

**University of Wisconsin–Madison
Consent to Participate in Research**

Parent Permission Form with Protected Health Information (PHI) Authorization

Study Name: Randomized, placebo-controlled, multicenter study to assess the efficacy, safety, and tolerability of **Oral Bacterial Extract** for the prevention of wheezing lower respiratory tract illness (**ORBEX**)

Study Investigator: Daniel Jackson, MD, (608) 263-7686

Co-Investigator: Robert F. Lemanske, Jr., MD, (608) 263-6184

Study Contact: Tanya Watson, RN, Study Coordinator, (608) 263-3360

INVITATION

Please read this form carefully. It has important information about this research study and it will help you decide whether or not you would like your child to take part. This consent form may contain words that you do not understand. Please ask the study doctor or the study staff to explain any words or information that you do not understand. You may take home an unsigned copy of this consent form to think about or discuss with your family or friends before making your decision.

Your child is being invited to join a research study at the University of Wisconsin–Madison. This study will see if a daily capsule of Broncho-Vaxom[®] will help young children at risk for developing asthma or wheezing.

Your child is invited because s/he is between 5 to 17 months old and has an increased risk of developing wheezing or asthma. Your child's participation is completely voluntary.

We, the study staff, will explain the study to you. This consent form describes the purpose, procedures, benefits, risks, discomforts and precautions of the study. If you decide to let your child participate, you must sign the pages at the end of this form to show that you agree for your child to be part of the study. This is called "giving parental permission."

WHY IS THIS STUDY BEING DONE?

This study is being done to find out if Broncho-Vaxom[®] given to high-risk infants for 10 days each month over a two-year period will prevent or reduce wheezing illnesses in the third year when the child is not taking it. Broncho-Vaxom[®] has been used in other countries all over the world, but it has not been approved by the U.S. Food and Drug Administration for use in the U.S. Therefore, the use of Broncho-Vaxom[®] for this study is considered investigational.

Broncho-Vaxom[®] is a mix of parts of different bacteria that often cause respiratory infections. It works like an immunization to stimulate the immune system in order to increase the body's natural defenses against a wide number of respiratory bacteria that cause children to have respiratory illnesses.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

The University of Wisconsin–Madison is one of 7 clinical centers in the U.S. doing this study. About 1076 children will participate in the study nationwide. About 154 children will be enrolled at this site.

WHAT WILL HAPPEN IF MY CHILD TAKES PART IN THIS STUDY?

Your child will be in the study for about 3 years. There is a 1-month run-in period, a 24-month treatment period, and a 1-year observation period. Each of these different study periods are described below with complete descriptions of common study interventions provided at the end of this section. There will be a total of 12 planned in-clinic study visits. There will also be telephone calls about once a month (in months with no clinic visit) for the duration of the study. If your child gets sick with a wheezing illness during the course of the study the research team will schedule a study visit with your child to evaluate this illness, and may prescribe medications to manage the wheezing illness.

RUN-IN PERIOD:

Visit 1 (about 2 hours): At the first visit we will explain the study to you. You will be asked to sign this consent form. We will ask you questions about your and your child's medical history. We will ask you to complete some questionnaires. The study doctor will do a physical exam on your child. We will give you some practice capsules (no active ingredients) to see if you can stay on the right schedule for giving your child the capsules during the run-in period. You will need to give your child one capsule daily for 10 days. The run-in period will last for about one month.

We will send you a text message once each week, and you will need to answer the text to let us know whether your child has had any breathing problems. We will send you another text message reminding you to start giving your child the study medication.

It is very important that you receive these text messages. It is also very important that we receive your text message answers. In order to participate in this research study, you must have a cell phone that can receive and send text messages throughout your child's participation in this study. At the first visit, we will ask if you have a cell phone that will be able to receive and answer text messages throughout the study.

TREATMENT PERIOD:

The treatment period will last for two years. This is when your child will be taking the study capsule for 10 days each month.

Visit 2 (about 4 weeks later) (about 2 hours): We will check the study capsules provided during the run-in period to make sure you have followed the directions on how and when your child takes the study capsules. We will check your ability to receive and answer the study text messages. We will also make sure your child is still able to participate.

