The UNIVERSITY OF CHICAGO
The Division of the Biological Sciences • The University of Chicago Medical Center

CONSENT/AUTHORIZATION BY SUBJECT FOR PARTICIPATION IN A RESEARCH PROTOCOL

Protocol Number: 14-1199 Name of Subject: _____
Medical History Number: _____

STUDY TITLE: Evaluating factors involved in Dymista's superior clinical efficacy to fluticasone propionate in the treatment of seasonal allergic rhinitis.

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You are being asked to participate in a research study. A member of the research team will explain what is involved in this study and how it will affect you. This consent form describes the study procedures, the risks and benefits of participation, as well as how your confidentiality will be maintained. Please take your time to ask questions and feel comfortable making a decision whether to participate or not. This process is called informed consent. If you decide to participate in this study, you will be asked to sign this form.

WHY IS THIS STUDY BEING DONE?
The purpose of this study is to investigate how a combination medication, Dymista, achieves its effectiveness in controlling the symptoms of seasonal allergic rhinitis (hayfever).

This research is being done because we do not know why this combination medication is more effective than its individual components Both the combination medication Dymista and the individual components (Flonase and Astelin) are approved by the FDA and are currently on the market for the treatment of hayfever.

You are being asked to be in this study because you are healthy and have seasonal allergies to either grass or ragweed,

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?
About 55 people will take part in this study at the University of Chicago.

WHAT IS INVOLVED IN THE STUDY?
You will undergo a screening evaluation to determine whether you can participate in the full study.

Screening Visit

- You will be asked about your allergy history and asked to complete a questionnaire about your nasal symptoms.
- You will be skin tested with common allergens (the stuff that causes hayfever), for example, ragweed, grass, cat, dustmites, tree mix, or mold. A skin test involves puncturing your skin with a tiny needle. If the test is positive, you will develop a red and itchy bump around the puncture site within 15 minutes that may last for a day. Only those people who test positive for grass or ragweed will be considered for this study.
- If you are a woman of childbearing age you will be asked to take a urine pregnancy test. Pregnant women will not be allowed to participate in this study.

If you have a history of mild asthma you will be asked to blow into a peak flow meter. If your FEV1 (a measure of lung function) is less than 80% of a predicted normal range for your age and size you will not be eligible for the study.

Screening nasal challenge

If your skin test is positive to grass or ragweed, we will perform a screening nasal challenge test.

- Before starting the screening challenge test we will spray your nose on both sides with 2 sprays of oxymetazoline 0.05% (a nasal decongestant) to prevent it from becoming too stuffy. Being too stuffy may interfere with the nasal lavage (wash).
- We will wash your nose with about 2 teaspoons of a salt solution (nasal lavage) before starting the challenges and 10 minutes after each challenge.

The lavages will be saved to test and count the cells associated with allergy.

This screening nasal challenge with antigen (the stuff that causes hayfever) is an experimental procedure that involves:

- On one side of the nose we will spray a diluent (a solution used to dilute the allergen) and then either grass or ragweed allergen. We will choose the allergen (grass or ragweed) based on the results of your skin prick test. If you are allergic to both we will choose the one you have the strongest response to.
- You will then be asked about your nasal symptoms (sneezing, stuffiness, runny nose and itchy nose/throat), and to count the number of sneezes.
- This nasal test is done once with the substance used to dilute the allergen extract (diluent) and then with two increasing doses of either grass or ragweed extract. This is done over a period of about 45 minutes. If you have a history of mild asthma the FEV1 will be repeated after each nasal challenge test.

If you have a positive response to the screening nasal challenge test, you will be allowed to have a 2 week washout period (a time when you do not take a drug or get a nasal challenge). After that you will return to the Nasal Physiology laboratory and receive one of the study drugs and undergo one nasal challenge every day for 3 days while still taking study drug. Another 2 week washout will follow followed by another round of treatment (with one of the other study drugs) and 3 nasal challenges on 3 consecutive days. Another 2 week washout will follow and the last drug will be given and your nose challenged for 3 consecutive days. Your participation in the study will then conclude.

All Participants in this study will receive 3 different drugs (A, B, and C as below). The order in which these medications are received will be randomly determined (like the roll of a die).

- Drug A: A steroid nasal spray (fluticasone propionate) approved by the Food and Drug Administration (FDA),
- Drug B: Placebo (spray with no active medicine in it),
- Drug C:Dymista (a combination of fluticasone propionate and azelastine hydrochloride) also approved by the FDA.

