University of Wisconsin-Madison
Research Subject Information and Consent Form
Core Consent

Study Title: Severe Asthma Research Program (SARP4)
Immunometabolic Phenotypes in adult Severe Asthma and disease progression

CONSENT FOR SUBJECTS WITH ASTHMA

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SUMMARY

You are invited to participate in a research study. The purpose of this research is to learn more about severe asthma by comparing people with severe asthma to those with milder forms of asthma over time. You are invited to be in this study because you have asthma. Your participation in this research will involve 4-5 in person visits and 3 phone calls; the study and will last approximately 36 months (3 years).

This is a quick summary of the study. There is more detailed information about the study on the next page. Participation in this study will involve questionnaires, breathing tests, blood draw, and sputum collection. All research studies involve some risks. Risks to this study that you should be aware of are dizziness from breathing tests, mild pain from the blood draw, and some coughing from the sputum collection. There is the possibility that you may benefit from participation in this study by understanding your asthma in more detail.

Your participation in this study is voluntary. You do not have to participate in this study if you do not want to. You will not lose any services, benefits, or rights you would normally have if you choose not to participate.

The remainder of this form contains a more complete description of this study. Please read this description carefully. You can ask any questions if you need help deciding whether to join the study. The person in charge of this study is Dr. Loren Denlinger. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study his contact information is: 600 Highland Ave Madison, WI 53792, phone 608-261-1552. If you have any questions, suggestions or concerns about your rights as a volunteer in this research, contact the UW Institutional Review Board at 608-263-2362 or UW Patient Relations at 608-263-8009.

Introduction

This consent form may contain words that you do not understand. Please ask the study physician or the study staff to explain any words or information that you do not clearly understand.

The purpose of this form is to give you information about the study, and by signing it you will give your permission to be in the study. The University of Wisconsin is part of a group of centers that are studying severe asthma. You should join in this study only if you want to do so. You may refuse to join or stop being in this study at any time. Your decision to join or not join this study will not affect your doctor-patient relationship or your medical treatment in any way. This study is voluntary.

What Is the Purpose of This Study?

You have been invited to join in a research study. This is a research study that is being done to learn more about severe asthma by comparing people with severe asthma to those with milder forms of asthma over time. You are being asked to join a research study to follow your overall health and the health of your lungs for three years. In this study, we will look at your breathing tests, your level of inflammation in your blood and breath, the number of and how bad your asthma attacks are, your medication use and other conditions related to asthma over time.

The job of the Severe Asthma Research Program (SARP) is to improve the understanding of severe asthma to develop better treatments. The SARP will gain a better understanding of asthma in adults, by looking at the disease level in a very detailed way. You are being asked to join in this study because you have asthma.

Who is Sponsoring the Study?

The University of Wisconsin is one of eight universities enrolling patients with severe asthma, funded mainly by the National Institutes of Health, and partially by the private industry-supported SARP Research Fund, working together to study severe asthma. A list of current and past industry sponsors is available upon request for this study. This group of sites is part of the SARP.

Because severe asthma is uncommon, the eight clinical centers were set up to work together to enroll enough people with severe asthma in research studies. Each of the centers will conduct a common protocol over time and will share the information, test results and research samples collected across all the centers. If you decide to join this research study at the University of Wisconsin, you will also be asked to allow the sharing of your study information and samples with other sites participating in this study. The data coordinating center for all sites will be Penn State University. There are also some research sites that will be helping to analyze data and specimens but will not enroll patients at their institutions. All of the institutions that are part of SARP are listed below.

Who are the other investigators involved in the SARP partnerships?

