms that we have not seen before. If you (or your partner) become pregnant while in this study, the sponsor may ask to follow the outcome of the pregnancy. If you agree to allow the study doctor to follow your pregnancy, you will be asked to read and sign a separate consent form for permission to follow the outcome of your pregnancy.

If you are a man taking part in the study and your partner becomes pregnant, the study doctor may ask you to ask your partner for permission to follow her pregnancy. If she agrees, she will be asked to sign a separate consent form mentioned above.

Before starting this research study, females able to have children will have a pregnancy test. Talk to your doctor about the best method of birth control to use while you are in this study. It is important that you call your study doctor at 502-588-4940 right away if you become pregnant or father a child during the course of this study. If you or your partner becomes pregnant, a decision may have to be made whether or not to end the pregnancy.

We do not know the effects of flunisolide on an unborn baby. There is a risk that your unborn baby could be harmed if you become pregnant during your participation in the study. (If you ask, your study doctor will discuss the possible risks to your unborn child and your options should you become pregnant while in this study.)

Flunisolide HFA in Children with Small Airway Disease

Benefits

The possible benefits of this study include improving your asthma control and having access to an inhaler device that may be easier to use than others (as it does not require a separate spacer).

Alternatives

Instead of taking part in this study, you could choose to not to participate in this study. You can discuss other medications and/or methods with your doctor to bring your asthma symptoms under control.

Research Related Injury

If you are injured by being in this research study, the study doctor will arrange for you to get medical treatment. The sponsor will pay for any reasonable medical costs related to the treatment of your injury. If you are injured, there is no money set aside for lost wages, discomfort, disability, etc. You do not give up your legal rights by signing this form. If you think you have a research related injury, please call your study doctor, Dr. Bickel at 502-588-4940.

Compensation

You will be paid \$50 by Visa gift card for your time, inconvenience, or expenses while you are in this study. Because you will be paid to be in this study the University of Louisville may collect your name, address, social security number, and keep records of how much you are paid. You may or may not be sent a Form 1099 by the University. This will only happen if you are paid \$600 or more in one year by the University. This will not include payments you may receive as reimbursement, for example mileage reimbursement. We are required by the Internal Revenue Service to collect this information and you may need to report the payment as income on your taxes.

Costs

You will not be billed for the following office visits, tests, medications, and procedures that are done for this research study that are done for the research study: Flunisolide HFA, spirometry and impulse oscillometry. The charges for these items will be paid for by the Sponsor.

You or your insurance company will be billed for all office visits, tests, medications and procedures that are part of your routine medical care outside of this research study. You will be responsible for paying your co-pay that is associated with any office visit, test, medication or procedure. Some insurance companies will not pay for medical bills for people who participate in a research study. It is your responsibility to find out what costs, if any, your insurance company will cover before taking part in the study. If you need help finding out what your insurance company will cover, please ask your study doctor for assistance. If your insurance company does not pay for your bills associated with this study, you will be responsible for paying them.”

Flunisolide HFA in Children with Small Airway Disease

HIPAA Research Authorization

The Health Insurance Portability and Accountability Act of 1996 (HIPAA) provides federal safeguards for your protected health information (PHI). Examples of PHI are your name, address, and birth date together with your health information. PHI may also include your medical history, results of health exams and lab tests, drugs taken and results of this research study. Your PHI may not be used or shared without your agreement, unless it meets one of the HIPAA exceptions.

State and federal privacy laws protect your health information. In most cases, health information that identifies you can be used or shared by the research team only if you give your permission by signing this form.

If you sign this form your health information will be used and shared to answer the research questions described above and to make sure that the research was done correctly. The time period when information can be used or shared ends when all activities related to this study are completed.

Your access to your health information will not be limited during this study

You do not have to sign this form. If you do not sign this form you may not participate in the study and health information that identifies you will not be shared with the research team.

Site(s) where health information about you will be used or shared for this research:

In our research, the research team will look at and may share information about you and your health. Federal law requires that health care providers and researchers protect the privacy and security of health information that identifies you. We may ask for your health information from the following:

Faculty Practice Group Sites:

University of Louisville Pediatric Pulmonology Clinic

Protected health information (PHI) that will be used or shared for research

Consultation reports
Healthcare Provider orders
History and physical exams
Laboratory, x-ray and other tests
Records about the study drug and other drugs you may be taking

Revocation of Research Authorization

You may cancel the permission you have given to use and share your protected health information at any time. This means you can tell us to stop using and sharing your protected health information. If you cancel your permission:

- We will stop collecting information about you.
- You may not withdraw information that we had before you told us to stop.

Flunisolide HFA in Children with Small Airway Disease

- We may already have used it or shared it.
- We may need it to complete the research.
- Staff may ask your permission to follow-up with you if there is a medical reason to do so.

To cancel your permission, you will be requested to complete a written “Revocation of Research Authorization” form located at the end of this document. You may also obtain a copy from your study doctor, designated personnel or from the Human Subjects Protections Program Office website (<http://louisville.edu/research/humansubjects/links-to-forms>).

Information Available on ClinicalTrials.gov

A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

Confidentiality

Total privacy cannot be guaranteed. We will protect your privacy to the extent permitted by law. If the results from this study are published, your name will not be made public. Once your information leaves our institution, we cannot promise that others will keep it private.