This study is double-blinded, meaning that neither you nor the study doctor or his research team will know which group you are in until the entire study is finished. However, this information can be obtained if it becomes medically necessary to know which study drug you are taking during the course of the study.

Nasal challenges

The nasal allergen challenge during the study visits will be performed on 3 consecutive days and will be as follows:

- You will come to the nasal laboratory and allowed to rest for 15 minutes so your nose gets used to the environment of the laboratory.
- You will be asked to fill in a score that reflects the severity of your nasal symptoms of sneezing, stuffy nose, runny nose, and itchy nose and we will count the number of sneezes.
- We will then wash your nose 5 consecutive times with about 2 teaspoons of a salt solution (nasal lavage).
- We will then spray your nose on both sides with 2 sprays of oxymetazoline 0.05% (a nasal decongestant) to prevent it from becoming too stuffy, as this may interfere with nasal lavage (wash).
- After a 10 minute wait, you will record sneezes and symptoms again and receive your study drug (as mentioned above) in the form of 1 spray in each nostril.
- After a 10 minute wait, we will apply 2 sprays of the diluent (a solution used to dilute the allergen) to your left nostril.
- After 10 minutes, we will record your sneezes and ask you to fill the score that reflects your symptom severity. We will also perform a nasal lavage.
- We will then spray your nose with 2 sprays of either grass or ragweed allergen followed 10 minutes later by a recording of sneezes and symptoms and a nasal lavage.
- We will then spray your nose with 2 sprays of the same allergen in a higher dose and 10 minutes later record sneezes and symptoms and perform a nasal lavage.
- You will then be discharged from the laboratory and asked to take your study drug in the evening and report the following day at approximately the same time with your study drug bottle. The same challenge and study drug will be administered the second day and the third day.
- After the third challenge, you will stop taking study drug and return to the laboratory 2 weeks later so your nose will have rested and returned to baseline.
- You will undergo consecutive 3 day challenges, except that another study drug will be used.
- The same sequence will then happen one last time using the last of the assigned study drug.
- The study will then be concluded after the third series of study administration and nasal challenges.

- The symptoms you record will allow us to determine how the different drugs are affecting the nasal challenge. We will use the washes to measure cells and substances that your nose releases during the allergic reaction. This will also allow us to determine the effect of the different drugs on these substances and cells and help us to understand how these treatments work.

During this study, Dr. Baroody and his research team will collect information about you for the purposes of this research. This information will include name, age, date of birth, sex, race, e-mail address, telephone number, address and social security number (for payment purposes only), and information about your medical history (past medical/surgical history, allergies, medications, family and social history and other routine information) and results of pregnancy test, skin test, and nasal challenges. This information will be used to analyze the results of the study and compare groups of subjects. This information will be kept in secure computers and offices of Dr. Baroody and his research staff.

HOW LONG WILL I BE IN THE STUDY?
We think you will be in the study for about 9 weeks.

Dr. Baroody may decide to take you off of the study without your consent if:

- You are unable to meet the requirements of the study;
- Your medical condition changes;
- New information becomes available that indicates that participation in this study is not in your best interest; or
- If the study is stopped.

WHAT ARE THE RISKS OF THE STUDY?
The likely and unlikely risks to subjects participating in this study are listed below:

Fluticasone
The risks associated with the administration of fluticasone propionate include:
Likely:

- sore throat
- nosebleed
- Nasal irritation
- blood in nasal mucus

Less Likely:

- headache
- Nasal burning
- nausea
- vomiting
- asthma symptoms and cough

Dymista:
Likely:

- a bitter taste

Less Likely:

- nose bleed

- headache
- sleepiness

Skin testing
The following side effects are:
Likely:
- skin itchiness, irritation

Less likely:
- discomfort

The following side effects below may require prompt treatment with adrenalin or other drugs. However, the risks of these side effects are not very likely and the described reactions are less serious if a person is under observation, as you will be in this study, and are readily reversible.

Unlikely:
- hives
- flushing
- low blood pressure

Very unlikely, but serious:
- asthma requiring treatment with adrenalin or other drugs,
- anaphylactic shock (a bad reaction to the antigen, the substance that causes allergies, causing someone to go into shock, that is to faint and have low blood pressure)

Nasal allergen challenge and nasal lavage
The antigen placed in your nose may cause sneezing, a runny nose and/or nasal congestion that may last up to 24 hours. Some people may find the reaction very uncomfortable. Other generalized reactions (hives, flushing or asthma) requiring additional treatment with epinephrine may occur. These are not serious if a person is under observation and are readily reversible. The nasal lavage may cause some mild discomfort at the site of collection.

