Children's Hospital of Pittsburgh

3705 Fifth Avenue
Pittsburgh, PA 15213-2583
www.chp.edu

CONSENT FOR A CHILD TO BE A SUBJECT IN MEDICAL RESEARCH AND AUTHORIZATION TO PERMIT THE USE AND SHARING OF IDENTIFIABLE MEDICAL INFORMATION FOR RESEARCH PURPOSES

**TITLE:** A Randomized, Double-Blind, Placebo-Controlled Trial of Antimicrobial Prophylaxis in Children with Vesicoureteral Reflux and Urinary Tract Infection

**Principal Investigator:** Alejandro Hoberman, MD (412) 692-5249

**Other Investigators:**

Nader Shaikh, MD (412) 692-8111
Sonika Bhatnagar, MD (412) 692-6682
Diana Kearney, RN CCRC (412) 692-6717
MaryAnn Haralam, CRNP (412) 692-8582
Carly Jenkins, RN, BSN (412) 692-7381
Marcia Pope, RN (412) 692-7381
Linette Milkovich, RN (412) 692-7381
Emma Hooper, BA (412) 692-7381
**Children's Hospital of Pittsburgh**
**Division of General Academic Pediatrics**
**Children's Hospital of Pittsburgh**
3705 Fifth Avenue
Pittsburgh, Pennsylvania, 15213-2583

Tracy Balentine, RN (724) 543-4597
Thomas Lynch, MD (724) 543-4597
**CCP Armstrong Pediatrics**
**Children's Community Pediatrics**
100 Medical Arts Building
Kittanning, PA 16201

Annette Seelhorst, RN (412) 680-2378
**The Children's Pine Center - Wexford**
11279 Perry Highway, 110
Wexford, PA 15090

Kristy Mackin, RN, BSN (412) 232-7751
**Primary Care Center – UPMC Mercy Health Center**
1515 Locust Street, Floor 3 Ambulatory Pediatrics
Pittsburgh, PA 15219

***Evening/Week-end Coverage: 412-999-3277 (999-EARS)***



University Of Pittsburgh Institutional Review Board
Approval Date: 2/1/2010
Renewal Date: 6/16/2010
IRB #: IRB0609070

**SOURCE OF SUPPORT**: National Institutes of Health

***What is this study about and why is it being done?***

You are being asked to volunteer your child for a research study because your child has had a urinary tract infection (UTI) and also has a condition called VUR (vesicoureteral reflux), a condition where urine from the bladder flows back toward the kidney. Please read this form carefully. As the research study staff discusses this informed consent form with you, please ask them to explain any words or information that you may not clearly understand.

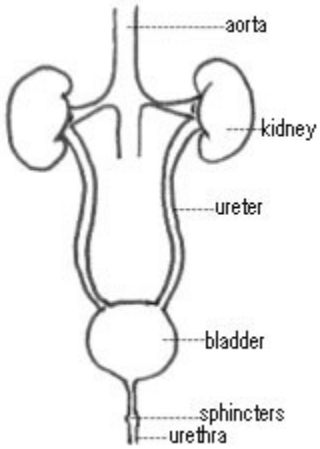
This research study will allow our medical team the chance to improve the care that they give to children with VUR. Taking part in this research study is entirely your choice. Your child will receive medical care for his/her VUR whether you allow your child to be in this study or not.

Our staff will explain how the study will be carried out and what you and your child will be expected to do. This form describes the importance of the study as well as the benefits and risks of taking part in the study. Our staff will answer your questions about the study. If you decide to volunteer your child to be in the study, please sign and date this form.

***What is my child's health condition?***

Your child had a urinary tract infection (UTI) and has also been diagnosed with vesicoureteral reflux. Normally, urine flows from the kidneys down the ureters into the bladder. Vesicoureteral reflux (VUR) means urine moves back (reflux) from the bladder (vesico) up the ureters (uretero) into the kidney. We are studying whether or not children with VUR need to take an antibiotic everyday to prevent more urinary tract infections from occurring.

***What is the urinary tract and how does it work?***




The Urinary System is made up of two kidneys, the bladder and two ureters. The kidneys remove waste from the body by making urine. The urine flows from the kidneys down through the ureters (tubes) to the bladder (balloon-shaped pouch). The ureters have a one-way valve that should only allow urine to flow down into the bladder.

