

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

**Efficacy of Antibiotics in Children with Acute Sinusitis:
Which Subgroups Benefit?**

PRINCIPAL INVESTIGATOR:

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

We are asking you and your child to take part in our research study because your child has sinusitis. Before you decide whether to participate, it is important for you to know why the research is being done and what it will involve. Ask us if there is anything that is not clear or if you would like more information. Please read this information and feel free to ask any questions before you agree to take part in the study. The purpose of this consent form is to help you decide if you want to have your child participate in this research study. This consent form contains information about why the study is being conducted, what will be involved if you agree to have your child participate, and what the risks and benefits are. You will be provided a copy of this consent document. Please read this consent form carefully before making your decision. Please ask the study doctor or study staff to explain anything you do not clearly understand.

Sinusitis (a sinus infection) is one of the most common illnesses in children. Many children currently being diagnosed as having acute sinusitis actually have an uncomplicated cold or upper respiratory infection that is caused by a virus. We cannot cure a viral infection with an antibiotic. Antibiotics are only helpful when the infection is caused by bacteria.

It can be hard for doctors to know whether your child's symptoms are due to a viral infection (which does not need to be treated with antibiotics) or a bacterial infection. Sometimes doctors decide to wait and watch to see if symptoms get better on their own. The term "watchful waiting" means that doctors do not give an antibiotic right away for possible sinus infection. Instead, doctors carefully watch how the child feels and acts over the next two to three days. This can be done because sinusitis is not usually a serious illness. In fact, symptoms often clear up without any antibiotic treatment. An antibiotic is only started if the symptoms get worse or do not get better. In some European countries, doctors have been using this "watchful waiting" approach for children with ear and sinus infections during the past 10 years. Recently, this has become more common among US doctors. If doctors use less antibiotics, this may help reduce the spread of resistant bacteria. Also, children who take antibiotics often have side effects, such as diarrhea, skin rash or allergic reaction.

Doctors used to believe that young children need to be treated with antibiotics, in order to get better faster or to prevent serious problems (an abscess or collection of bacteria in a pocket or a bone infection in the skull). We now know that these problems are very rare (about 2 out of 1000 children) and can happen even if your child is on antibiotics. We are trying to find out which of the two strategies, "watchful waiting" or treatment with antibiotics, is better for children with sinusitis.



What are my child and I being asked to do?

About 688 children in Pittsburgh and three other cities in the US, between the ages of 2 and 12 years, with sinusitis will be enrolled in the study. If you enroll your child in this study, your child will be given either the antibiotic Augmentin™ (also known as amoxicillin clavulanate) or placebo for 10 days. Placebo looks and tastes like the antibiotic but does not contain any antibiotic. Augmentin is approved by the Food and Drug Administration for the treatment of sinus infections, ear infections, and pneumonia. The dose will be calculated based on your child's weight. If you agree to have your child join the study, he/she will be assigned by chance, like the flip of a coin, to receive Augmentin or placebo.

Today, we will ask you about your child's medical history and any medicines he/she is currently taking. A focused assessment of your child's face and nose will be performed. Your child's temperature and weight may be checked if this has not already been done. We will ask you how your child is feeling and discuss any concerns you may have. We will get a little bit of mucus from your child's nose at the first visit with a flexible swab. The results of the nose culture may help us understand which germs are in your child's nose. This information may help us to figure out which children are more likely to improve if they are prescribed antibiotics.

You will be asked to let us know about your child's symptoms in an electronic diary each day. A text message or email will be sent with a link to complete the daily diary. This is called the PRSS score (Patient Reported Sinus Symptoms). This should not take more than 5 minutes to complete. You will also write down when you give your child the study product. While enrolled in the study, we ask parents to refrain from administering intranasal medications (e.g., corticosteroids, decongestants and systemic medications that contain antihistamines, decongestants or corticosteroids) to your child.