Brigham and Women's Hospital, Boston, MA	Bruce Levy, M.D.; Elliot Israel, M.D.
Boston Children's Hospital, Boston, MA	Wanda Phipatanakul, M.D.
Carnegie Mellon University, Pittsburgh, PA	Ziv Bar-Joseph, Ph.D.
Cleveland Clinic, Cleveland, OH	Suzy Comhair, Ph.D.; Mark Aronica, M.D.
National Jewish Health, Denver, CO	Max Seibold, Ph.D.
Penn State University, Hershey, PA	Dave Mauger, Ph.D.
Rainbow Babies and Children's Hospital, Cleveland, OH	Kristie Ross, M.D.
Stanford University, Stanford, CA	Purvesh Khatri, Ph.D.
University of Arizona, Tucson, AZ	Deborah Meyers, Ph.D
University of California San Francisco, CA	Prescott Woodruff, M.D.
University of Iowa, Iowa City, IA	Eric Hoffman, Ph.D.
University of Kansas, Kansas City, KS	Mario Castro, M.D.
University of Pittsburgh, Pittsburgh, PA	Sally Wenzel, M.D.
University of Virginia, Charlottesville, VA	Gerald Teague, M.D.
University of Wisconsin, Madison, WI	Loren Denlinger, M.D.
Wake Forest School of Medicine, Winston-Salem, NC	Wendy Moore, M.D.
Washington University, St. Louis, MO	Cajal Sumino, M.D.

What Does this Study Involve?

This study will last three years and will involve between 4 and 5 clinic visits, and up to four phone contacts from research study staff. There will be 400 subjects with asthma enrolled in this study across all centers. The University of Wisconsin will have 120 people with asthma sign the consent in order to enroll approximately 60 subjects with asthma.

A detailed study grid can be found at the end of this consent form. An explanation of each procedure can be found below.

SARP Registration:

If you have participated in the prior SARP study you are already enrolled in the SARP Registry and can skip to the study procedures section. If you are a new participant, before you enroll in SARP, you must first be entered into the SARP Registry. This Registry has been set up to collect basic background information that will not change over time. This information is limited to: your initials, date of birth, gender, and race/ethnic identification. Your Registry information will be coded with a unique SARP identification number. No information that directly identifies you will be entered into the SARP database or sent to the Data Coordinating Center (Penn State University, Hershey, PA). Registry data help us track your study over time and is useful in data analyses.

Your agreement to provide the information for the SARP Registry is voluntary. However, if you choose not to provide it, you cannot be screened for or enrolled into SARP. Once you

consent to be entered into the Registry, your information cannot be removed and will be maintained in the study database into the future. You will only be asked to supply Registry information one time during your participation in SARP. Registration happens before or during your first study visit (Visit E1).

Study Procedures:
There is a chart that shows the timing of study procedures on the last page of this consent. Please refer to this to help you understand when certain procedures would be done as part of the study.

Below are detailed descriptions of each of the study procedures. For some procedures we will ask you to not take your asthma medications before you come into the clinic for testing. If your asthma symptoms get worse and you feel that you need to take your medication, please take your asthma medicine and call the study staff to let them know.

I. QUESTIONNAIRES

Questionnaires will be done at Visit E1, Visit E2, Visit E3, and Visit E4 as well as phone visits for a total of 7 contacts over 3 and one half years. Some of these later questionnaires will be done over the phone while you will need to come to the clinic for others.

This will include information on the development of asthma or breathing problems, current symptoms, your home and work environment, present and past treatment of shortness of breath, exacerbating factors (triggers) and how your breathing affects your life. In addition, you will be asked to give information on your age, place of birth and your parent's medical history. The questionnaires will take you approximately 1 hour to complete.

RISKS: The questionnaires are not tests; there are no right or wrong answers. A risk for completing questionnaires includes breach of confidentiality. There are no known risks to answering the questionnaires. The questionnaires might be considered long with repeating questions. You can skip any question you feel uncomfortable answering.

II. PULMONARY FUNCTION TESTING

Pulmonary Function Testing will be done each year at Visit E1, Visit E2, Visit E3, and Visit E4. for a total of 3 and one half years.

Pulmonary function testing (PFT) is a standard test that is used regularly by doctors to test breathing. You will be asked to breathe into a machine called a spirometer (spirometry). The technician will ask you to take a few normal breaths, then breathe in a deep breath, and then breathe out hard and fast. You will need to repeat this task several times. To make sure we measure all of your breaths exactly, you will be asked to wear nose clips. PFT’s take approximately 10 minutes to complete.

Maximum Bronchodilation: After you perform pulmonary function testing, we will ask you to take 4 puffs of albuterol (an inhaled medicine to relax the airways). 15 minutes later you will perform spirometry again and take another 2 puffs of albuterol. 15 minutes later you will repeat spirometry. If there is little to no difference between the last two sets of spirometry values, the test will stop. If comparison of the last two sets of spirometry values shows a

continued increase in your breathing, you will take 2 more puffs of albuterol, and spirometry will be repeated one last time. For this test, you will receive no more than 8 puffs of albuterol.