Your child will have a physical examination with the study doctor. We will ask some questions about your child's medical history and we will ask you to complete a few questionnaires. We will draw some blood from your child (10 ml or about 2 teaspoons). We may ask to draw blood at a later visit if we are unable to get your child's blood sample at this visit.

Your child will be randomly assigned to take either a capsule containing Broncho-Vaxom® or a placebo capsule. The placebo capsule looks like the study capsule, but it has no active ingredient. Randomly assigned means that there is an equal chance of your child receiving either treatment. It is similar to flipping a coin and having the treatment decided by whether the coin lands heads up or tails up. Neither you nor the study doctor will know which capsule your child is taking. It will be kept a secret and the capsule your child is taking will not change throughout the entire study. However, this information can be released if medically necessary.

The study capsule contains a little bit of powder that you can mix with fruit juice or other liquid for your child to drink. You will need to give your child the study capsule for 10 days each month.

You will be given enough study capsules to last until the next visit.

Visit 3 (1 month later), and visits 4 through 8 (every 4 months) (about 1 ½ hours):

The study doctor will do a brief physical exam on your child. Your child will be asked to do some breathing tests at Visit 8. We will check to make sure your child is taking the study capsule as required, and that you are receiving and answering the study text messages.

You will be given enough study capsules to last until the next visit.

Visit 9 (month 24) (about 2 hours): The study doctor will do a brief physical exam on your child. Your child will be asked to do the breathing tests. We will check to make sure your child has taken the study capsule as required, and that you are receiving and answering the study text messages. We will also obtain another blood sample from your child (about 2 teaspoons).

Visits 10 (month 28) and 11 (month 32) (about 1 hour): The study doctor will do a brief physical exam on your child. Your child will be asked to do the breathing tests. We will check that you are receiving and answering the weekly text messages.

Visit 12 (last visit, month 36) (about 2 hours): The study doctor will do a physical exam to see how your child is doing. We will draw a blood sample from your child (about 2 teaspoons). Your child will be asked to do the breathing tests. We will ask you some questions and ask you to complete questionnaires.

Telephone calls (10 minutes): We want to see how your child is doing about once a month during the study. During months when you do not have an in-clinic visit, we will call you to see how your child is doing. We will ask questions about your child's asthma or wheezing symptoms, medication use, and whether your child has seen the doctor. There will be about 26 telephone calls over the 3-year study.

Unscheduled visits: If your child has wheezing symptoms we may ask you to bring your child into the clinic for a physical exam with the study doctor. The study doctor might prescribe medications for the wheezing illness. This visit will take about 2 hours.

PROCEDURES:

Physical examination includes weight and height measurements, and looking at your child's lungs, skin, nose, and mouth.

Medical history is an interview that tells us about the overall health of your child.

Questionnaires will tell us about your child's health and how this affects you and your child's life. They will also tell us about your child's lifestyle and home environment. You will also complete questionnaires about your child's and your family's medical history.

Blood samples will be taken 3 times. The blood will be collected by putting a needle in a vein in your child's arm or by a needle stick to the heel of your child's foot. The blood test is to see what your child might be allergic to and to test for inflammation. This sample may also be used to test your child's genetics; however, this will only occur if you agree on a separate part of this consent.

Nasal washes/swabs using salt water similar to tears will be done at some study visits. First, the coordinator will use a spray bottle to spray both sides of the inside of the nose with a salt water similar to tears. Next, the coordinator will gently swab both sides of the nose using a cotton swab. This is to look for bacteria or viruses in your child's nose.

Breathing tests will include spirometry and impulse oscillometry. These tests will be done at visits 8, 9, 10, 11, and 12.

Spirometry: Your child will wear a nose clip and will be asked to breathe out forcefully into a machine for a few seconds. The machine measures how much air comes out of the lungs and how fast it comes out. Not all children will be able to perform spirometry, but will hopefully get better at it as they get older.

Impulse Oscillometry (IOS): Your child will wear a nose clip and be asked to breathe normally into a machine for about 20 seconds while holding their cheeks. This will be repeated a few times per session.

