

**Consent Form Template v 13**

**TITLE OF STUDY:** *Randomized Intervention for Children with VesicoUreteral Reflux*

(RIVUR)

**PRINCIPAL INVESTIGATOR:**

**PHONE NUMBER:**

*Evening/Week-end Coverage: 24 Hour Phone Number*

**ADDRESS:**

**CO-INVESTIGATORS:**

**SPONSOR:** National Institutes of Health (NIH)

**NAME OF SUBJECT:** \_\_\_\_\_ **MEDICAL RECORD NUMBER:** \_\_\_\_\_

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. This form will help you understand your child's condition, and what can be done to treat it. Please read this form carefully. As the research study staff discusses this informed consent form with you, please ask him/her to explain any words or information that you may not clearly understand.

This research study will allow your 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 participate in this study or not.

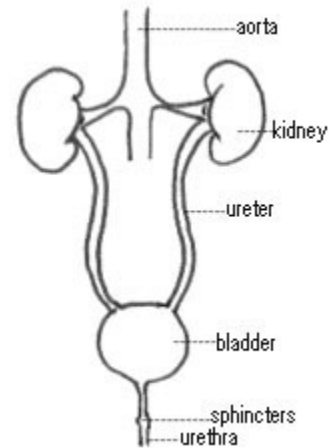
The researcher will explain how the study will be carried out and what you will be expected to do. This form describes the importance of the study as well as the benefits and risks of taking part in the study. The researcher will answer your questions about the study. If you decide to volunteer your 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 (VUR). VUR is the backflow of urine from the bladder up into the kidney. We are studying whether or not children with VUR need to take an antibiotic everyday in order 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 downward 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 backwards 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.

### ***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 infections is called prophylactic antibiotic treatment. The prophylactic use of an antibiotic does not stop the backflow of urine. Prophylactic antibiotic treatment prevents your child 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 prophylactic 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 repair 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 antibiotics. The study will tell us if prophylactic antibiotic treatment will effectively prevent urinary tract infections in children with VUR and will give more information on prophylactic 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 prophylactic antibiotics. By conducting this study, we hope to determine which of the two strategies, (1) careful follow-up of every illness with fever OR (2) treatment with daily low-dose antibiotic is more appropriate for children with VUR.

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 (SITE) is to recruit (NUMBER AT SITE). The staff is being reimbursed from the National Institutes of Health for the time and materials involved in carrying out 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 participate. Your child may leave this research study at any time. There will be no penalty or loss of health care benefits if your child does not participate or withdraws from this study. This form will help you understand what we think is hurting your child's health, and what we think can be done to treat your child's condition. 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. This means that neither you nor your doctor will know which treatment your child will be given. Randomization means that a computer will choose the treatment to be given in a manner similar to that of flipping a coin. There is an equal chance of receiving either treatment. Information about which treatment your child is receiving will be available to your doctor in case of emergency. Your child will have a 50% chance of receiving one of the following treatments during the study: 1) Prophylactic antibiotic; or 2) placebo (no active medication.) A prophylactic medication is one that may *prevent* a medical condition. The placebo will look and taste exactly like the prophylactic antibiotic.

Trimethoprim-sulfamethoxazole will be used as the prophylactic antibiotic unless your child has an allergy to trimethoprim-sulfamethoxazole (TMP/SMZ). If your child is allergic to TMP/SMZ (or any medication that contains sulfa), then your child is not eligible for this study. If your child develops an allergy to TMP/SMZ or the placebo for TMP/SMZ during the study, then your child will remain in the study but will discontinue study medication and be treated according to standard care practices for UTI and VUR.