RISKS: Pulmonary function testing can cause tiring, mild chest tightening and coughing. If your breathing is difficult after or during the test, we will give you 2-4 puffs of albuterol, an inhaled medicine to relax the airways (bronchodilator). In some people, albuterol can make your heart race, make you feel jittery or nervous, increase your blood pressure and cause nausea or headache. These feeling are temporary and should be gone within 15-30 minutes.

III. METHACHOLINE INHALATION CHALLENGE

A Methacholine Inhalation Challenge may be done at Visit E1 (only subjects new to SARP).

This test measures the reactivity or sensitivity of the airways. This consists of measuring the degree of narrowing that occurs after inhaling methacholine. The Methacholine Challenge is an approved standard test used by physicians to test if a person has asthma or test how "sensitive" the airways are in people with asthma. Methacholine will cause some people's breathing tubes to narrow, especially if you have asthma. We will ask you to inhale increasing doses of a mist containing methacholine and then we will measure your breathing capacity by having you blow into a spirometer. You will receive albuterol after the test to reverse any shortness of breath or wheezing the test has caused. An inhalation study using methacholine will take approximately 60 minutes of your time. This will be done in the beginning of the protocol (Visit E1), but you may need to come back on a different day to do the test. If you have previously participated in an NIH study involving Methacholine Inhalation Challenge, you may not need to complete this procedure.

RISKS: Methacholine may cause your breathing tubes to narrow slightly after you inhale it, causing shortness of breath. You may feel this as tightness in your chest or experience a coughing sensation. These symptoms usually go away in 10-15 minutes without treatment, but they can be reversed quickly with 2 puffs of albuterol at the end of the test. We have performed these tests on many people in the last 20 years and very few have had any difficulty. If your breathing is very bad (less than half of what is considered normal breathing), we will not perform this test.

IV. BLOOD SAMPLING

Blood collection will be done each year at Visit E1, Visit E2, Visit E3, and Visit E4.

You will be asked to donate a small amount of blood from your vein on Visits E1, E2, E3 and E4. About 4-6 tablespoons will be collected at each visit.

At all Visits blood will be drawn for blood cell counts, including eosinophils (white blood cells important in asthma) and the storage of blood fluids (serum and plasma). At Visit E1, the blood draw will also include blood tests for environmental allergies.

A fasting blood draw will take place at Visit E1 and Visit E4 to look at metabolic health measures and cellular and chemical activity. We will ask you not to eat for 12 hours before these blood draws. You will be allowed to drink water, and we would like you to drink plenty of water so that you do not get dehydrated. If you cannot fast or choose not to, then you will

still be eligible for the study and we will go on with the study procedures by making a note that you have not fasted.

We will be collecting blood for DNA at Visit E1 in the people new to SARP to study genes that may be related to the development of asthma, allergy and related diseases. DNA (deoxyribonucleic acid) is the genetic material contained in all the cells of your body, including blood cells. This genetic material (genes) influences such things as your physical features, hair, and eye color. As part of this research project, your DNA will be studied in an effort to find out if there are genes that contribute to medical conditions that are part of this study.

RISKS: You may experience a slight bruise or some discomfort at the site of the blood draw. Some people may feel faint or lightheaded during blood draws. The study doctor and nurse are available in these cases. There is also a very small risk of infection at the site of the needle insertion. With fasting, there is a risk that your blood sugar will get too low. To avoid this, we will encourage you to eat snacks (please bring your own snack) after your blood draw. Please let us know if you have a medical condition that could be made worse by fasting or if you have had a low blood sugar or any problems with blood draws in the past.

V. URINE

Urine collection will be done each year at Visit E1, Visit E2, Visit E3, and Visit E4.

The urine sample collected will be used to look for signs of inflammation that might be related to your asthma. For females, at all visits you will also be asked to provide a small amount of urine for pregnancy testing if you are a female of childbearing potential to make sure you are not pregnant before taking any study medication or doing some study procedures. You will not be enrolled if you are pregnant or breastfeeding. If you become pregnant during the study you can stay in the study, but we will ask that you let us know.