Your information may be shared with the following:

- The sponsor (MEDA Pharmaceuticals) and others hired by the sponsor to oversee the research
- The University of Louisville Institutional Review Board, Human Subjects Protection Program Office, Privacy Office and others involved in research administration at the University
- The local research team
- People responsible for billing, sending and receiving payments related to your participation in the study
- Government agencies, such as:
 - Office for Human Research Protections
 - Office of Civil Rights
 - Food and Drug Administration

Security

The data collected about you will be kept private and secure in the UL Pediatric Pulmonology Clinic in a locked office. Data stored on a computer will be kept in a secured, password protected location which will be accessible only by those authorized by the study.

Conflict of Interest

This study involves a conflict of interest because: the institution and investigator will be compensated for your participation. The investigator may also receive compensation from the sponsor in exchange for sharing your study results and your protected health information with the sponsor. This

Flunisolide HFA in Children with Small Airway Disease

compensation is used to pay for the costs of doing this study. If you want to know, please ask the investigator how the institution and investigator will benefit by your participation in the study.

Voluntary Participation

Taking part in this study is completely voluntary. You may choose not to take part at all. If you decide not to be in this study, you won't be penalized or lose any benefits for which you qualify. If you decide to be in this study, you may change your mind and stop taking part at any time. If you decide to stop taking part, you won't be penalized or lose any benefits for which you qualify. You will be told about any new information learned during the study that could affect your decision to continue in the study.

Termination

Your study doctor or the study sponsor has the right to stop this study at any point. Your study doctor may take you out of this study with or without your okay. Reasons why this may occur include:

- The study doctor believes it is best for you to stop being in the study.
- You are a female and become pregnant
- You do not follow directions about the study.
- The sponsor stops the study for any reason.

Participation in Other Research Studies

You may take part in this study if you are currently in another research study. It is important to let your doctor know if you are in another research study.

Contact Persons

If you have any questions, concerns, or complaints about the research study, please contact Dr. Bickle at 502-588-4940.

Flunisolide HFA in Children with Small Airway Disease

Research Subject's Rights

If you have any questions about your rights as a research subject, you may call the Human Subjects Protection Program Office at (502) 852-5188. You may discuss any questions about your rights as a research subject, in private, with a member of the Institutional Review Board (IRB). You may also call this number if you have other questions about the research, and you cannot reach the study doctor, or want to talk to someone else. The IRB is an independent committee made up of people from the University community, staff of the institutions, as well as people from the community not connected with these institutions. The IRB has approved the participation of human subjects in this research study.

Concerns and Complaints

If you have concerns or complaints about the research or research staff and you do not wish to give your name, you may call the toll free number 1-877-852-1167. This is a 24 hour hot line answered by people who do not work at the University of Louisville.

Acknowledgment and Signatures

This informed consent document is not a contract. This document tells you what will happen during the study if you choose to take part. Your signature indicates that this study has been explained to you, that your questions have been answered, and that you agree to take part in the study. You are not giving up any legal rights to which you are entitled by signing this informed consent document. You will be given a copy of this consent form to keep for your records.

Subject Name (Please Print)

Signature of Subject

Date Signed

Printed Name of Legal Representative (if applicable)

Signature of Legal Representative

Date Signed

Relationship of Legal Representative to Subject

Printed Name of Person Explaining Consent Form

Signature of Person Explaining
Consent Form (if other than the Investigator)

Date Signed

Printed Name of Investigator

Signature of Investigator

Date Signed

List of Investigators:
Nemr Eid, MD
Scott Bickel, MD

Phone Numbers:
502-852-3772
502-558-4940

Flunisolide HFA in Children with Small Airway Disease

REVOCAION OF AUTHORIZATION FOR USE AND DISCLOSURE OF YOUR HEALTH INFORMATION FOR RESEARCH

PI Address: <u>571 S Floyd St., Suite 414</u> <u>Louisville, KY 40202</u> <u>Phone: 502-588-4940</u>	Return To:	Institutional Review Board MedCenter One, Suite 200 501 E. Broadway Louisville, KY 40202
	OR	

Do not sign this letter unless you are withdrawing from this research. You will be sent confirmation that this notice was received.

To Whom It May Concern:

I would like to discontinue my participation in the research study noted above. I understand that health information already collected will continue to be used as discussed in the Authorization I signed when joining the study.

Your options are (**choose one**):

Withdraw from Study & Discontinue Authorization:

Discontinue my authorization for the future use and disclosure of protected health information. In some instances, the research team may need to use your information even after you discontinue your authorization, for example, to notify you or government agencies of any health or safety concerns that were identified as part of your study participation.

Withdraw from Study, but Continue Authorization:

Allow the research team to continue collecting information from me and my personal health information. This would be done only as needed to support the goals of the study and would not be used for purposes other than those already described in the research authorization.

Printed Name and Signature of Subject

Date Signed

Signature of Subject's Legal Representative (if subject is unable to sign)

Date Signed

Printed Name of Subject's Legal Representative

Birthdate of Subject

Relationship of Legal Representative to Subject

Subject's Address

Subject's Phone Number

Optional:

I am ending my participation in this study because: _____