The study may last for up to 2 years. Participation includes the following study clinic visits and telephone contacts described below:

**Baseline Visit:** This visit will help to determine whether your child is eligible for this study. The details of the study will be explained to you and you will be asked to sign this consent form if you have not already done so. To help determine your child's eligibility in the study, we will be asking you questions about your child's medical history and about your child's recent health and any medical problems. You will be asked to complete a short self-administered questionnaire. We will also collect from your child a small stool sample from a rectal swab, a teaspoon size sample of blood, and a urine sample. Your child will have a physical exam and will be scheduled for a nuclear renal scan (DMSA scan); if one has not already been done in the course of your child's medical care for his/her UTI. At the end of the visit, you will be given study medication (it will be either an antibiotic or placebo) that your child will take daily for the duration 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. A small blood sample (about one-tenth of a teaspoon) will be collected. You will be given additional study medicine and your empty or used bottles of study medicine will be collected. 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 for another DMSA scan to monitor any changes in your child's renal scarring since the baseline DMSA.

**End of Study Visit (24 Month Visit):** 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 teaspoon sample of blood, and a urine sample. Radiographic VCUG and DMSA imaging performed at the beginning of the study will be repeated or scheduled at this visit.

**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 baseline DMSA scan shows moderate renal scarring, then your child will have a DMSA scan after each UTI that causes a fever. If any DMSA scan shows worsening of the renal scarring, then your child will be taken off the study medication and be treated with a prophylactic antibiotic prescribed by your doctor. Your doctor may discuss the option of surgical repair of the VUR. Your child's continued participation in the study will still be important to us even though his/her treatment has changed. We will still continue the study clinic visits and phone calls.

**Special procedures for children with new or worsening scarring on the 12-month DMSA scan:** If the 12-month DMSA scan shows a new renal scar or worsening of a previous scar, then your child will be taken off the study medication and be treated through routine clinical care, for example, a prophylactic antibiotic may be prescribed by your doctor. Your doctor may discuss the option of surgical repair of the VUR. Your child's continued participation in the study will be important to us even though his/her treatment has changed. We will still continue the study clinic 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 prophylactic antibiotic prescribed by your doctor. Your doctor may discuss the option of surgical repair of 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 continue the study clinic visits and phone calls, and will schedule your child for a DMSA scan 4 months after he/she stops receiving the study medication.

**Release of additional medical information:** We will ask you to sign a Release of Medical Information form so that we can find out details of 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 (SITE). We will also ask you to allow us to contact a family member or other individual you've identified if (SITE) 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 participating in this study. We will send your primary care doctor reminders that your child is participating in this study. We are doing this so your primary care doctor knows how to treat your child if he/she gets a UTI.

### ***What are the risks of participating in this research study?***

Potential risks to your child while participating in the study are described below. You should discuss these with the researcher and/or your regular doctor.

**Risks of Study Medication – Antibiotic group:** The study medication (TMP/SMX) is commonly used in the treatment and prevention of UTI, and has an established record of safety in children. However, patients may have adverse reactions to these medications. The study medications may cause allergic reactions that range from mild (skin rash, nausea, vomiting) to severe (difficulty breathing, severe allergic reaction), although severe reactions are extremely rare. Other potential side effects include sun sensitivity, vaginal irritation, low white blood cell count, and dizziness. Other drugs may be given to make side effects less serious and uncomfortable. 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 cannot predict.

There is a chance that daily treatment with antibiotics, such as the study drug, may lead to the development of UTIs with resistant bacteria. This may require treatment with intravenous (IV) antibiotics.

**Risks of Study Medication – Placebo group:** If daily antibiotic prophylaxis protects children against recurrence of UTI and renal scarring, then your child will be exposed to a higher risk of recurrent UTI and renal scarring.

**Risks of Blood Drawing:** Risks associated with drawing blood from your child's arm include minimal discomfort and/or bruising. Infection, excess bleeding, or clotting (blockage of the vein) are also possible, although very rare.

**Risks of a voiding cystourethrogram (VCUG):** A voiding cystourethrogram (VCUG) is an x-ray examination of the bladder and lower urinary tract. A VCUG involves inserting a catheter through the urethra and filling the bladder with contrast material, both of which can be uncomfortable to children. A series of X-rays are taken as the contrast material is voided from the bladder. The radiation exposure from a VCUG is similar to the natural background radiation during one year.