RISKS: There are no known risks for the collection of urine.

VI. EXHALED BREATH CONDENSATE

Exhaled Breath Condensate will be done at Visit E1.

Exhaled breath condensate (EBC) is a liquid collection of the air you breathe out into a tube. We will ask you to collect a liquid version of your exhaled breath (EBC) by breathing into a tube for 10 minutes, which will allow the collection of exhaled breath vapor.

RISKS: Risks of these procedures include tiring, mild chest tightness and coughing. A medication (albuterol) can be given to open the air passages if wheezing develops.

VII. NITRIC OXIDE MEASUREMENT

Nitric Oxide Measurements will be done each year at Visit E1, Visit E2, Visit E3, and Visit E4.

People with asthma are known to have inflammation in their airways. This test is a way to look at this inflammation. Nitric oxide (NO) is a gas in your breath that we can measure with a

machine. We will ask you to undergo measurement of NO by having you blow out slowly through a mouthpiece while wearing nose clips. It feels much like blowing up a balloon. When breathing out you will notice some resistance (similar to blowing through a straw). You will be asked to repeat this maneuver up to two times. This test takes approximately 10 minutes to complete.

RISKS: Risks of this procedure includes tiring, mild chest tightness and coughing. A medication (albuterol) can be given to open the air passages if wheezing develops.

VIII. PHYSICAL EXAM

A physical exam will be done at Visit E1 and Visit E4. Vital signs only at Visit E2 and Visit E3.

Vital signs (blood pressure, temperature, height and weight) will be collected by a study coordinator or designated representative at Visit E1, Visit E2, Visit E3, and Visit E4.The study doctor will listen to your heart and lungs, and look at your eyes, ears, nose and throat at Visit E1 and Visit E4. If needed a study physician is available to see you during other visits also.

RISKS: There are no known risks for Physical Exams.

IX. SPUTUM INDUCTION

Sputum induction will be done at Visit E1 and Visit E4.

Sputum induction is a method of obtaining fluid secretions from your breathing airways to better understand airway inflammation in asthma. You will be asked to inhale a nebulized mist of 3% saline solution (salt solution) and collect your airway secretions in a cup. Prior to inhaling saline solution, you will be given 4 puffs of albuterol to help prevent you from developing wheezing from inhaling the salt solution, which may happen in some subjects. You will be asked to inhale this saline mist for 12 minutes. During this period, you will be encouraged to cough and your secretions will be collected in a cup. If you develop difficulty breathing or excessive coughing during this procedure, the inhalation of saline will be stopped. Before and after the inhalation period, you will also be asked to perform a pulmonary function test. Subjects with low lung function will not be asked to inhale the saline mist. These subjects will be asked to spontaneously cough and their secretions will be collected in a cup.

RISKS: This is a commonly performed procedure to try to obtain a sputum (respiratory secretions) sample from patients in the hospital to see if they have pneumonia. You may experience some discomfort or coughing but this will only be temporary. Some patients experience bronchospasm (narrowing of the airways) from inhaling saline, which may cause some chest tightness, wheezing, and shortness of breath. This is reversible with a bronchodilator (albuterol). If you experience any of these symptoms and/or your breathing decreases by 20%, you will be given 2 puffs of a bronchodilator. In addition, should you develop any symptoms during the inhalation of saline the procedure will be stopped. You should experience no other effects from the inhalation of the saline solution.

X. STOOL COLLECTION

Stool collection will be done at Visit E1 and Visit E4.

A stool sample will be collected to look for signs of inflammation (biomarkers) that might be related to asthma. You will be asked to take a kit home with you to collect a stool sample that will be mailed in later.

RISKS: There are no known risks for Stool Collection.

What are the Benefits of Study Participation?

You are not guaranteed any benefit from participation in this study, but you may benefit from a more detailed assessment of your asthma. Your participation in this study will help researchers understand more about severe asthma. The results from this study may help us find a better way to treat asthma and may benefit other asthma patients in the future.

Will it cost me to take part in this study?

There is no cost to you for taking part in this study.

Will I be Paid for My Participation?