***What is VUR and when do we worry about VUR?***

VUR happens when the valve where the ureter meets the bladder is not working properly. This allows urine to flow back up to the kidney after it has already been in the bladder. This backflow of urine is a problem if germs enter the bladder and infect the urine. VUR can then allow germs in the infected urine to flow backward up to the kidney and cause a kidney infection. Children can have kidney scarring (damage) after the infection. Kidney damage may lead to high blood pressure or kidney failure or to high blood pressure during pregnancy (pre-eclampsia).

***How is VUR usually treated?***

Children with VUR take a low dose of antibiotic once a day to prevent UTIs. A low daily dose of antibiotic to prevent infection is called prophylactic antibiotic treatment. This use of an antibiotic does not stop the backflow of urine. Daily antibiotic treatment prevents children from getting a urinary tract infection by killing germs in the infected urine that backflows toward the kidney. Preventing UTIs may prevent kidney damage. Children with VUR are usually treated with a daily antibiotic until the VUR disappears. VUR often disappears as children get older, but it may take from one to more than five years. Sometimes it never disappears. Some children have surgery to fix the VUR when it does not go away as the children grow.

***What is the purpose of this study?***

The purpose of this study is to learn whether or not all children with VUR should be treated with daily antibiotics. The study will tell us if daily antibiotic treatment will prevent urinary tract infections in children with VUR and will give more information on daily antibiotic use and kidney scarring. New research suggests that if a child with VUR has close follow-up with his/her doctor for every illness with fever, a UTI can be treated early with antibiotics and kidney scarring can be prevented without the use of an antibiotic everyday. Kidney scarring can cause high blood pressure, kidney failure or high blood pressure during pregnancy (pre-eclampsia). By doing this study, we hope to find if (1) careful follow-up of every illness with fever OR (2) treatment with daily low-dose antibiotic is better for children with VUR.

A second thing that we would like to learn about the use of daily antibiotics is whether or not this practice will result in the bacteria that naturally appear in some children becoming resistant to the antibiotic that they receive. Many children carry bacteria such as Escherichia coli (E. coli), Streptococcus pneumoniae (S. pneumoniae) or Staphylococcus aureus (Staph aureus) on their bodies without any evidence of infection. Although children who have these germs are not usually sick, under certain circumstances these bacteria may lead to an infection. If the use of daily antibiotics leads to the development of antibiotic resistance (where antibiotics no longer kill the bacteria) in these germs, infections caused by these bacteria could be harder to treat. It is important to know whether or not this happens. This can be done by obtaining samples of stool and mucous from the front and back of the nose while children are receiving daily antibiotics. We will look for bacteria and test for antibiotic resistance in the laboratory.

This study will include children from across the United States and Canada. About 600 children, ages of 2–72 months, will take part in this study. Our goal at Children's Hospital of Pittsburgh is to enroll 150 children. The staff is being reimbursed from the National Institutes of Health to do this study.

***What are my child and I being asked to do?***

You are being asked to volunteer your child for a research study. Taking part in this research study is your choice. Your child does not need to be in this study. Your child may leave this research study at any time. There will be no penalty or loss of health care benefits if your child is not in the study or drops out. This form will help you understand what we think is hurting your child's health, and what we will ask you and your child to do in this study. This form tells you what will happen in the research study. This form also tells you about the risks, discomforts, and other information about the research study. Medical language may be hard to understand. If there is anything which you do not understand, please ask questions.

This is a double-blind, randomized study. Randomization means that a computer will choose what your child will receive. Your child will have a 50% chance of receiving either: 1) Prophylactic (daily) antibiotic; or 2) placebo (no active medication). There is an equal chance of getting either one. The placebo will look and taste exactly like the prophylactic antibiotic. Neither you nor your child's doctor will know if your child will be given daily antibiotic or placebo. Your child's doctor will be able to get the information about what your child is receiving in case of emergency.

The study nurse will show you how to give your child the study medication or placebo. The study medication or placebo will be liquid. The study nurse will show you how to measure the liquid medication/placebo with a dosing syringe and give it to your child. You will give a dose of the medication/placebo once every day until the end of the study.

Trimethoprim-sulfamethoxazole (TMP/SMZ) will be used as the daily antibiotic. TMP/SMZ is approved by the FDA for use in children for the treatment of urinary tract infection. If your child is allergic to TMP/SMZ (or any medication that contains sulfa), then your child cannot be in this study. If your child develops an allergy to TMP/SMZ or the placebo for TMP/SMZ during the study, then your child can remain in the study but will stop study medication and be treated according to standard care practices for UTI and VUR.