A stool sample will be collected at visits 2, 9 and 12. We will give you a collection kit and instructions. You will need to scoop a small amount of your child's stool into a collection tube at home before the visit.

Text messages will be sent to you once each week. You will need to answer the text to let us know whether your child has had any breathing problems.

If you do not do this task a majority of the time, your child may be asked to withdraw from the study.

Email messages may be used during the study to remind you about study visits.

AT HOME PROCEDURES:

You will need to give your child the study capsule for 10 days each month. You will need to answer the weekly text messages every time you receive them. You should try

hard to keep appointments and phone calls. Call the study coordinator if you must change your appointment. Study capsules should be brought with you to every study visit. They should not be thrown away.

The study capsules should be stored at room temperature under dry conditions away from heat and direct sunlight. The study capsules must be taken ONLY by the child participating in the study. The study capsules should only be taken as directed and should be kept out of the reach of other children.

CAN MY CHILD STOP BEING IN THE STUDY?

Your child's participation is voluntary. You may refuse for your child to participate in this study. If you decide your child can take part in the study, you may remove your child from the study if you change your mind at any time.

WHAT RISKS, SIDE EFFECTS OR DISCOMFORTS CAN I EXPECT FROM MY CHILD BEING IN THE STUDY?

Physical examination, medical history, impulse oscillometry, and stool collection: there are no risks to these procedures.

Questionnaires may make you feel uncomfortable. You do not have to answer any question if you do not want to.

Text messages: Text messages can be distracting. Text messages could increase your risks of having an accident if you try to read or reply while you are doing something that requires your attention, like walking or driving a car. You should know that it is illegal in some states to text while driving. You should continue to use good judgment about this while your child is in this study. Text messages used in this study are not encrypted or secure when they are sent, so there is a chance someone could access them.

Email messages: We are requesting your email address so we can remind you about study visits. Email is generally not a secure way to communicate about your health as there are many ways for unauthorized users to get access to email. You should avoid sending sensitive, detailed personal information by email. Email should also not be used to convey information of an urgent nature. If you need to talk to someone immediately, you should contact the study team at (608) 263-3360. You do not have to provide your email address to participate in this study.

Blood samples: There may be pain from the skin puncture, as well as bleeding or bruising of the skin. There is a rare risk for infection at the place of puncture of the skin.

Local anesthetic cream (a medicine to numb the skin) may be put on the skin before the needle is inserted. This may reduce the pain of the needle poke. The use of this cream is optional. If you would like to use this cream, it must be on your child's skin 30-60 minutes before the needle poke. The cream might cause temporary paleness, redness, changes in feeling heat and cold, swelling, itching, and rarely, rash.

Nasal washes can cause minor discomfort and nasal stuffiness that is short lived.

Spirometry may make your child feel dizzy. This will go away when the test stops.

Broncho-Vaxom®: It is possible that your child will experience diarrhea (6 out of 100), or headache (5 out of 100) when taking study capsules. Undesirable effects that are infrequent (between 1 out of 100 and 10 out of 100) are abdominal pain, nausea, vomiting, a skin rash accompanying a disease or fever, hives, difficult or labored breathing, cough, asthma, and tiredness. Undesirable effects that are rare (less than 1 out of 100) are fever and allergic reactions. There are no severe risks known to taking Broncho-Vaxom®, but it is possible that unknown risks may exist.

Albuterol, an inhaled short-acting beta-agonist, will only be used if your child has trouble breathing. Potential risks with albuterol are palpitations (abnormally rapid beating of the heart), increased blood pressure, tremor, nausea, headache, nervousness, lightheadedness, coughing, and dizziness.

Fluticasone, an inhaled corticosteroid, will only be used if your child develops asthma symptoms. Research studies of fluticasone in children less than 5 years of age have shown no meaningful differences in the rate of adverse effects compared to placebo when given for 12 weeks. The biggest concern for young children is the possible growth delay. “Catch-up” growth after stopping fluticasone has not been fully studied. The growth of all children in the study will be carefully measured at each study visit. Other possible side effects are headache (11%), throat irritation (8%), upper respiratory inflammation (2%), sinusitis (6%), hoarseness (2%), and oral candidiasis (2%).