You will be paid for your participation. The amount you receive depends on which parts of the study you complete. If you qualify for the study after screening and complete all the study visits outlined in this consent form for which you are eligible, you will be paid up to $585.00. If you stop participating before the end of the study or if the study is discontinued through no fault of yours, you will receive a partial payment based upon your participation in the study.

You will be provided with free parking or other transportation arrangements as needed for each in-person study visit. In addition, for study visits that take longer than 4 hours, you may receive a meal voucher for the UWHC cafeteria or be provided with small snacks. Nonmonetary incentives such as tote bags, water bottles, or other small gifts may be given at certain study visits.

Visit E1	Questionnaires	$25.00
	Spirometry with maximum reversibility	$35.00
	Methacholine (if applicable	$30.00
	Exhaled Nitric Oxide	$15.00
	Exhaled Breath Condensate	$20.00
	Blood Draw	$15.00
	Urine Collection	$10.00
	Sputum Collection	$30.00
	Stool Sample	$15.00
	Total:	**$195.00**
6 month telephone follow up		$15.00
Visit E2	Questionnaires	$25.00
	Spirometry with maximum reversibility	$35.00
	Exhaled Nitric Oxide	$15.00
	Blood Draw	$15.00
	Urine Collection (Females only)	$10.00
	Total:	**$100.00**
12 month telephone follow up		$15.00
Visit E3	Questionnaires	$25.00
	Spirometry with maximum reversibility	$35.00
	Exhaled Nitric Oxide	$15.00
	Blood Draw	$15.00
	Urine Collection (Females only)	$10.00
	Total:	**$100.00**
18 month telephone follow up		$15.00
Visit E4	Questionnaires	$25.00
	Spirometry with maximum reversibility	$35.00
	Exhaled Nitric Oxide	$15.00
	Blood Draw	$15.00
	Urine Collection	$10.00
	Sputum Collection	$30.00
	Stool Sample	$15.00
	Total:	**$145.00**

What Are My Alternatives to Participating?
Your participation in this study is voluntary. You may choose not to participate in this research study.

Who Will See The Study Records?
To the extent possible, your participation in this study will remain private. The principal investigator as well as people from the NIH (National Institutes of Health) and the Data and Safety Monitoring Committee may review your medical records about this study. However, private industry supporters will not have access to your medical records about the study. The SARP investigators will have access to the information that you have agreed to share. The results of this study may be published in scientific journals or be presented at medical meetings; however, individual patients will not be identified by name. The data will be coded with a number. Only the Investigator and his/her study staff at this site have access to the code that links your name with your study number and data. Paper copies are kept in a locked file cabinet in locked rooms, electronic data is password protected.

What About My Health Information?
In this research study, any new information we collect from you and information we get from your medical records or other facilities about your health or behaviors is considered Protected Health Information. The information we will collect for this research study includes**:** questionnaire information, testing procedures results, blood, stool, DNA, sputum cells, and bronchoscopy fluid.

If this research study involves the diagnosis or treatment of a medical condition, then Protected Health Information collected from you during this study may be placed in your medical record, and may be used to help treat you, arrange payment for your care, or assist with the University of Wisconsin operations.

We will make every effort to keep your Protected Health Information private. We will store records of your Protected Health Information in a cabinet in a locked office or on a password protected computer. Only the following people or organizations will be granted access to your Protected Health Information:

1) The study investigator and his/her staff, or others at the University of Wisconsin who oversee research

2) Other people or laboratories providing services for this research project on behalf of the University of Wisconsin

3) Brigham and Women's Hospital, Boston, MA
Boston Children's Hospital, Boston, MA
Carnegie Mellon University, Pittsburgh, PA
Cleveland Clinic, Cleveland, OHNational Jewish Health, Denver, CO
Rainbow Babies and Children's Hospital, Cleveland, OH
Stanford University, Stanford, CA
University of Arizona, Tucson, AZ
University of California San Francisco, CA

University of Iowa, Iowa City, IA
University of Kansas, Kansas City, KS
University of Pittsburgh, Pittsburgh, PA
University of Virginia, Charlottesville, VA
Wake Forest Baptist Health, Winston-Salem, NC
Washington University, St. Louis, MO

4) FDA (Food and Drug Administration)

5) SARP Data Coordinating Center, Penn State University College of Medicine, Hershey PA

6) SARP Data Safety Monitoring Board (DSMB)

7) NIH/NHLBI (National Institutes of Health/ National Heart, Lung, and Blood Institute)

8) Investigators from the Precision Interventions in Severe and Exacerbation prone Asthma (PrecISE) network, another severe asthma network sponsored by NHLBI.