During the study, we will collect specimens to look at whether or not the bacteria that live there are resistant to the antibiotic TMP/SMZ. These specimens will consist of a small amount of stool and a sample of mucous from the front and back of the nose.

This study may last for up to 2 years. If you decide to have your child join the study, we will ask you to come to the Children's Hospital Primary Care Center for the enrollment visit. If it is more convenient for you, follow-up visits may be completed at CCP Armstrong Pediatrics, The Children's Pine Center in Wexford, or the Primary Care Center at UPMC Mercy Health Center.

**First Visit (today):**

This visit will help to find out if your child can be in this study. If you want your child to be in the study, you will be asked to sign this consent form. Your child will have a physical exam. We will ask questions about your child's health and any medical problems and ask you to fill out a short questionnaire. We will also collect from your child a small stool sample (using a small swab), a sample of mucous from the front and back of the nose, a sample of blood (about 1 teaspoon), and a urine sample. At the end of the visit, you will be given study medication (it may be antibiotic or placebo) that your child will take daily until the end of the study.

**Follow-up Visits (6, 12, and 18 Month Visits):**

Your child will have a physical exam and we will ask you about any medical problems that have happened since the last visit. You will be given more study medicine and your empty or used bottles of study medicine will be collected. At each visit, we will collect a small sample of blood (about 1 teaspoon), a sample of mucous from the front and back of the nose, a small stool sample (using a small swab), and a urine sample. You may also be asked to fill out a short questionnaire about your child's health and wellbeing. At the 12-month visit, your child will be scheduled to have a repeat DMSA scan to look for kidney scarring since the first DMSA scan.

**End of Study Visit (24 Month Visit):**

Your child will have a physical exam and we will ask you questions about any medical problems that have happened since the earlier study visits. At this visit, we will also collect from your child a small stool sample (using a small swab), a sample of mucous from the front and back of the nose, a sample of blood (about 1 teaspoon), and a urine sample. The VCUG and DMSA scans done at the beginning of the study will be repeated or scheduled at this visit.

A voiding cystourethrogram (VCUG) is a test that can diagnose reflux. VCUGs are common tests done when children have VUR and are part of routine care. This test uses a catheter (tube) that is placed into the child's bladder. The catheter is used to fill the bladder with X-ray dye or radioactive material. An x-ray is used to watch the dye move while the child urinates, and if the dye moves toward the kidneys rather that towards the bladder, the diagnosis of reflux is made. This x-ray will take about 30-60 minutes. It is important for your child to remain as still as possible.

A dimercaptosuccinic acid (DMSA) scan is a test that can look at the shape of the kidneys and evaluate how much scarring is present. A DMSA scan is a common test done when children have VUR and is part of routine care. Your child will have a small amount technetium-99m (a radioactive chemical), injected into a vein of the arm or hand. After the injection, you will be able to leave the radiology department and then return in approximately 3-4 hours after the injection. This delay will allow the kidneys to absorb the radioactive chemical. When you return, we will ask your child to urinate and then we can start the imaging. The imaging will take about 30-60 minutes. It is important for your child to remain as still as possible.

**Phone calls:** We will call you every 2 months during the study to find out how your child is doing. We will ask questions about the study medicine and about any medical problems that have happened since we last talked with you.

**Special procedures for children with moderate scarring on the first DMSA scan:** If your child's first DMSA scan shows moderate kidney scarring, then your child will have a DMSA scan if your child has a UTI that causes a fever. If any DMSA scan shows worsening of the kidney scarring, then your child will be taken off the study medication and be treated with a daily antibiotic given by your doctor. Your doctor may discuss the option of surgical repair of the VUR. We would want your child to stay in the study even though his/her treatment has changed. We will still continue the study visits and phone calls.

**Special procedures for children with recurrent UTIs:** If your child has 2 UTIs with fever during any 12 month period or 4 UTIs with or without fever during the entire study, then your child will be taken off the study medication and be treated with a daily antibiotic given by your doctor. Your doctor may discuss the option of surgical repair of the VUR. We would want your child to stay in the study even though his/her treatment will have changed. We will continue the study visits and phone calls, and will schedule your child for a DMSA scan 4 months after he/she stops receiving the study medication.