Montelukast, an oral anti-inflammatory, will only be used if your child develops asthma symptoms. It is approved for use in children twelve months old and above with asthma. The most common side effects with a frequency of about 2% include fever, cough, abdominal pain, diarrhea, headache, rhinorrhea, rash, ear pain, and conjunctivitis.

Prednisolone, an oral corticosteroid, will only be used if your child develops asthma symptoms. Oral corticosteroids can produce hoarseness, sore throat, and yeast infection of the mouth or throat if taken in high doses for lengthy periods of time. They can also cause weight gain, growth delay, bruising of the skin, cataracts, and diabetes if taken at high doses over a long time. These side effects are not expected in this study because of the short length of time (4 days at a time) that it will be used.

CLINICAL FINDINGS

Some of the tests we will do are routine breathing tests such as spirometry, and routine lab tests such as a complete blood count and allergy tests. There is a chance of finding something unexpected. You will be told of findings of clear clinical significance. Clear clinical significance means that the problem may be treatable and we know the risks of not treating the problem. You will not be told of findings with unclear or no known clinical significance.

There may be benefits to learning about unexpected findings, such as treatment of the condition. There may also be risks to learning the results, such as feelings of worry if no treatments are available. Study doctors will follow up with you to answer any questions you may have. If you believe your child is having symptoms that require testing, you should contact your primary care physician.

You are encouraged to share these results with your child's primary care physician. You may also choose to have your child's physician informed of results that we report to you. If you choose to have your child's physician informed of any findings of clinical significance, that report will likely be placed in your child's medical record.

Please indicate your preference by checking the appropriate box:

- Please inform my doctor of findings of clinical significance –OR–
 Please do not inform my doctor of findings of clinical significance

If you do wish us to report any findings to your child's physician you must provide us with the name and location of the primary physician, prior to your [breathing tests, blood tests, etc.]:

Name of primary physician _____

City or clinic _____

WHAT BENEFITS CAN MY CHILD EXPECT FROM BEING IN THE STUDY?

Your child may or may not benefit in the long-run from being in this study. If effective, Broncho-Vaxom[®] has the potential to prevent or reduce the development of wheezing illness in these high-risk children. The children who receive placebo are not expected to benefit directly from taking the study drug. This study may help other young children in the future because we will learn more about using Broncho-Vaxom[®] in toddlers who may be at risk for developing asthma.

WHAT CHOICES DO I HAVE IF MY CHILD DOES NOT TAKE PART IN THE STUDY?

You may choose for your child to participate or not without penalty or loss of benefits to which your child is otherwise entitled. Your child does not have to take part in this study. You can choose to have your child join another wheezing or asthma study. Participation in this study is not a replacement for your child's usual health care.

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?

There are no costs to you or your child for being part of this study, other than your time. There is a chance you could be charged for study text messages if they are not covered under your current cell phone plan.

WILL MY CHILD BE PAID FOR PARTICIPATION IN THIS STUDY?

Your child will be paid a total of \$1360 if you and your child complete all study visits and phone calls. You will receive \$70 for each of the 12 clinic visits s/he completes. You will also receive \$20 for completing each of the 26 phone calls and for responding to weekly text messages. Your child will only be reimbursed for study visits and phone calls that

have been completed. It is important to know that payment for participation in a study is taxable income. We will ask that you provide your child's social security number for this purpose. Other incentives such as small toys may be given to children at each visit.

SOURCE OF FUNDING

This study is funded by the National Institutes of Health's National Heart, Lung and Blood Institute (NIH NHLBI).

CAN MY CHILD LEAVE THE STUDY EARLY?

Yes, your child can leave the study early. Taking part in this research study is voluntary. No matter what decision you make, there will be no penalty to you or your child and your child will not lose any of her/his regular benefits. By signing this form, your child does not give up any personal legal rights s/he may have as a participant in this study. You will be told of any new information which may affect your willingness for your child to continue. If you decide not to participate, any relationship you have with the University of Wisconsin-Madison (UW-Madison) or the University of Wisconsin Hospitals and Clinics (UWHC) will not be affected in any way. If you decide to quit the study, you will be asked to return study-related items to the study coordinators.

