UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Study Title: STEP-UP YELLOW ZONE INHALED CORTICOSTEROIDS TO PREVENT EXACERBATIONS (STICS)

This is a medical research study. Your child's study doctor(s), Michael Cabana, MD, MPH and Ngoc Ly, MD, MPH from the UCSF Department of Pediatrics or one of their research coordinators will explain this study to you.

Medical research studies include only people who choose to take part. Take your time to make your decision about your child participating. You may discuss your decision with your family and friends and with your health care team. If you have any questions, you may ask your child's study doctor.

Your child is being invited to join a research study about asthma action plan strategies to prevent asthma attacks. Your child is being invited because he/she is between 5-11 years of age and had at least 1 bad asthma attack in the past year.

Why is this study being done?

Most people with asthma use an action plan to guide their asthma treatment. Written asthma action plans are usually color-coded. "Green" means that asthma symptoms are well controlled. "Yellow" means that asthma symptoms are not well controlled and asthma treatment may need to change. "Red" means a severe worsening of symptoms. Red zone treatment is usually an oral corticosteroid like prednisone.

The purpose of this study is to find the best yellow zone action plan strategy for children with asthma. Finding the best yellow zone strategy may prevent children from entering the red zone and having to take prednisone. The study is also trying to determine which yellow zone strategy leads to the least total corticosteroid (oral and inhaled) use for children with asthma.

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

How many people will take part in this study?

UCSF is one of 9 clinical research centers in the country doing this study. A total of about 250 children will be in this study. At least 25 children will be included in the study at UCSF. There is no upper limit to the number of children enrolled at each site.

What will happen if my child takes part in this research study?

This study has 8 study visits and 6 study telephone calls over a year. More study visits or telephone calls may happen if your child's asthma worsens. Most visits will take about one hour. The first 2 visits will be about two hours each. The telephone calls will take less than 15 minutes each.

ASTHMANET REGISTRATION: Before your child is enrolled in an AsthmaNet study, he/she must first be entered into the AsthmaNet Registry. This Registry has been set up to collect basic background information that will probably not change over time. This information is limited to: initials, date of birth, gender, and race/ethnic identification. Your child's Registry information will be coded with a unique AsthmaNet identification number and entered into the AsthmaNet database (Data Coordinating Center, Penn State University, Hershey, PA). Data collected from your participation in the STICS study might be combined or used with data from other studies for analyses performed by AsthmaNet investigators and their collaborators. Registry data help us track your child's participation in multiple AsthmaNet studies over time. Knowing that your child was in more than one study is useful in certain types of data analyses.

Your agreement to provide the information for the AsthmaNet Registry is voluntary. However, if you choose not to provide it, your child cannot be screened for or enrolled in any AsthmaNet study. Once you consent to have your child entered into the Registry, his/her 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 child's participation in AsthmaNet studies. Registration happens before or during your child's first study visit.

RUN-IN: The first 4 weeks of the study is called the run-in. All children will be asked to take fluticasone 44 mcg/puff, 2 puffs twice a day. Fluticasone is also called Flovent®. Your child will also be asked to do peak flow measurements and complete electronic diary entries once daily. You and your child will be given a written asthma action plan. The action plan will help you know if your child is in the green, yellow or red zone. **Please make sure you and your child understand this asthma action plan.**

The run-in is used to make sure that your child qualifies for the study. Breathing tests and questionnaires will be completed. The run-in is also used to make sure your child can follow the study instructions. If your child's asthma is not well controlled during the run-in or has problems doing daily home procedures, he/she may be asked to leave the study. If your child continues to qualify for the study, he/she will begin the treatment period.

During the Study 48-WEEK **TREATMENT PERIOD**: Your child will take Fluticasone 44 mcg/puff, 2 puffs twice a day in the green zone, and will be randomly assigned to one of two yellow zone treatments which are:

- Fluticasone 44 mcg/puff, 2 puffs twice a day for 7 days
- Fluticasone 220 mcg/puff, 2 puffs twice a day for 7 days

You and the study team will not know which yellow zone treatment your child has been assigned to. However, this information can be found out, if necessary.

The following sections cover medication and study procedure details.