**Special procedures for children with new or worsening scarring on the 12-month DMSA scan:** If the 12-month DMSA scan shows a new kidney scar or worsening of a kidney scar, then your child will be taken off the study medication and be treated through routine clinical care, for

example, with a prophylactic antibiotic that may be prescribed by your child's doctor. Your child's doctor may discuss the possibility of surgery for the VUR. Your child's continued participation in the study will still be important to us even though his/her treatment will have changed. We will still continue the study clinic visits and phone calls.

**Release of additional medical information:** We will ask you to sign a Release of Medical Information form so that we can find out about any medical problems, particularly as they may relate to any urinary tract infections, for which your child has received care from doctors other than those at Children's Hospital of Pittsburgh. We will also ask you to allow us to contact a family member or other individual you've identified if CHP staff is unable to make contact with you during the study. We will ask for permission to release medical information to your child's physician regarding your child's care in the study.

***Will my child's primary care doctor be notified about his/her participation in this study?***

Your primary care doctor will be told that your child is in this study. We will send your child's primary care doctor reminders that your child is in this study. We are doing this so your child's primary care doctor knows how to treat your child if he/she gets a UTI.

***What are the risks of being in this research study?***

Potential risks to your child while being in the study are described below. You can discuss these with Dr. Hoberman and our study staff and/or your child's regular doctor.

**Trimethoprim/Sulfamethoxazole:** The study medication (TMP/SMX) is commonly used in the treatment and prevention of UTI, and has a record of safety in children. TMP/SMX is approved by the FDA for the treatment of urinary tract infection in children. However, patients may have side effects to antibiotics. Antibiotics may cause common (10-25 out of 100 children) side effects such as skin rash, nausea and vomiting. Other side effects include sun sensitivity, vaginal irritation, low white blood cell count, and dizziness. Allergic reactions, including hives, joint pain and shock can rarely (1 out of 100 children) happen with TMP/SMX just like with any other antibiotic, although severe reactions are extremely rare. TMP/SMX can also (rarely, 1 out of 100 children), cause Stevens Johnson syndrome, a very serious skin rash. Many side effects go away soon after the drugs are stopped. In some cases, side effects can be serious, long lasting or permanent. There also may be other side effects that we don't know about yet. There is a chance that daily treatment with an antibiotic, may lead to the development of UTIs with resistant bacteria. Having a resistant bacteria means that something has changed about the germ so that it is not killed by the antibiotic. This may require treatment with intravenous (IV) antibiotics for some infections.

**Placebo**: There is no active medicine in the placebo. The same flavoring and coloring and powder mixers used in the regular TMP/SMX are in the placebo (to make it look and taste like the real medicine). A child could rarely (less than 1 out of 100) be allergic to one of these powders. There is also a chance that daily antibiotic use protects children against recurrence of UTI and kidney scarring, and then children in the placebo group will be exposed to a higher risk of UTI and kidney scarring. Kidney scarring can cause high blood pressure, kidney failure or high blood pressure during pregnancy (pre-eclampsia).

**Blood Drawing:** Risks of drawing blood from your child's arm are discomfort (likely about 25 out of 100) and/or bruising (infrequently, 1-10 out of 100). Infection and excess bleeding are possible, but rare (less than 1 out of 100). Lightheadedness and inflammation at the site of injection are rare (less than 1 out of 100). Localized clot formation may occur, but this is rare (less than 1 out of 100). Fainting may occur infrequently (1-10 out of 100), during or shortly after having blood drawn.

**Voiding Cystourethrogram (VCUG):** A voiding cystourethrogram (VCUG) is a video x-ray of the bladder and lower urinary tract. A VCUG involves inserting a catheter through the urethra and filling the bladder with a special liquid, both of which can commonly (10-25 out of 100) be uncomfortable for children. A series of X-rays are taken as the special liquid is urinated from the bladder. The radiation exposure from a VCUG is similar to the natural background radiation during one year.

**DMSA scans:** A DMSA kidney scan is used to show areas of kidney infection or kidney damage. A DMSA scan requires inserting an intravenous (IV), injecting a radioactive substance into the blood stream, and taking a pictures of the kidney with a special camera. Commonly (10-25 out of 100), children may have some discomfort with the placement of the IV. IVs can fall out and some fluid can go into the arm outside of the vein, but this is rare (1 out of 100). The radiation exposure from a DMSA scan is les than half of the natural background radiation during one year.