The study sponsor or study doctor may decide to stop your child's participation without your permission. This could happen if the study doctor thinks that being in the study may cause your child harm or if the study outcome is found out early. If you do not do use the study capsules or answer the text messages a majority of the time, your child may be asked to withdraw from the study.

WHAT HAPPENS IF MY CHILD IS INJURED BECAUSE MY CHILD TOOK PART IN THIS STUDY?

In the event that your child is physically injured as a result of participating in this research, emergency care will be available. You will be responsible for the charges for the emergency care. There is no commitment to provide any compensation for research-related injury. You should realize that you have not released this institution from liability for negligence. Please contact the study investigator Dr. Daniel Jackson at (608) 263-7686 if your child is injured or for more information.

INFORMATION ABOUT CONFIDENTIALITY AND USE OR DISCLOSURE OF PROTECTED HEALTH INFORMATION

The University of Wisconsin–Madison has rules to protect information about your child. Federal and state laws also protect your child's privacy. This part of the consent form tells you what information about your child may be collected in this study and who might see or use it.

Generally, only people on the research team will know that your child is in the research study and will see your child's information. A unique number and your child's initials will be used in place of your child's name on samples and for data entry.

The people working on the study will collect information about your child. This includes things learned from the procedures described in this consent form. They may collect other information including:

- Medical history
- Results of tests, exams, and questionnaires collected for this study (called study records)
- As a part of this study, the researchers may ask to see your child's healthcare records from your child's other health care providers. Your child's past medical records may include personal information such as your child's social security number, medical record number, address, date of birth, and other details.
- Your cell phone number will be transmitted to Twilio.com, which sends and receives the weekly and monthly study text messages. Your cell phone number will be erased right after you receive your message and send your answers.

The research team will need to see your child's information. Other organizations may see, use and share your child's identifiable health information during this study. These include:

- Governmental agencies that have the right to see or review your child's health information, such as the Office for Human Research Protection (OHRP) and the Food and Drug Administration (FDA). There is a possibility that your child's medical research record, including identifying information, may be inspected by officials of Federal or State government agencies, and/or organization representatives but only to the extent necessary to satisfy legitimate Federal, State, or University responsibilities
- Study funder: National Institutes of Health (NIH) National Heart, Lung, and Blood Institute (NHLBI)
- Members of the ORBEX Data Safety Monitoring Board set up by the funding agency to ensure the study is being done properly
- ORBEX Data Coordinating Center, Penn State University College of Medicine, Hershey, PA
- Doctors and staff at other places that are participating in this study
- Twilio.com, San Francisco, CA (the company that will temporarily receive your cell phone number in order to send you the scheduled study text messages and send your answers to the Data Coordinating Center)
- Tucson Genetics of Asthma Lab, University of Arizona, Tucson, AZ (genetics lab, storing DNA and plasma) (ONLY if you agree to the optional genetics sample collection described later in this consent)
- Other labs contracting with the study for analysis of blood or other biological specimens
- OM Pharma, SA (provider of Broncho-Vaxom)
- Other people or organizations assisting with this research effort (this may include drug manufacturers, distributors, and/or their designees)

We cannot do this study without your permission to use and give out your child's information. You do not have to give us this permission. If you do not, then your child may not join this study.

WILL MY CHILD'S STUDY-RELATED INFORMATION BE KEPT CONFIDENTIAL?

We will do everything we can to protect your and your child's privacy and to keep your child's health information confidential. Records will be stored in locked spaces accessible only to research staff. People outside the University of Wisconsin–Madison who receive your child's information may not be covered by this promise. We try to make sure that everyone who needs to see your child's information keeps it confidential – but we cannot guarantee this. Personal information regarding your child's participation in this study may be disclosed if required by state law.

The researchers might use information learned from this study in scientific journal articles or in presentations. None of this information will identify you or your child personally. A description of this clinical trial will be available on www.ClinicalTrials.gov, as required by U.S. law. This website will not include information that can identify your child. At most, the website will include a summary of the results. You can search this website at any time.