If required by law or court order, we might also have to share your Protected Health Information with a judge, law enforcement officer, government agencies, or others. If your Protected Health Information is shared with any of these groups it may no longer be protected by federal or state law.

Any Protected Health Information collected from you in this study that is maintained in the research records will be kept for an indeterminate period of time. This authorization does not expire and any research information entered into your medical record will be kept for as long as your medical record is kept by [Institution Name]. You will not be able to obtain a copy of your Protected Health Information in the research records until all activities in the study are completely finished.

You can tell Dr. Denlinger that you want to take away your permission to use and share your Protected Health Information at any time by sending a letter to this address:

Dr. Loren Denlinger
600 Highland Ave
Madison, WI 53792

However, if you take away permission to use your Protected Health Information you will not be able to be in the study any longer. We will stop collecting any more information about you, but any information we have already collected can still be used for the purposes of the research study.

By signing this form you give us permission to use your Protected Health Information for this study.

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 Web site at any time.

Certificate of Confidentiality

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National

Institutes of Health. With this Certificate, the researchers cannot be forced to disclose information any demands for information that would identify you, except as explained below.
The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

The Certificate of Confidentiality does not prevent the researchers from disclosing voluntarily, without your consent, information that would identify you as a subject in the research project if required by law (e.g. child abuse, reportable communicable disease, threat of harm to self or others) or as required by state or federal agencies who may review our records under limited circumstances, (e.g. such as a U.S. Department of Health and Human Services (DHHS) request for information for an audit or program evaluation or an FDA request under the Food, Drug and that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The researchers will use the Certificate to resist Cosmetics Act.)

Will There Be Any Costs To Me?
There will be no charge to you for participation in this study.

Will There Be Compensation For Injury?
If you are injured or get sick because of this study, medical care is available to you through UW Health, your local provider, or emergency services, as it is to all sick or injured people.

- If it is an emergency, call 911 right away or go to the emergency room.For non-emergency medical problems, contact the study team for instructions.Call the Lead Researcher, Dr. Loren Denlinger, at 608-261-1552 to report your sickness or injury.

Here are some things you need to know if you get sick or are injured because of this research:

- If the sickness or injury requires medical care, the costs for the care will be billed to you or your insurance, just like any other medical costs.
- Your health insurance company may or may not pay for this care.
- No other compensation (such as lost wages or damages) is usually available.
- UW-Madison and UW Health do not have a program to pay you if you get sick or are injured because of this study.
- By signing this consent form and taking part in this study, you are not giving up any legal rights you may have. You keep your legal rights to seek payment for care required because of a sickness or injury resulting from this study.

If I Start This Study, Can I Stop?
If you choose not to participate in this study, your doctor will continue to treat your asthma. Your participation is voluntary. You are free to refuse to participate in the study and may stop participating in the study at any time without any change in the quality of medical care to which you are entitled. Your physician may also end your participation in the study if he/she judges it to be in your best

interest. Your participation in the study may be stopped for any of the following reasons:

A. Failure to follow the investigator's instructions
B. A serious adverse reaction, which may require evaluation
C. If the investigator feels it is in the best interest of your health and welfare

In addition the investigator or the NIH may end your participation in the study at any time with or without your consent.

Sample Storage and Shared Procedures: Below, we describe the different kinds of information that we will collect about you for this research study.