Participation in this research study involves exposure to radiation from a DMSA scan. The amount of radiation exposure that your child will receive from this procedure is approximately 0.14 rem (a unit of radiation exposure) to your child's kidneys, with minimal exposure of other body areas. For comparison, radiation workers are permitted, by federal regulation, a maximum annual radiation exposure of 20 rems to the most sensitive organs of their body. There is no known minimum level of radiation exposure that is recognized as being totally free of the risk of causing genetic defects (abnormal cells) or cancer. However, the risk associated with the amount of radiation exposure that your child will receive from this study is considered to be low and comparable to everyday risks.

**Storage of Blood and Urine for Research Purposes:** Rarely (less than 1 out of 100), there is a risk of loss of confidentiality. To minimize the risk of loss of confidentiality, before your child's sample is sent, the sample will be labeled with the study identification number only. Personal identifying information such as name, address, and date of birth will be removed from the sample. Personal information that could link the sample to your child's identity will be kept in locked cabinets and password-protected computers that are only used by study staff.

**Peri-Rectal Swab:** The area around the anus will be wiped with a small swab or a small sample of stool will be collected from a soiled diaper. This can commonly (10-25 out of 100) cause some minor discomfort.

**Nose Swab**: A swab of mucous from the front and back of the nose to test for bacteria in your child's nose will be done. This can commonly (10-25%) cause minor discomfort and gagging.

**Confidentiality:** Rarely (less than 1 out of 100), there is a risk of loss of confidentiality. In order to minimize the risk of loss of confidentiality, all records related to study data will be kept in

locked cabinets, and access to this information will be restricted. A password system (like an electronic lock) will be used to control access to all information stored on a computer. All reports or articles based on this study will be prepared such that no individual patient can be identified.

***What if problems occur during this study?***

Your child's health is more important than following the research plan. If any changes are needed to protect your child's health, we will talk with you about them before they are made. We will also tell you if a better treatment is discovered somewhere else. If you want this treatment, your child's doctor can provide this in place of or in addition to the treatment your child is receiving at the time.

The researchers have taken steps to minimize the known or expected risks. However, your child may still have problems or side effects. It is important that you tell our staff about any injuries, side effects, or other problems that your child has during this study. You will have our phone number to call at any time 412-692-3277. This is a 24 hour cell phone to either Dr. Hoberman or the other study staff.

A Data Safety and Monitoring Board, an independent group of experts, will be looking at the data from this research throughout the study to provide further safety and ethical assurances.

We will inform you of new information from this or other studies that may affect your child's health, welfare, or your willingness to stay in this study.

You can withdraw your child from this study at any time, without penalty. The researchers also have the right to stop your child's participation at any time. This could be because your child has had an unexpected reaction, or you have failed to follow instructions, or because the entire study has been stopped.

If you withdraw your child or are withdrawn from the study early, you may be asked to come in for one more clinic visit. This visit will allow your study doctor to collect final (outcome) data about your child. Your child will have a physical exam. We will ask you questions about your child's health and any medical problems that have happened since the earlier study visits. At this visit, we will also collect from your child a small stool sample from a rectal swab, a sample of mucous from the front and back of the nose, a sample of blood (about a teaspoon) and a urine sample. Radiographic VCUG and DMSA imaging performed at the beginning of the study may be repeated or scheduled at this visit.

***What are the possible benefits of my child being in this study?***

There is no guarantee that your child will get any direct benefit from being in this study. The information that is collected will be useful scientifically and possibly helpful to others. We hope that this study may benefit society by showing which of these two methods is better for children with VUR, but this is not guaranteed.

The testing in this study will provide information about your child's disease that may benefit your child. For example, the DMSA scan could allow early discovery of kidney scars. This would alert the doctors to closely monitor your child so that the risk of new scars might be less. The blood and urine tests may also provide early information about kidney damage.

**Placebo:** Children in the placebo group may be less likely to become infected with resistant germs that would require treatment with intravenous (IV) antibiotics. Children in this group will not develop the allergies or side effects caused by daily antibiotic use.

**Trimethoprim/Sulfamethoxazole:** If daily antibiotic use protects children from UTI and kidney scarring, then children in the antibiotic group may have fewer UTIs and less risk of kidney scarring.

***Will I or my insurance provider be charged for the costs of any procedures performed as part of this research study?***

While your child is in the study, you will not be charged for the study medication, the physical examinations, blood tests, stool tests, nasal swabs, or the DMSA kidney scan. If the doctor suspects that your child has a new urinary tract infection, the urine tests and the medication to treat the infection will be billed to you or your insurance company in the standard manner. All costs not paid by your insurance will be your responsibility. Please ask about any expected added costs or insurance problems.