MEDICATIONS

GREEN zone treatment:

Daily study inhaler: Fluticasone propionate (Flovent 44 mcg/puff) is an inhaled corticosteroid. It is commonly prescribed for the treatment of asthma. The daily dose in this study is thought to be the lowest effective dose to control asthma symptoms. It is FDA approved for use in children 4 years and older. Fluticasone has been studied a lot in children and is described as safe and well tolerated. Your child will be asked to take 2 puffs twice a day for the entire study unless instructed otherwise. It will always be active drug and we call this “open label”. It will never be fake or placebo.

As needed rescue inhaler: Albuterol (90 mcg per puff) is a short acting bronchodilator. Your child may take 2 puffs whenever he/she would typically use albuterol.

YELLOW zone treatment: The yellow zone treatment is blinded, meaning that neither you nor the study team will know which treatment it is. Yellow zone treatment will be either the same daily dose of fluticasone as described above or five times the daily dose of fluticasone. That is, it will be either 44 mcg/puff, two puffs twice daily or 220 mcg/puff, two puffs twice daily. It will never be fake or placebo. Yellow zone treatment lasts for 7 days. During this time, your child may use the albuterol rescue inhaler 2 puffs as needed.

If your child enters the yellow zone, he/she must STOP their open label (green zone) fluticasone and BEGIN the blinded yellow zone treatment. At the end of the 7 day yellow zone treatment, your child should restart their open label (green zone) fluticasone again. You should call the study coordinators within 72 hours (3 days) if your child starts yellow zone treatment.

The fluticasone 220 mcg/puff inhaler is FDA approved for use in children 12 years of age and above and in adults. It is considered experimental in this study of children between 5-11 years of age. The FDA is aware of this and has provided us permission to use fluticasone 220 mcg/puff inhalers in this study.

RED zone treatment: Prednisone is an oral steroid used to treat severe worsening of asthma. The dose will be calculated based on your child’s weight and will not be more than 60 mg a day. If red zone treatment is needed, your child will take one dose for 2 days and then a lower dose for 2 more days. It will never be fake or placebo. Red zone treatment follows what doctors normally do in their office. If you are concerned that your child is in the red zone, the signs of which will be described on the Action Plan, you should contact the study coordinators and a study doctor will decide whether your child should start prednisone. While in the red zone, your child may use the albuterol rescue inhaler 2 puffs as needed. For safety reasons, if your child needs red zone treatment too often, he/she may be asked to leave the study.

In brief summary:

- Your child will use fluticasone 44 mcg/puff 2 puffs twice a day as their **GREEN** zone daily inhaler.
- If your child enters the **YELLOW** zone, he/she must STOP the daily open label fluticasone inhaler and begin taking the yellow zone fluticasone treatment for 7 days.
- If your child enters the **RED** zone, you will need to contact the study center to determine if he/she should STOP the yellow zone fluticasone and begin taking prednisone for 4 days.
- It is possible that your child will never enter the yellow or red zone.
- Study location: All study procedures will be done at the UCSF pediatric clinical research center located at Parnassus, SFGH or Mission Bay.

PROCEDURES

Please see the study plan below for a list of procedures done at each visit. A description of each procedure follows:

Spirometry. Your child will wear a nose clip and will be asked to breathe out forcefully into a machine for 6 or more seconds. The machine measures how much air comes out of the lungs and how fast it comes out. Spirometry will be done at every visit.

- Spirometry takes effort and concentration. Your child must be able to do this procedure well in order to qualify for the study.
- Your child's spirometry values must be within a certain range at visit 1 and visit 2 to qualify for the study.

Maximum reversibility test. Spirometry will be done before and after 4 puffs of albuterol. The purpose of this test is to measure how much albuterol opens your child's airways. This test is done at Visit 1.

Methacholine challenge. Methacholine is a drug that can cause narrowing of the airways. Your child will be asked to breathe in gradually increasing doses of methacholine. Spirometry will be performed after each dose to measure any change in the airway. The test will stop once your child's airways narrow at least 20% or your child was given the highest dose of methacholine. This test might make your child feel like they are having a mild asthma attack. At the end of the challenge, your child will be given albuterol to reverse symptoms.