To further protect your privacy, the ORBEX researchers have been granted a Certificate of Confidentiality from the FDA. This will help further protect information that may identify your child. The Certificate prevents the investigator from being forced to disclose identifying information for use in court. The investigator may not even be forced by court subpoena. Courts that may be prevented from getting your child's information include any federal, state, local civil, criminal, administrative, legislative, or other court proceeding.

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 child's involvement in this research. The investigator may not withhold information if you give your insurer or employer permission to receive information about your child's participation in this research. This means that you and your family must also actively protect your own privacy.

The Certificate does not prevent the researchers from taking steps, including reporting to authorities, to prevent serious harm to your child or others.

HOW LONG WILL MY PERMISSION TO USE MY HEALTH INFORMATION LAST?

By signing this form, you are giving permission for your health information to be used for this study and shared with the individuals, companies, or institutions described in this form. Unless you withdraw your permission in writing to stop the use of your health information, there is no end date for its use for this research study. You may withdraw your permission at any time by writing to the person whose name is listed here:

Daniel Jackson, MD

600 Highland Avenue
Mailstop 9988
Madison, WI 53792

Beginning on the date you withdraw your permission, no new health information will be used. Any health information that was shared before you withdrew your permission will continue to be used. If you withdraw your permission, you can no longer actively take part in this research study.

GENETIC BLOOD DRAW AND TESTING SECTION (OPTIONAL)

WHAT IS THE PURPOSE OF GENETIC TESTING?

Your child is also being asked to take part in an optional part of this study, which involves giving a blood sample for genetic testing (DNA analysis). Deoxyribonucleic acid (abbreviated DNA) is the genetic material contained in all cells of your body, including blood cells. DNA stores information in the form of a code. It is the material that determines, among other things, your physical characteristics such as your height and the color of your eyes. Genetic testing can be used to find out if a person is more likely to develop a particular disease or to determine how one might respond to different medications. Another purpose of genetic testing is to identify genes and/or variations in genes. Genes are parts of DNA that have complete messages for building the proteins that make our bodies work.

We will try to find out if your child's DNA results are associated with their response (or lack of response) to different medications or study drugs, and whether those results are related to information we collect about your child in the study. We will also look for genes and/or variations in genes related to asthma, allergies, and related diseases. Identifying genes and their variations may help develop a new treatment for people with asthma who have certain genes. We will also perform a test for proteins present in the plasma leftover from your child's blood sample. Other tests on the plasma may be performed at a later time, but they have not yet been defined. Any future tests will need to be approved by the ORBEX Steering Committee. The ORBEX Steering Committee supervises how the study is run, and is made up of investigators from each study site.

Your child can still take part in the main study even if you refuse to give an optional genetic blood sample.

WHAT DOES PARTICIPATION INVOLVE?

If you agree to genetic testing, we will use a needle to collect about 10 ml (2 teaspoons) of blood from a vein in your child's arm. This will be done at the time of the regular study blood draw so there will not be an additional stick, if possible. DNA will be removed from the blood sample and stored in a lab. Plasma (the liquid part of blood in which blood cells are suspended) leftover from the DNA removal process also will be stored for future research in the areas of asthma, allergies and related diseases.

HOW WILL MY CHILD'S BLOOD BE HANDLED?

Your child's blood sample collected for genetic testing will be labeled with a code number, their initials, and blood draw date and transferred to the Tucson Genetics of Asthma Lab in Tucson, Arizona for DNA removal and storage, and storage of the leftover plasma. The Data Coordinating Center in Hershey, Pennsylvania, will provide the Tucson lab with a new genetics code number (unrelated to the original), along with your child's gender and birth year (not complete date of birth). The genetics code number will not contain any information about your child or your clinical site. After the DNA removal process is complete, the genetics lab will have access only to the new genetics code number, your child's gender, and year of birth to identify their samples. The Tucson lab will not store your child's initials with their samples and will not be able to see their initials in the study database following processing of your child's sample.