***Will my child or I be paid for taking part in this research study?***

To help cover any expenses such as transportation or time off from work, you will be given $50 today at the first visit and $25 at the 6, 12, and 18 month visits. There will be an additional $25 given at the 24 month visit, if you bring your child to all follow up visits. If you park in our parking lot, you will receive free parking.

***May I refuse to give my OK for the use of my child's medical information for the purpose of this research study?***

Your OK to use and share your child's medical information for the purpose of this research study is completely up to you. However, if you do not provide your OK, your child will not be allowed to be in this study.

***What alternatives are available to my child if I don't give my OK for him/her to participate in this study?***

Children with VUR are usually treated with daily antibiotics to prevent infections. If you choose not to enroll in the study, your child's doctor may use daily antibiotics to decrease the risk of your child having a UTI. For certain children, surgery may be an alternative treatment. Participation in this study is entirely up to you. Choosing not to participate in this study will not affect you or your child's present or future relationship with the Children's Hospital of Pittsburgh or any affiliated health care provider of the University of Pittsburgh.

***Consent for Storing Blood, Tissue, or Body Fluid for research purposes***

**Biological Sample**: During the blood and urine specimen collection at the first visit and the 24 month visits, we would like to collect another small amount of blood and urine to send to the National Institutes of Diabetes and Digestive and Kidney Diseases (NIDDK), of the National Institutes of Health (NIH) Central Repository. The purpose of this collection is to provide samples for future research of VUR and UTIs. Collecting samples for a repository is also called specimen banking. Sending samples to the Repository may give scientists valuable research material that can help them to develop new diagnostic tests, new treatments, and new ways to

prevent disease. The amount of extra blood will be about 1-2 teaspoons at each visit that the specimens are drawn for the Repository, depending upon your child's age.

The Repository will take measures to protect your privacy, although no guarantee of confidentiality can be absolute. Before your child's sample is sent to the Repository, the sample will be labeled with the study identification number. Personal identifying information such as name, address, and date of birth will be removed. The Repository will have some data about your child such as age, sex, race, and diagnosis. You will not be given any information, nor will any appear in your child's medical record, as to how these samples are used.

You will not get any direct benefit or payment for letting us draw the extra blood, but your child's sample may benefit other people with VUR. It is possible that data from the use of your child's sample may be used in a research publication. If that happens, your child's name and other personal information will not be included.

There is no cost to you or your insurance company for the storage and use of the specimens. Your child's donation does not entitle you or your child to compensation from any commercial use of the products that may be come from the specimen. You and your child will not be informed about future use or results. Your child's donation is voluntary, and if you choose not to have your child be in this part of the study, your child can still be in the rest of the study. Your child will need to sign a new consent form at age 18 for the continued use of their research specimens.

If you agree to have your child's sample stored in the Repository, you can change your mind up until the end of the study. All that is needed is an instruction from you to the study researchers and they will destroy your child's sample and all information that identifies your child. Once the study is over, the sample will stay in the Repository indefinitely.

Any tissue, blood, cell, or other biologic samples that your child provides as a participant in this research study are donations of these samples to the NIH. You and your child will not have any property rights to the samples, nor will you or your child have any property rights to or be entitled to compensation of any type for any products, data, or other items or information that is developed from the samples. If you would like your sample to be destroyed you can contact Dr. Alejandro Hoberman at 412-692-7382.

Consent for blood specimen banking (Only for children over 20 pounds):

Yes Initials _____

No Initials _____

Consent for urine specimen banking:

Yes Initials _____

No Initials _____

**Genetic Sample**: Also during the first visit, we would like to collect another small amount of blood that will be sent to the NIDDK Genetic Repository at Rutgers University. The amount of extra blood will be about 1-2 teaspoons depending on your child's age. The same standards and guidelines outlined above for the Biological Samples apply to the Genetic Samples. Scientists

will look at DNA (heredity material in cells) of the blood to help them develop new diagnostic tests, new treatments, and new ways to understand diseases. The genetic sample will only be used for research on UTIs and VUR. Banked samples will be identified by a code number. You will not be informed of the results of future genetic testing of this sample because at this time we don't know how this information would be helpful. The DNA that your child provides as a participant in this research study is a donation to the NIH. You and your child will not have any property rights to the samples, nor will you and your child have any property rights to or be entitled to compensation of any type for any products, data, or other items or information that is developed from the samples. If you would like your child's sample to be destroyed, you can contact Dr. Alejandro Hoberman at 412-692-7381.