Exhaled nitric oxide (FeNO). Your child will be asked to gently blow into a small machine for a few seconds to measure exhaled nitric oxide. Exhaled nitric oxide is a possible measure of airway inflammation and might predict who does better on 1 treatment versus another.

Peak flow and E-diary. Your child will be asked to measure their peak flow daily by blowing into an electronic peak flow meter called a Spirotel®. The Spirotel® is also an electronic diary. You or your child must toggle through and answer questions about asthma symptoms and medication usage daily. Your child will be asked to take their fluticasone immediately after the peak flow measurements and diary questions. It may take 5-10 minutes daily to complete these tasks. The Spirotel® device must be returned at the end of the study.

- If peak flows, diary completion and fluticasone puffs are not done often enough, your child may be asked to leave the study.

Physical examination includes weight, height, and examining 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 asthma and what your child might be exposed to in the environment. You will be asked how asthma affects you and your child's life, and about household income and family education level. You will be asked to complete an anonymous study satisfaction questionnaire at your child's final visit.

A blood sample will be taken at visit 2. About 1.5 tablespoons (20 ml) of blood will be taken. The blood tests include cell counts, markers of inflammation and allergy. Your child will be asked to provide an optional blood sample for genetic testing. Optional genetic testing is described separately in this consent form.

A urine pregnancy test will be performed at visits 1 and 2 on every female who has begun menstruation (that is, has had at least one period). The pregnancy test is done to find out if the participant is eligible for the study. If the pregnancy test is positive, she will not be able to join the study.

A nasal mucus sample will be obtained to find out which respiratory germs are present. It will be collected by nose-blowing into a baggie. Your child's nasal mucus will be collected at visit 2 and at home with each yellow zone. We will teach you how to collect and store the mucus and give you all supplies.

PARTICIPATION RESPONSIBILITIES

You should try hard to keep appointments and phone calls. Please call the study coordinator if you must change your appointment 866-913-8477.

Your child will have tasks to do at home every day for the entire study. You and your child should understand the asthma action plan and take study medication as directed. ONLY the study participant may take the study medications. The study medications should be stored at room temperature. Keep the medication dry and away from direct sunlight. Keep the study medications out of the reach of people who cannot read or understand the labels on the medications. Study tools and medications (used and unused) should be brought with you to every study visit. <u>They should not be thrown away</u>.

Asthma attacks can be life threatening. If asthma symptoms worsen you should immediately call the study coordinator at 866-913-8477, not your primary care provider. If serious asthma symptoms develop contact the closest Emergency Department (ER) or Urgent Care immediately.

Study Plan

Specific tests and procedures performed at each visit are listed in the table below:

Week	0	4	12	20	28	36	44	52
Visit Number	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
Consent	X							
Medical History	X							
Full Physical Exam	X							
Brief Physical Exam		X	X	X	X	X	X	X
Questionnaires	X	X	X	X	X	X	X	X
Exhaled Nitric Oxide		X	X	X	X	X	X	X
Spirometry	X	X	X	X	X	X	X	X
Maximum Reversibility	X							
Methacholine Challenge		X						
Blood Test		X						
***Urine Pregnancy Test**	X	X						
****Nasal Mucus Sample**		X						
Review Action Plan	X	X	X	X	X	X	X	X
Review spirotel® Data		X	X	X	X	X	X	X

*Urine pregnancy testing will be asked of all females who have had their first period.

**We will ask you to obtain nasal mucus samples at home with each yellow zone episode.

Telephone calls will occur between visits.

How long will my child be in the study?

This study has 8 study visits and 6 study telephone calls over a year (52 weeks). More study visits or telephone calls may happen if your child's asthma worsens.

Can my child stop being in the study?

Yes. You or your child can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop your child's participation safely.

The study doctor or study sponsor may stop you from taking part in this study at any time if he/she believes it is in your child's best interest, if you do not follow the study rules, or if the study is stopped.

You will be told of any new and significant findings that may affect your willingness to continue in the study.

What side effects or risks can I expect from being in the study?