**Risks of DMSA scans:** A DMSA renal scan is a diagnostic imaging procedure that is used to show areas of kidney infection or kidney damage. A DMSA scan requires inserting an intravenous (IV), injecting a radioisotope (radioactive substance) into the blood stream, and taking pictures of the kidney with a special camera. Your child may experience some discomfort associated with the placement of the IV. IVs can be dislodged and some fluid can go into the arm outside of the vein. The radiation exposure from a DMSA scan is less than half of the natural background radiation usually received during one year.

**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 physician can provide this in place of or in addition to the treatment you are receiving at the time.

The researchers have taken steps to minimize the known or expected risks. However, your child may still experience problems or side effects. It is important that you tell the researchers about any injuries, side effects, or other problems that your child experiences during this study.

A Data Safety and Monitoring Board, an independent group of experts, will be reviewing 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 you have had an unexpected reaction, or have failed to follow instructions, or because the entire study has been stopped.

If you withdraw your child 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 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 teaspoon sample of blood, 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 your child being in this study?***

There is no guarantee that you will receive any direct benefit from participating in this study. The information which is obtained will be useful scientifically and possibly helpful to others. We hope that this study may benefit society by showing which of these two approaches is better for children with VUR, but this is not guaranteed.

The standard testing in this study will provide information about your child's disease that may be beneficial to your child's wellbeing. 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 decreased. The blood and urine tests may also provide early information about kidney damage.

**Benefits of Study Medication – Placebo group:** Children in the placebo group may be less likely to become infected with resistant organisms that would require treatment with intravenous (IV) antibiotics. Children in this group will not develop the potential allergies or adverse events caused by antibiotic prophylaxis.

**Benefits of Study Medication – antibiotic group:** If daily antibiotic prophylaxis is protective against recurrence of UTI and renal scarring, then children in the antibiotic group may have fewer UTIs and less risk of renal scarring.

### ***What are the financial costs of this study?***

You will not be charged for the study medication or any of the study examinations while your child is a participant in this study. You will not be charged for testing of the stool specimen, or for the special blood test measuring kidney function. All other laboratory tests and radiographic imaging are considered routine care (the normal course of treatment for your child's illness) and

will be billed to you or your insurance company. All costs not paid by your insurance will be your financial responsibility. Please ask about any expected added costs or insurance problems. Financial Counselors are available to discuss insurance, costs and other issues.

***How will my child and I be compensated for taking part in this research study?***

To help cover any expenses such as transportation or time off from work during the clinic visits, you will be given \$25 for each visit. If you complete every follow-up during the study, you will also receive a \$25 bonus at the last visit.

***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 antibiotics to prevent infections. If you choose not to enroll in the study, your child's doctor may prescribe 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 (SPECIFIC SITE) or any affiliated health care provider.

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

**Optional Biological Samples:** During the already planned blood and urine specimen collection at baseline and the 24 month visit, we would like to collect an additional small amount of blood and urine to send to the National Institutes of Diabetes and Digestive and Kidney Diseases (NIDDK) Central Repository. This is also referred to as specimen banking. The purpose of specimen banking is to provide available samples for future research. 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 RIVUR 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 receive any direct benefit or payment for participating, but your child's sample may benefit other people with VUR. It is possible that data resulting from use of your child's sample may eventually 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 derived 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 participate in this portion of the study, your child can still participate in the rest of the study

If you agree to have your child's sample stored in the NIDDK Central Repository, you can change your mind up until the end of the RIVUR 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 has concluded, the sample will stay in the Repository indefinitely.

You understand and agree that 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 at any time during the study you would like your child's blood or urine sample to be destroyed, you can contact SITE PERSONNEL NAME at SITE PHONE NUMBER.

If you consent to the use of your child's biological (urine and blood) samples for future scientific studies, please initial one or both of the statements below. If you do not consent to the use of your child's biological samples, then leave the statements blank

**Statement of Consent for blood specimen Banking:**

\_\_\_\_\_ I **do** give permission for my child participate in the blood sample  
Initials            Date            banking part of the study.

**Statement of Consent for urine specimen Banking:**

\_\_\_\_\_ I **do** give permission for my child to participate in the urine sample  
Initials            Date            banking part of the study.