Consent for genetic sample banking:

Yes Initials _____

No Initials _____

***Consent for Collecting Additional Laboratory Samples***

In order to check the quality of laboratory results, we would like to send matching samples of blood, urine and stool from approximately 10 children. The extra sample of ¼ of a teaspoon to 1 teaspoon of blood would be obtained at the same time as the study sample and only from children whose weight is over 20 pounds. The urine will only be sent if there is enough urine after the regular study sample is measured. The stool sample would be obtained by a second rectal swab.

Blood Sample: Yes Initials _____

No Initials _____

Urine Sample: Yes Initials _____

No Initials _____

Stool Sample: Yes Initials _____

No Initials _____

***What if my child's doctor is one of the investigators for this research study?***

If your child's doctor is an investigator in this research study, he/she will be interested both in your child's medical care and in this research. Before putting your child in this study or at any time during the study you may discuss your child's care with another doctor at CHP, a doctor who isn't at CHP or your child's pediatrician or family doctor who is in no way associated with this research project. It is entirely up to you whether to let your child be in any research study offered by your child's doctor.

***Do any of the investigators on this study have any other conflicts of interest?***

This study is supported by the National Institutes of Health. Investigators in the study do not

receive individual compensation from your child's participation in this trial.

***What if there is new information while my child is in this study?***

If any information is learned that might affect your willingness to have your child continue to be in this study, you will be informed.

***How will my child's privacy rights be protected?***

Under the Health Insurance Portability and Accountability Act (HIPAA), your child's private health care information cannot be used for the research purposes of this study without your OK. You will be informed of the specific uses and disclosures of your child's medical information for the purpose of this research study and who will have access to your child's health information.

***What uses of my child's medical information will this research involve?***

This research study will involve the recording of existing medical information as well as medical information that will become available while your child participates in this study from your child's hospital and/or physician records. From this material, case report forms will be prepared so that your child's medical information, such as prior treatments, medical history and diagnosis can be compared to that of other children participating in this research. These forms will be analyzed by the investigators; the information on the form will not contain any information identifying your child. The research information will be shared, now and in the future, with other doctors who are studying UTI or reflux. If the results of this study are published, information concerning your child will be in a form such that he/she cannot be identified.

During your child's participation in this clinical study, the study staff will collect your child's age, gender (male or female), medical history and information on the health and ethnic origin of your child. This information will be reported to the NIH, Data Coordinating Center at the University of North Carolina. We will store and process the information about your child using a computer. Your child's personal identity (name, address, and other identifiers) will remain confidential. In the database, your child will only be referred to by a code number and initials. Only the study staff will be able to link the code number to your child's name. The NIH, the Children's Hospital Institutional Review Board or regulatory authorities may directly access your child's medical records in order to determine the accuracy of the reported data. These representatives will observe professional secrecy and keep your child's identity confidential to the extent permitted by law.

***Will participation in this research result in medical information being placed in my child's medical records?***

Your child's participation in this study may result in health information being placed in the Children's Hospital of Pittsburgh medical chart, electronic medical record, outpatient chart, or research record, regarding the usual tests that would be useful for your child's doctor to know. Information from the genetic testing will not be placed in your child's medical chart.

***Who will have access to my child's medical information related to his/her participation in this research study?***

In general, research records are kept confidential. Paper records are stored in locked cabinets and computerized records are password protected. There are, however, some disclosures of your

child's research-related medical information that may occur. In addition to the investigators listed on the first page of this authorization form and their research staff, the following persons may have access to your child's identifiable private health information related to your child's participation in this research study.