Your child may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen. Side effects may be mild or very serious. Your child's health care team may give him/her medicines to help lessen side effects. Many side effects go away soon after you stop taking *them.*

Please make sure that the study team knows about all of your child's drug allergies. Serious allergic reactions to the drugs used in this study are rare. If an allergic reaction occurs, 1) stop the drug immediately, 2) get emergency medical care, and 3) contact the study coordinator 866-913-8477. The most common risks side effects for the study medications and procedures are listed below.

You should talk to your child's study doctor about any side effects your child experiences while taking part in the study.

STUDY MEDICATIONS

Your child's asthma treatment might change when they join this study. It is possible that changing your child's asthma medication might worsen his/her asthma control.

FLUTICASONE PROPIONATE (FLOVENT): A concern for children is the possible effect of fluticasone on growth. It is possible that the fluticasone 220 mcg/puff yellow zone inhaler could have more effects on growth than the fluticasone 44 mcg/puff inhaler, even when used for short periods of time. This has not been studied before and is an important part of this study. Therefore, the growth of all children in the study will be carefully measured at each study visit. "Catch-up" growth after stopping fluticasone has not been fully studied.

Long-term use of steroid medications taken by mouth or inhaled like fluticasone can weaken the body's ability to handle stress from other medical conditions like infections. The risk is greater when the steroid doses are high and used for a long time. Although these side effects are not expected in STICS because your child will not be taking a high dose of steroids for a long period of time, there is no scientific evidence to confirm this.

Less Likely:

- Headache (11%)
- Throat irritation (8%)
- Sinusitis (6%)
- Upper respiratory inflammation (2%)
- Hoarseness (2%)
- Oral thrush (2%)

ALBUTEROL:

Likely:

- Faster heart beat

Less Likely:

- Shaky /nervous
- Sick to stomach
- Lightheaded
- Dizzy

Your child probably already uses albuterol so you may know how he/she responds to this medication.

PREDNISONE:

Likely:

- Increased appetite
- Fussiness / Restlessness
- Trouble sleeping / wakefulness

Less Likely:

- Sore throat
- Yeast infection of the mouth or throat
- Hoarseness

Rare but serious:

- Weakening or break down of hip bone
- Cataracts
- Diabetes
- Growth delay
- Weight gain
- Skin bruising

The side effects listed as rare but serious tend to occur with long-term use and are not expected in this study because, if prednisone is given, it will only be for 4 days at a time

and cannot be used for more than 2 courses in 6 months or 3 courses in 1 year in this study.

PROCEDURES

SPIROMETRY:

Breathing fast and hard into a spirometry machine or peak flow meter can cause side effects which should go away shortly after the test is finished.

Likely

- Coughing
- Lightheadedness
- Chest tightness

MAXIMUM REVERSIBILITY TEST:

Taking the 4 puffs of albuterol may cause the below side effects. These symptoms usually go away in less than an hour.

Less likely

- Fast heart rate
- Jittery feeling
- Increase in blood pressure
- Nausea
- Headache

METHACHOLINE CHALLENGE:

This test could cause the below side effects. Your child will receive albuterol at the end of this test to reverse any symptoms. In the unlikely event that your child's symptoms are severe, albuterol will be given immediately and the challenge will be stopped.

Likely

- Coughing
- Chest tightness
- Shortness of breath
- Wheezing

PREGNANCY TESTING: There are no known risks with performing the pregnancy test. There may be unknown risks to the fetus/unborn child if the study participant becomes pregnant while in this study.

QUESTIONNAIRES: Questionnaires are not tests. There are no 'right' or 'wrong' answers. You and your child may skip any question that makes you uncomfortable.

BLOOD SAMPLES:

Likely:

- Pain
- Bleeding or bruising

Less likely:

- Lightheadedness and fainting

Rare but serious:

- Infection

A LOCAL ANESTHETIC CREAM (a medicine to numb the skin): This may be placed 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.

Less Likely:

- Paleness
- Redness
- Changes in feeling heat and cold
- Swelling
- Itching
- Rash (rare)

MEDICAL HISTORY, PHYSICAL EXAMS, EXHALED NITRIC OXIDE AND NASAL MUCUS SAMPLES: There are no risks that go with these procedures.

Unknown Risks: The experimental treatments may have side effects that no one knows about yet. For more information about risks and side effects, ask your child's study doctor.