**Optional Genetic Sample:** Also during the baseline visit, we would like to collect another small amount of blood that will be sent to the NIDDK Genetic Repository. The amount of extra blood will be about 1-2 teaspoons depending on your child's age. The same standards and guidelines outlined above regarding protection of privacy for the Biological Samples apply to the Genetic Samples. Cells collected from your child's blood that can be used to make DNA (heredity material) will be stored indefinitely for future research purposes. Scientists will use this DNA of the blood to help them develop new diagnostic tests, new treatments, and new ways to understand diseases.

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 derived 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 participate in this portion of the study, your child can still participate in the rest of the study.

If you agree to have your child's DNA stored in the NIDDK Genetic Repository, you can change your mind up until the end of the RIVUR 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 has concluded, the sample will stay in the Repository indefinitely.

You understand and agree that any DNA that your child provides as a participant in this research study is a donation 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 at any time during the study you would like your child's DNA sample to be destroyed, you can contact SITE PERSONNEL NAME at SITE PHONE NUMBER.

If you consent to the use of your child's genetic samples for future scientific studies, please initial the statement below. If you do not consent to the use of your child's genetic samples, then leave the statement blank

**Statement of Consent for genetic sample Banking:**

\_\_\_\_\_ I do give permission for my child participate in the genetic sample  
Initials            Date            banking part of the study.

***What if you have more questions?***

For questions about the study or a research-related injury, contact the study coordinator at SITE PHONE NUMBER. A member of the study team will be available to speak to you 24 hours per day, 7 days per week at SITE PHONE NUMBER. If additional questions arise, you can also speak with your doctor.

This research study has been reviewed and approved by the Human Research Review Board, whose purpose is to see that the rights and welfare of research participants are adequately protected, and that risks are balanced by potential benefits. A member of this committee is available to speak to you or your child about any questions or complaints. The SITE INSTITUTION Human Research Review Board can be reached at SITE IRB PHONE NUMBER.

If you choose to participate, you will receive a copy of this consent form. You may also request a copy of the protocol (full study plan).

***Will information be kept confidential?***

Research information collected during the study will be sent to the RIVUR Data Coordinating Center at the University of North Carolina and will not contain your child's name, address, or phone number. Data from this study will be identified with a code number. The match between your child's name and this code will be stored in a locked file cabinet at SITE INSTITUTION. Data and biological samples that we collect from your child during this study may be shared with other researchers in the future, and may be linked together with other information such as your child's age, gender, ethnicity, and medical diagnosis. Also, scientific data from this study may

be presented at meetings and published so that it may be useful to others, as long as your child is not identifiable.

Your child's personal information may be disclosed if required by law. Organizations that may inspect and/or copy your child's medical and research records for quality assurance and data analysis include:

- The research team, which includes personnel listed on this form and other persons involved in this study at SITE INSTITUTION.
- The SITE INSTITUTION Human Research Review Board
- The National Institutes of Health (NIH), the Food and Drug Administration (FDA) and/or other regulatory agencies, including the Data Coordinating Center team at the University of North Carolina.
- Doctors and other researchers coordinating this study at other participating institutions.

Because this study could affect your medical care, a copy of this consent form will be placed in your permanent medical record. This will allow the doctors caring for you to obtain information about what drugs or procedures you are receiving in the study and treat you appropriately, if you have other health problems or needs during the study.

***Permission to proceed and Statement of Consent***

The signing of this consent does not absolve the study doctors from the responsibility for proper medical care at all times.

When you sign this form, you agree that you have read the above description of this research. You also agree that your questions have been answered, and that you want to take part in this research.

**Statement of consent**

I understand the above information. The study has been explained to me and my questions have been answered. I, the undersigned, give permission for \_\_\_\_\_ to participate in this study.

\_\_\_\_\_  
Signature of subject or authorized representative

\_\_\_\_\_  
Date

\_\_\_\_\_  
Relationship to the child

**The proposed research study and consent has been explained to you by:**

\_\_\_\_\_  
Name of Principal or Co-Investigator

\_\_\_\_\_  
Signature of Principal or Co-Investigator