The following side effects are:
Likely:
- sneezing
- itchy nose
- runny nose
- nasal congestion

Less likely:
- discomfort
- hives
- asthma

FEV1 measurements
There are minimal to no risks associated with the tests performed to measure nasal congestion and your lung function.

Reproductive risks
Women: There may be unknown risks to the unborn child if you are pregnant or if you become pregnant during the study. Therefore, you may not enter this study if you are pregnant, or plan to become pregnant, or breast-feed an infant during the study period. If you become pregnant during the study, you will be taken off study for safety reasons. If you become pregnant within 28 days after your participation in the study, we ask that you contact your study doctor for safety monitoring. In either case, please make your obstetrician aware of your study participation. Your study doctor will ask that you, or your obstetrician, provide updates on the progress of your pregnancy and its outcome. The study doctor will make this information available to the study sponsor for safety monitoring follow up.

Men: If you are a male and your spouse or partner thinks she has become pregnant during the study or within 28 days after your participation in the study, tell your study doctor immediately. The study doctor will make this information available to the study sponsor for safety monitoring follow-up.

There may be other risks that could arise which are not reasonably foreseeable. If new information becomes available which could influence your willingness to continue, this new information will be discussed with you.

ARE THERE ANY BENEFITS TO TAKING PART IN THE STUDY?
If you agree to take part in this study, there may be little or no direct medical benefit to you. We hope the information learned from this study will benefit other individuals with seasonal allergic rhinitis in the future.

WHAT OTHER OPTIONS ARE THERE?
Participation in this study is voluntary. Instead of being in this study you may choose to not participate. The decision whether or not you wish to participate in this study will not affect your care at the University of Chicago Medical Center.

WHAT ARE THE COSTS?
Clinical services provided during a clinical trial are either research-related or related to usual medical care. Research-related services are done to complete the research and the costs are not the responsibility of you or your insurance.

The costs that are considered research-related for this study include the following:

- Steroid nasal spray (fluticasone propionate)
- Placebo
- Dymista
- All nasal challenges with allergen or diluent
- All Nasal lavages
- All labs
- Skin test
- Urine pregnancy test

- Lung function test
- Oxymetazoline 0.05% (nasal decongestant)

Usual medical care costs include any and all services that are considered medically necessary for your disease. The cost of this usual, ongoing medical care will be the responsibility of you or your insurance, and may include deductibles and co-payments. Similarly, this care will be subject to all the same requirements and restrictions of your insurance.

If you suffer an unanticipated injury as a direct result of this research and require emergency medical treatment, the University of Chicago Medical Center will provide such treatment at the University of Chicago Medical Center at no cost to you. Costs of related non-emergency care for an unanticipated research injury will be covered if that care is provided at the University of Chicago Medical Center. You must notify Dr. Baroody as promptly as possible after your injury in order to receive this care. An injury is "unanticipated" if it is not one of the known effects of a study drug, medical device or procedure. If you think that you have suffered a research related injury, you must let Dr. Baroody know right away.

WILL I BE PAID FOR MY PARTICIPATION?

For participation in this study you will receive up to $575. There is no compensation for undergoing the skin test. Subjects undergoing the nasal screening challenge will be compensated $25 whether or not they are eligible to participate in the study. You will receive $50 for completing each of the 9 subsequent study visits and $100 as a bonus for completing the study and completion of the final visit. If you withdraw from this study early, you will only be compensated for the study visits you completed.

As policies at the University of Chicago require that these payments be given in the form of a check, you will need to complete a tax form. Therefore we will be collecting personal information about you including your name, address, and social security number. In addition, because the process for requesting a check oftentimes takes several weeks, we will mail your check to you when it is ready. Please note that it may take 3-4 weeks after conclusion of your study participation in order for you to receive your payment.

WHAT ABOUT CONFIDENTIALITY?

Study records that identify you will be kept confidential. We will store study information in locked offices and/or in computers in Dr. Baroody's offices and labs that are password protected and have limited physical access. Only Dr. Baroody and his study personnel will have access to the study information.