The clinical site where your child is being seen for study visits will not have access to the genetics code number linked to their samples. Therefore, it would be very difficult for staff at the clinical site or at the Tucson lab to identify the person belonging to any given DNA/plasma sample.

In the future, with the permission of the ORBEX Steering Committee, your child's DNA and/or plasma samples may be transferred to other laboratories for analysis. In each case, only the genetics code number, gender, and birth year will be transferred with their samples.

HOW WILL THE GENETICS INFORMATION BE HANDLED?

The coded results (that do not identify your child) of the genetic testing will be sent to our central Data Coordinating Center in Hershey, Pennsylvania. The Hershey site will keep the links among all the code numbers and will be able to join the clinical data from the study, such as results of your child's breathing tests, with genetics data in order to perform analyses. The Hershey site does not have access to your child's name, address, social security number or other personal identifying information.

The coded analysis results will only be released to other scientists working on this study. It is almost impossible for the genetics results to be associated with your child personally, unless your clinical site gives additional identifying information to the Data Coordinating Center (which it will not do) or unless the Data Coordinating Center gives additional information to your clinical site (which it may do under specific conditions which require approval as outlined in the next paragraph).

In the future, we may want to perform studies where it would be necessary to get in touch with you based on your child's genetic information. Only your specific clinical site will have enough information to do this, with your approval. Your specific clinical site will only be provided enough information to contact you based on your child's genetic information if **both** the ORBEX Steering Committee approves **and** the local clinical site's Human Subjects' Protection Board agrees that doing such testing and contacting you are appropriate. If you agree to future contact, you will always be able to opt out of (not take part in) the future study.

WHO WILL SEE THE RESULTS OF THE GENETICS TESTING?

Coded (not identifiable to your child) genetic information will be seen by the ORBEX study investigators or by other NIH/NHLBI research centers/investigators with whom the ORBEX study investigators agrees to share such information.

Currently, individual genetic results will not be known and you will not be notified of your child's results. Therefore, your child's genetic results will not become part of their medical record. In the future, ORBEX investigators might do studies based on previous genetic testing. For example, if you agree to have your child provide a blood sample for genetic testing in this study, those results might be useful for recruitment in future genetic studies. Future studies would only be done with the approval of the Human Subjects Protection Board. At that point, if approved by the ORBEX Steering Committee and the Human Subjects' Protection Board, only the investigators at your site would be made aware of any results linked to your child and would contact you to find out if you are interested in providing more information or having your child participate in a study. You can tell us whether or not you would like to be contacted for this purpose at the end of this section.

HOW LONG WILL MY CHILD'S SAMPLES AND INFORMATION (DATA) BE STORED AND USED FOR RESEARCH?

Your child's DNA and plasma samples will be stored for as long as they are useful to the ORBEX researchers. There is no limit on the length of time your child's information will be stored for research.

WILL THE GENETIC SAMPLES HAVE COMMERCIAL VALUE?

This genetic testing or other follow-up studies may lead to the development of a test that might tell in advance if a person will respond to certain asthma treatments, but you or your heirs will not be able to share in the profits made by the company that sells it.

WHAT IF I CHANGE MY MIND?

Your agreement to allowing your child to provide a blood sample for DNA analysis and plasma storage is voluntary. You may refuse to have your child provide a blood sample without any loss of rights or privileges to which your child is otherwise entitled. If you do not wish to allow your child to provide a sample for DNA analysis, your child can still take part in the main study.

As explained above, it will be very difficult to link your child's blood sample to them. It will be very challenging to withdraw your child's sample after it has been sent for genetic analysis, but we will make a good faith effort to ensure that all stored genetic material is destroyed upon receiving your written request. Please think very carefully about your decision to have your child provide a blood sample for DNA analysis.

If you wish to withdraw your permission for your child's DNA and/or plasma to be used for this research study, please contact Dr. Daniel Jackson by calling 608-263-7686.

RISKS AND DISCOMFORTS RELATED TO GENETIC TESTING:

Blood Draw. The risks with taking blood include pain from the needle poke and bruising. There is a rare risk for infection at the place of puncture of the skin. Dizziness and fainting rarely occur.