- Authorized representatives of the University of Pittsburgh Research Conduct and Compliance Office may review your identifiable research information (which may include your child's identifiable medical information) for the purpose of monitoring the appropriate conduct of this research study. In unusual cases, the investigators may be required to release identifiable information (which may include your child's identifiable medical information) related to your child's participation in this research study in response to an order from a court of law. If the investigators learn that you or someone with whom you are involved is in serious danger or potential harm, they will need to inform, as required by Pennsylvania law, the appropriate agencies.
- Authorized representatives of the NIH, including the Data Coordinating Center team at the University of North Carolina, the Office for Human Research Protections (OHRP) and the Food and Drug Administration (FDA) may review and/or obtain your child's identifiable medical information for the purpose of monitoring the accuracy and completeness of the research data, for performing required scientific analyses of the research data, and reanalysis of the research data at a later date and to be sure that the research is being conducted according to the guidelines of each institution. While these organizations have provided their assurance that they will not release your child's identifiable medical information to anyone else, the Children's Hospital of Pittsburgh cannot guarantee this. In unusual cases, the investigators may be required to release your child's research information in response to a court order.
- Research investigators may be required under Pennsylvania law to report any suspicion of child abuse to child protection services. If the investigators learn that you or someone with whom you are involved is in serious danger of potential severe harm, they may need to warn those who are in danger and contact other agencies to ensure safety.

***May I have access to my child's medical information resulting from participation in this research study?***

In accordance with the Children's Hospital of Pittsburgh's Notice of Privacy Practices document which you have been provided, you are allowed to look at information (including information resulting from your child's participation in this research study) contained within your child's medical records unless specifically stated. In this study, the researcher or you will not know which medicine your child is taking (active or dummy medication). After the study is finished and the results have been studied, we will send you a letter that tells you which medication your child received.

***Can I stop my child's participation in this study and may I withdraw my OK for the use of my child's medical information for the purpose of this research study?***

You have the right to stop your child's participation in this study at any time. If your child does not complete the study medication, he/she may still need additional medication and follow-up by

your primary care provider. Your child's participation in the study may also be discontinued without your consent, by your doctor, the NIH, Office for Human Research Protections or the FDA, if based on their judgment it might improve your child's medical care or if you fail to follow the study schedule. Your child will receive the same quality of care at this hospital whether or not he/she is in the study. Additionally, you may withdraw, at any time, your OK for the use of your child's medical information for the purpose of this research study. Of course, if you withdraw your OK for the use of your child's health information, your child may no longer participate in this research study. To the extent that researchers have already used your child's health information in data analysis and/or scientific publication, this information cannot be withdrawn. Any publication of information will be such that your child's information will not be identifiable. If you decide to withdraw your OK, you should notify your child's study doctor in writing along with the date of your decision. Your decision to withdraw your OK for the use of your child's private health information for this research study will have no effect on your or your child's current or future medical care at Children's Hospital of Pittsburgh, a UPMC Health System Hospital or affiliated health provider or the University of Pittsburgh.

***For how long will the investigators be permitted to use my child's identifiable health information?***

Dr. Hoberman and his study staff will be permitted to use your child's identifiable health information indefinitely. In addition, they will contact you a few months after you finish the study to share information about the study findings and to discuss other urinary tract infection research opportunities you might find of interest.

***Will there be any compensation if my child is injured or becomes ill as a result of participating in this study?***

There is the possibility with any medical treatment or research that a patient may suffer some physical illness or injury. In the event of an injury or illness resulting from this research, any immediate emergency treatment that may be necessary will be provided without charge. There is no plan for monetary compensation. You do not, however, waive any legal rights by signing this form. You may contact Dr. Hoberman to obtain information about treatment if needed.

**Voluntary Consent and Authorization**

All of the above has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions about any aspect of this research study during the course of this study, and that such future questions will be answered by the researchers listed on the first page of this form. Any questions which I have about my child's rights as a research participant will be answered by the Human Subjects Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668). Dr. Hoberman (412-999-3277) will be available for questions about this research, my child's rights, and any possible research related injury. I will receive a signed copy of this consent form.

_____

Printed Name of Child (Research Subject)

_____

Printed Name of Parent/Guardian

_____ _____

Signature of Parent/ Guardian Date

## Certification of Person Explaining the Research

I have explained the nature and the purpose of this research and the disclosure of the child's medical information to the parent(s) or legally authorized guardian(s). He/she/they have had the opportunity to ask questions. Based on this conversation, I believe that he/she/they understand what this research project involves.

_____

Printed name of person explaining the research

_____ _____

Signature of person explaining the research Date

## Certification of Informed Consent

I certify that I have explained the nature and purpose of this research study to the above-named individual and I have discussed the potential benefits and possible risks of study participation. Any questions the individual has about the study have been answered and we will always be available to address future questions as they arise. I further certify that no component of this protocol was begun until after this consent form was signed.

_____ _____

Signature of Investigator Date

_____ _____

Printed Name of Investigator Date