The data collected in this study will be used for the purpose described in the form. By signing this form, you are allowing the research team access to your medical records, which include Protected Health Information. Protected Health Information (PHI) consists of any health information that is collected about you, which could include your medical history and new information collected as a result of this study. The research team includes the individuals listed on this consent form and other personnel involved in this study at the University of Chicago.

As part of the study, Dr. Baroody and his research team will report the results of your study-related procedures and tests explained above to Meda, the company sponsoring the study. The information that will be sent will be coded prior to being sent to the sponsor only initials will be use. This information is

being sent in order to analyze the results of the study and to determine how the nasal sprays help control the symptoms of allergic rhinitis. This information will be used to analyze the results of the study and compare groups of subjects. The study sponsor or their representatives, including monitoring agencies, may also review your medical record. Please note that these individuals may share your health information with someone else.

Your name, address, and social security number will be shared with the University of Chicago Controller's Office in order to issue payment.

Your records may be reviewed by federal agencies whose responsibility is to protect human subjects in research including the Food and Drug Administration (FDA) and Office of Human Research Protections (OHRP). In addition, representatives of the University of Chicago, including the Institutional Review Board (IRB), a committee that oversees the research at the University of Chicago, may also view the records of the research to make sure that the study information is correct. If your research record is reviewed by any of these groups, they may also need to review your entire medical record. Because of the need to provide information to these parties, absolute confidentiality cannot be guaranteed.

If health information is shared outside the University of Chicago, the same laws that the University of Chicago must obey may not protect your health information.

During your participation in this study, you will have access to your medical record. Dr. Baroody is not required to release to you research information that is not part of your medical record.

This consent form will be kept by the research team for at least six years. The study results will be kept in your research record and be used by the research team for at least six years. At the time of study completion, either the research information not already in your medical record will be destroyed or information identifying you will be removed from study results. Any research information in your medical record will be kept indefinitely.

Data from this study may be used in medical publications or presentations. Your name and other identifying information will be removed before this data is used. If we wish to use identifying information in publications, we will ask for your approval at that time.

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

WHAT ARE MY RIGHTS AS A PARTICIPANT?

Taking part in this study is voluntary. If you choose not to participate in this study, your care at the University of Chicago/University of Chicago Medical Center will not be affected. You may choose not to participate at any time during the study. Leaving the study will not affect your care at the University of Chicago/University of Chicago Medical Center.

If you choose to no longer be in the study and you do not want any of your future health information to be used, you must inform Dr. Baroody in writing at the address on the first page. Dr. Baroody may still use your information that was collected prior to your written notice.

We will tell you about significant new information that may affect your willingness to stay in this study.

You will be given a signed copy of this document. This consent form document does not have an expiration date.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?
You have talked to Dr. Baroody or his research coordinator about this study and you had the opportunity to ask questions concerning any and all aspects of the research. If you have further questions about the study, you may call Dr. Baroody at 773-702-4790, or by mail at The University of Chicago, Section of OHNS, 5841 S. Maryland Ave., MC 1035,
Chicago, IL 60637.

If you have a research related injury, you should immediately contact Dr. Baroody at 773-702-4790 during office hours or you can call the paging service at 773-702-1000 and an OHNS resident on call will be paged and call Dr. Baroody as needed.

If you have any questions concerning your rights in this research study you may contact the Institutional Review Board, which is concerned with the protection of subjects in research projects. You may reach the Committee office between 8:30 am and 5:00 pm, Monday through Friday, by calling (773) 702-6505 or by writing: Institutional Review Board, University of Chicago, 5841 S Maryland Ave., MC7132, I-625, Chicago, Illinois 60637.

CONSENT

SUBJECT
The research project and the procedures associated with it have been explained to me. The experimental procedures have been identified and no guarantee has been given about the possible results. I will receive a signed copy of this consent form for my records.

I agree to participate in this study. My participation is voluntary and I do not have to sign this form if I do not want to be part of this research study.

Signature of Subject: _____

Date: _____ Time: _____ AM/PM (Circle)

PERSON OBTAINING CONSENT
I have explained to _____ the nature and purpose of the study and the risks involved. I have answered and will answer all questions to the best of my ability. I will give a signed copy of the consent form to the subject.

Signature of Person Obtaining Consent: _____

Date: _____ Time: _____ AM/PM (Circle)

INVESTIGATOR/PHYSICIAN:
Signature of Investigator/Physician _____
Date: _____ Time: _____ AM/PM (Circle)