Sharing and Storing of Questionnaires, Test Results and Samples: During the course of this study, the study investigator Dr. Loren Denlinger, or a member of the study team will ask you to answer questionnaires about your medical history including information on your asthma, current symptoms, present and past medical treatment, asthma triggers and the impact of asthma on your life, your age and place of birth. You will also be asked to do breathing tests, blood tests and other research related studies, and collect sputum cells/fluid, urine, exhaled breath condensate and blood samples. The results of these questionnaires, tests, and some of the samples will be used now. Some of the information and left over samples will be stored for studies to be done in the future. The information and samples may be stored indefinitely to look at scientific questions related to asthma, allergies and related diseases. The questionnaires, test results and samples will be handled in a manner that protects your privacy; they will only be identified by a code. Only Dr. Loren Denlinger and the University of Wisconsin Health study team will have the link between the code and your name. The investigators may share the stored questionnaire data, test results or tissue/samples with other investigators in the SARP or other groups for research related to asthma, allergy and inflammation. However, your identity will be kept private as only the code will identify your sample now and in the future.

The sharing and storing of the questionnaire data, test results and samples is not optional. If you do not want to have your questionnaire data, test results or samples shared or stored with the other investigators in SARP or other groups researching asthma, allergy and inflammation, you will not be allowed to join this study.

Genetic Studies –
Work with your DNA will be done at Wake Forest Baptist Health (Winston-Salem, NC) and a small number of other SARP centers as well. Your name and participation in these studies will be private. Your genetic samples will be identified only by an ID number (not your name), and no genetic testing will be performed other than that associated with asthma, allergy, respiratory and related diseases. Any identifying data is kept in a locked drawer or in a password protected computer file. Only the Principal Investigator of this study and his designated data manager will have access to the numeric code, which identifies you by name. These results will NOT be put in your medical records. No HMOs or insurance companies will ever be allowed access to the genetic results.

This DNA sample may be shared with our collaborators for research purposes. You authorize the University of Wisconsin and members of its professional staff to use your DNA sample for these purposes. Your DNA sample will be used only for research purposes and will not be sold. Because

we do not know how the results of this DNA study relate to your individual health, the results of the research will not be given to you or your doctor without your permission. These results will also not be placed in your medical records. The findings from this research may result in the future development of products that are of commercial value. There are no plans for you to share in any profits that may occur as a result of this research.

As part of genetic studies performed in SARP, a sample containing your genetic information may generate data about your genetic code using Genome Wide Association Studies (GWAS) chips or Whole Genome Sequencing (WGS). Both GWAS and WGS analyses evaluate a very detailed picture of your genetic information for researchers spanning the 3 billion genetic markers that make up the entire human genome. WGS is an analysis of your complete genetic code and has the capability to identify nearly all genetic mutations in your genetic information.

In addition, your genetic information and clinical information will be sent to the National Institutes GWAS database of Genotypes and Phenotypes (dbGaP), and the WGS in a National Institutes of Health repository for the Trans-Omics for Precision Medicine (also known as TOPMed) consortium where it will undergo genome-wide analyses and be shared with other investigators for research purposes. Genetic information sent to the dbGaP and TOPMed will help researchers better understand how genes affect the risk of developing diseases such as asthma, cancer, diabetes, and heart disease, and may lead to better methods to select the best treatment options. Before your information is sent to the GWAS data repository it will be de-identified, which means that we will remove any identifying information such as your name, date of birth, address, etc. The code that once linked the data back to you will be removed prior to the data being sent to the NIH dbGaP and TOPMed data repositories. Thus, researchers using your DNA and clinical data will not be able to link this information back to you and therefore you will not receive any results.

The laboratories that are processing genetic information are research facilities and do not have the ability to provide genetic test results or genetic counseling. Genetic information about you or other information obtained from your sample will not be given to you, your family or your doctor. You may withdraw consent for the use of your genetic information at any time by contacting Dr. Loren Denlinger at 608-261-1552.

a) Although the genetic information about you is shared with other investigators in the network, it is identified with a code number and not your name or other identifiable information. Only researchers at the University of Wisconsin will be able to link your information with your name.

b) Results from research using your samples may be presented in publications and meetings but individual names will not be identified.

c) Absolute privacy cannot be guaranteed as the U.S. Department of Health and Human Services has the right to inspect your medical records relating to this research for the purposes of verifying data. Demographic information on the subjects is released only to characterize our populations for the National Institutes of Health.

d) In order to protect records, 1) only allowed users will be able to see the records, 2) the records will be kept in offices that are locked when not in use, and 3) access is strictly controlled. The records collected in this study will be subject to the Privacy Act. Records will not be shown to any person or

agency, unless the person who the records are about gives a written request or prior consent. The request should be made in writing to the Privacy Act Coordinator, NHLBI, NIH, Building 31, Room 5A10, 9000 Rockville Pike, Bethesda, MD 20892.