Randomization risks: Your child will be assigned to a treatment program by chance, and the treatment your child receives may prove to be less effective or to have more side effects than the other study treatment or other available treatments.

Are there benefits to taking part in the study?

Taking part in this study may or may not make your child's health better. While doctors hope the yellow zone treatments will prevent future red zone exacerbation there is no proof of this yet.

Your child will receive physical examinations and breathing tests at no cost during the study. Your child may benefit by receiving frequent asthma check-ups during the study. However, you and your child are not expected to benefit in the long-run from being in this study. This study may help other children in the future because we will learn more about yellow zone strategies to prevent asthma attacks.

What other choices do I have if I do not take part in this study?

There are many asthma treatments available today. Your child does not have to join this study to get treatment for his/her asthma. If you decide to let your child take part in this study, you must agree to use only the medications allowed while your child is in the study.

How will information about me be kept confidential?

Participation in research involves some loss of privacy. We will do our best to make sure that information about your child is kept confidential, but we cannot guarantee total privacy. Records will be coded and stored in locked spaces accessible only to research staff.
Some information from your child's medical records will be collected and used for this study. If your child does not have a UCSF medical record, one will be created for you. Your signed consent form and some of your child's research tests will be added to his/her UCSF medical record. Therefore, people involved with your future care and insurance may become aware of your child's participation and of any information added to your medical record as a result of your child's participation. Study tests that are performed by research labs, and information gathered directly from you or your child by the researchers will be part of your child's research records but will not be added to your child's medical record. Your child's personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your child's name and other personal information will not be used.

We may need to contact your child's personal doctor during the study to discuss study findings. We may also ask you to contact your child's personal doctor if your child is having medical problems that are unrelated to the study. You must provide us with the contact information for your child's personal doctor, so that we may contact them in the event of a medical emergency.

A Certificate of Confidentiality has been received from the Department of Health and Human Services. Once it is received, the Certificate prevents the investigator from being forced to disclose identifying information for use in court. The investigator may not be forced even 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.

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.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The University of California
- AsthmaNet Data Coordinating Center, Penn State University College of Medicine, Hershey, PA
- AsthmaNet Data and Safety Monitoring Board (DSMB)
- Study sponsor and/or its agents: AsthmaNet (other facilities and investigators involved with this study), NIH/NHLBI
- Food and Drug Administration (FDA)
- MedGraphics, St. Paul, MN (spirometry data; also will house data from spirotel e-diary/PEF meter)
- Medical International Research Inc. (MIR), Waukesha, WI and Rome, Italy (makers of spirotel e-diary/PEF meter device)
- Respitech Medical, Inc., Lancaster, PA (servicing of spirotel devices)
- Aerocrine Inc, Morrisville, NC (maker of NIOX MINO for FeNO testing)
- Spirometry overreader, Madison, WI (Rick Kelley, who serves as our grader)
- ADx Labs, National Jewish Health, Denver CO (ImmunoCAP analysis)
- Tucson Genetics of Asthma Lab, University of Arizona, Tucson, AZ (genetics lab; storing DNA and plasma)
- University of WI – Madison Lab, Madison, WI (nasal sample lab)
- Microbiology Lab, Washington University – St. Louis, MO (nasal sample lab)
- Ding Lab, The Genome Institute, St. Louis, MO (nasal sample lab)
- GlaxoSmithKline (provider of fluticasone and albuterol)
- Other labs contracting with AsthmaNet for analysis of blood, urine or other biological specimens (e.g., local labs)
- Other people or organizations assisting with AsthmaNet research efforts (this may include drug manufacturers, packagers/distributors, and/or their designees)

What are the costs of taking part in this study?

You will not be charged for any of the study activities. All study tests, medications, visits and phone calls are provided without cost. If your child receives health care outside of study visits, you or your insurance company will be responsible to pay the bill. This includes physician, ER or Urgent Care visits or hospitalizations.

Will I be paid for taking part in this study?