Confidentiality/Disclosure. Information about your child's participation in a genetics study may influence insurance and/or employers regarding their health status. If a result is accidentally disclosed and you or your child are considered a high insurance risk as a result, this could lead to loss of health insurance, difficulty obtaining insurance, or an increase in premiums. If your employer becomes aware of the result, this could lead to the loss of your job or make it harder to get a new one. To help prevent disclosure, information about your child's participation and the results of the research will not be placed in your medical records. In addition, your child's blood sample will be coded and the key to the code kept in a separate locked physical or password-protected electronic file at the clinical site. Once the sample is processed at the genetics lab in Tucson, Arizona, a new unrelated code number will be used and no key linking your child's identity (name, address, etc.) to the DNA and plasma samples will exist. Not sharing information about your child's participation in this study with others will lower these risks. Although every effort will be made to keep your child's participation confidential, the investigators cannot guarantee absolute confidentiality. Even though we will remove identifying information and do not intend to tell you or anyone else the results of the genetic testing on your child's sample, there is a very small chance that this information could accidentally become known to you, your doctor, or others.

To further reduce your risks, there is a new Federal law, called the Genetic Information Nondiscrimination Act (GINA). This law makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

All employers with 15 or more employees must follow this law as of November 21, 2009. Be aware that this new Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Other Risks. There might be other risks associated with genetic testing that we do not know about yet.

As we learn more about asthma-related genetic testing, we may contact you to provide or request more information.

Do you agree to genetic testing and the sharing of your child’s coded genetic samples with ORBEX and NIH/NHLBI research centers/investigators for the purposes of identifying genes and/or variations in genes related to asthma, allergies, and related diseases (to be performed only with the agreement of the ORBEX Steering Committee)?

(Please initial) YES _____ NO _____

Do you agree to the storage and sharing of leftover plasma from your (or your child’s) genetics blood sample with ORBEX and NIH/NHLBI research centers/investigators for use in future research in the areas of asthma, allergies and related diseases?

(Please initial) YES _____ NO _____

Do you agree to allow your clinical site to identify and get in touch with you based on the results of genetic testing (to be performed only with the agreement of the ORBEX) Steering Committee and the local Human Subjects’ Protection Board?

(Please initial) YES _____ NO _____

WHO CAN ANSWER MY QUESTIONS ABOUT THE STUDY?

You can talk to your study doctor about any question, concerns, or complaints you have about this study. You can reach Dr. Jackson at (608) 263-7686.

If you have questions about your child’s rights as a participant in this study or to discuss other study-related concerns or complaints with someone who is not part of the research team, you may contact the UWHC Patient Relations Representative at (608) 263-8009.

REQUEST FOR PERMISSION TO CONTACT YOU ABOUT FUTURE STUDIES:

Occasionally we may want to contact subjects who did our studies in the past to see if they are interested in new studies. Your child’s name, contact information, and health information gathered during screening for this study will be kept in a database at the University of Wisconsin Asthma, Allergy and Pulmonary Research Unit. If you agree to have your child’s information be in this database, you may be contacted in the future to see if you are interested in having your child participate in more studies. There is a chance that an outside investigator, who is still part of the UW, would like to conduct a study that your child might qualify for. With your permission, your contact information may be passed along to the investigator to screen for another study. The database is password protected, and only immediate research staff will have access to the information. There is a very small chance that your child’s name and contact 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 for my child.

_____ I DO NOT want to be contacted for future research studies for my child.

CONSENT AND AUTHORIZATION

I have read this form and I am aware that my child is being asked to participate in a research study. I have had the opportunity to ask questions and have had them answered to my satisfaction. I voluntarily agree to have my child participate in this study. I am not giving up any of my child's legal rights by signing this form. I will be given a signed copy of this form.

Printed name of child

Printed name of person authorized to consent for the child

Signature of person authorized to consent for the child

Date (mm/dd/yyyy)

Relationship to the child

Investigator/Research Staff

I have explained the research to the participant's representative before requesting the signature above. A copy of this form will be given to the participant's representative.

Printed name of person obtaining consent

Signature of person obtaining consent

Date (mm/dd/yyyy)