Some of the tests we will perform on your blood, tissue, etc. will be genetic testing, which is done on your DNA. DNA, or deoxyribonucleic acid, carries the genetic instructions for the cells that make up your body. Genes tell your body how to do things like form your spine, or what color your eyes should be. We will do whole genome testing for this study. Your “genome” is the complete DNA instruction book. “Whole genome testing” means making a list of the entire order, or sequence, of the DNA in your genome.

The DNA samples and information sent to other researchers will not include personal information like your name or your birthdate. However, even without your name or other identifiers, your genetic information is unique to you, like a fingerprint. Scientists expect that over the next few years, researchers will be able to look at your genetic information and be able to trace the data back to you (and potentially also to your blood relatives).

There may be other risks related to genetic testing that we don’t know about right now. This is because the field of genetics is moving forward very quickly.

Future Contact
Occasionally we may want to contact subjects who did our studies in the past to see if they

are interested in new projects. Your name and contact information will be kept in a database at the University of Wisconsin. If you agree to be in this database, you may be contacted in the future to see if you are interested in participating in more studies. The results of your breathing tests will be included in this database, and this information may be used to see whether you qualify for future research studies. The database is password protected, and only immediate research staff will have access to the information. There is a very small chance that your name, contact information and your screening information could, in error, be made public. Please let us know whether you would like to be called or not by putting your initials in one of the spaces below.

_____I would like to be contacted for future research studies.

_____I DO NOT want to be contacted for future research studies.

Who Will Answer Questions?
You may freely ask questions about this informed consent or the study now or at any time during the study. If you experience an adverse reaction, have questions about the research or experience a research related injury you may contact Dr. Loren Denlinger or one of his associates at the University of Wisconsin

If you have questions about your rights as they relate to your participation in this study, you may

contact the Institutional Review Board at the University of Wisconsin by telephone at 608-263-2362. The Institutional Review Board is a group of people who review research to protect your rights.

Agreement to Participate in the Research Study
You do not have to sign this form. If you refuse to sign, however, you cannot take part in this research study.
If you sign the line below, it means that:

- You have read this consent and authorization form.
- You have had a chance to ask questions about the research study, and the researchers have answered your questions.
- You want to be in this study.
- You give authorization for your protected health information to be used and shared as described in this form.

<u>Please initial to indicate your preference:</u>

________I agree that my family doctor can be told I am in this research study.

________I **DO NOT** agree that my family doctor can be told I am in this research study.

- -

____
Printed Name of Research Participant

____
Signature of Research Participant   Date

____
Signature of Person Obtaining Consent and Authorization   Date

****You will receive a copy of this form****

WFU School of Medicine
Institutional Review Board
IRB Number: IRB00066576
Meeting Date Approved 11/10/2021
Version Valid Until: 6/23/2022

Visits and Procedures

Minimum Procedure Set	Visit E1[1]	Phone call	Visit E2	Phone call	Visit E3	Phone Call	Visit E4
		6 months	12 months	18 months	24 months	30 months	36 months
Consent and eligibility	x						
Questionnaires	x	x	x	x	x	x	x
Validated questionnaires	x	x	x	x	x	x	x
Physical exam	x						x
Vital Signs/Height/Weight/BMI	x		x		x		x
Spirometry	x		x		x		X
Maximum bronchodilation	x		x		x		x
Methacholine (subjects new to SARP)	x[2]						
Urine pregnancy test	x		x		x		x
Urine collection	x						x
Sputum induction	x						x
Exhaled nitric oxide	x		x		x		x
Exhaled breath condensate	x						
Blood sample – complete blood count (CBC)	x		x		x		x
Blood sample – serum/plasma (blood fluids)	x		x		x		x
Blood sample – fasting metabolic health	x						x
Blood sample – DNA (subjects new to SARP)	x						
Blood sample – allergy tests	x						
Stool	x						x

[1]Testing in E1 may be completed on several days as determined by individual site standard operating procedures. [2]Methacholine challenge will be performed only if subject does not have acceptable documentation of a previously positive methacholine challenge.