In return for your time, effort and travel expenses, you and your child will receive a total of $600 if your child completes every visit and phone call during the study. If you or your child quits before the last visit, your payment will be prorated. That means you get payment only for visits and phone calls that have been completed. If you receive more than $599 in a calendar year for study participation, UCSF must follow IRS guidelines and report this income to the IRS. UCSF may issue you a 1099 form. We will ask that you provide your social security number for this purpose. You will be responsible for reporting this compensation when you file your tax return. Non-monetary incentives such as toys may be given to children at study visits.

$80 for completion of the first visit
$100 for completion of the randomization visit (visit 2)
$25 for completion of visits 3, 4, 5, 6, 7, 8
$25 for bringing the electronic diary and study medications to visits 3, 4, 5, 6, 7, 8
$20 for completion of each of 6 phone calls

What happens if my child is injured as a result of taking part in this study?

It is important that you tell your study doctor, Michael Cabana, MD, MPH or Ngoc Ly, MD, MPH, if you feel that your child has been injured because of taking part in this study. You can tell the doctor in person or call him/her at 866-913-8744.

Treatment and Compensation for Injury: If your child is injured as a result of being in this study, the University of California will provide necessary medical treatment. The costs of the treatment may be billed to you or your child's insurer just like any other medical costs, or covered by the University of California, depending on a number of factors. The University and the study sponsor do not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Committee on Human Research at 415- 476-1814.

What are my rights if my child takes part in this study?

Taking part in this study is your choice. You may choose either to have your child take part or not to take part in the study. If you decide to have your child take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and your child will not lose any of his/her regular benefits. Leaving the study will not affect your child's medical care. Your child can still get medical care from our institution.

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 hurt your child or if the study outcome is found out early.

We will tell you about new information or changes in the study that may affect your child's health or your willingness to have them continue in the study.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

Who can answer my questions about the study?

You can talk to your study doctor about any questions, concerns, or complaints you have about this study. Contact your child's study doctor(s) Michael Cabana, MD, MPH or Ngoc Ly, MD, MPH at 866-913-8477.

If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers or if you wish to voice any problems or concerns you may have about the study, please call the Office of the Committee on Human Research at 415-476-1814.

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.

GENETIC BLOOD DRAW AND TESTING SECTION (OPTIONAL)

WHAT IS THE PURPOSE OF GENETIC TESTING?

Your child is 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, 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 AsthmaNet Steering Committee.

Your child can still take part in this 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 (two teaspoons) of blood from a vein in your child's arm. DNA will be removed from their 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 AsthmaNet 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 AsthmaNet 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 study investigators at your site and in the AsthmaNet and by other NIH/NHLBI research centers/investigators with whom the AsthmaNet 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, AsthmaNet 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 AsthmaNet 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 AsthmaNet 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 this 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 Michael Cabana, MD, MPH in writing.

RISKS AND DISCOMFORTS RELATED TO GENETIC TESTING:

Blood Draw. If possible, the genetic blood sample will be taken when other blood samples are needed for the study so that your child will not have to undergo an extra needle stick. 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 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. However, this law does not protect you against 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 (DNA) with AsthmaNet 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 AsthmaNet Steering Committee)?

(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 AsthmaNet Steering Committee and the local Human Subjects' Protection Board)?

(Please initial) YES_____ NO_____

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

(Please initial) YES_____ NO_____

CONSENT

Request Permission for Future Contact

1. May we contact you for future studies conducted by UCSF or AsthmaNet? If yes, we may need to look at your child's Protected Health Information (PHI) to check for study eligibility.	___ Yes	___ No
2. May other UCSF physicians conducting asthma research contact you? If yes, your child's PHI may be shared with those physicians.	___ Yes	___ No

Taking part in future studies is optional. If you agree to being contacted, you may still refuse joining those future studies. Also, you can ask us at any time to take your child's name off of our contact list.

You have been given copies of this consent form and the Experimental Subject's Bill of Rights to keep.

You will be asked to sign a separate form authorizing access, use, creation, or disclosure of health information about you.

PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right to decline to participate or to withdraw at any point in this study without penalty or loss of benefits to which your child is otherwise entitled.

If you wish to have your child participate in this study, you should sign below.

_____
Print Child's Name

_____
Print Relationship to Child

Date	Parent or Legal Guardian
Date	Parent or Legal Guardian
Date	Legally Authorized Representative
Date	Person Obtaining Consent