If a PRSS score is missing or was not been completed we will call the next morning to see how your child is doing. The phone call should not take more than 5 minutes. We can also text you a link to the electronic diary. In addition, you can call us on the study cell phone anytime (412-692-7668). We would like to see your child anytime you feel he/she is not better or is worse. If the study cell phone network is not working, you may reach Dr. Shaikh through the Children's Hospital operator at 412-692-5325. If at any time your child does not look well, you may go to the emergency room, or have your child seen by their primary care doctor. Some reasons that we want you to call us are continued fever, severe face pain or headache. You should also call if you are worried about your child in any way. We will see your child within 24 hours and we will reimburse you for transportation as at the other visits. At a sick visit, we will ask you how your child is feeling and talk about any concerns you may have. If your child has an allergic reaction (hives), or if your child gets worse, we may stop the study product and provide a prescription for an antibiotic.

Summary of each visit:

- Visit 1 (today)
 - Read and discuss the Informed Consent Document
 - Record medical and medications history
 - Record temperature and weight, if necessary
 - Focused assessment of face and nose
 - Nose swab
 - First dose of study medication
 - Review how to do diary entries
 - This visit will take about 30 minutes

- Sick visit (if needed):
 - Record medical history since the last visit
 - Discuss questions or concerns
 - Focused assessment of face and nose
 - Measure temperature
 - This visit will take about 20 minutes

- Visit 2 (final visit, day 12-18)



- Record medical and medications history since the last visit
- Discuss questions or concerns
- Return bottle(s) of study product
- This visit will take about 20 minutes

What are the benefits and risks of participating in this research study?

Risks

Augmentin

The most common (10-25 out of 100 children) side effect from Augmentin is diarrhea. Infrequently (1 to 10 out of 100 children), children may have vomiting, nausea or yeast diaper rash, stomach pain, gas and headache. An increase in liver enzymes is rare, (less than 1 out of 100 children). Rare (1 out of 100 children) allergic reactions, including hives, joint pain and shock or anaphylaxis, a severe form of allergy, which may lead to death, can occur just like with any other antibiotic. Most of the reported side effects have been mild to moderate and stop when the medicine is stopped.

Placebo

There is no active medicine in the placebo. The same flavoring and coloring and powder mixers used in regular Augmentin are in the placebo (to make it look and taste like the real medicine). A child could rarely (1 out of 100 children) be allergic to one of these powders. A possible but rare (less than 1 out of 1000) risk is of developing an abscess or collection of infection or an infection of the skull while on placebo.

Nose Swab

A nose swab to test for bacteria in your child's nose will be done. This can commonly (10-25%) cause minor discomfort.

Confidentiality

Rarely (<1%), there is a risk of loss of confidentiality. All of the study data will be stored in locked file cabinets that are kept in the research area and computer records are password protected. Electronic diary entries will be stored on a secure server that requires an account with a password in order to obtain access. Each computer has a password only available to the study staff. All specimens and electronic diary entries will only have the patient study identification number on them. Identifying codes that could be used to link your child with this identification number will be kept in a locked file cabinet in the research office.

Internet Communication/Text Messaging

Although every reasonable effort has been taken, confidentiality during Internet communication activities cannot be guaranteed and it is possible that additional information beyond that collected for research purposes may be captured and used by others not associated with this study. Text message are not encrypted or secure during their transmission. Text messages could be intercepted and used by others not associated with this study.

Benefits

In this study both treatment options include the potential for benefit. If your child is placed in the part of the study where the children are placed on an antibiotic it provides potential for clinical improvement if the child's symptoms are caused by a bacterial infection. The children who are placed on placebo also may have benefits if the child's symptoms are not due to a bacterial infection but are due to a viral infection which does not need and cannot be treated with an antibiotic. It is difficult to know, based on symptoms alone, if the symptoms are due to a bacteria or a virus. For the children who do not receive an antibiotic, they may also have the benefit of avoiding the side effects of antibiotics such as rash, diarrhea, or allergic reaction. Exposure to antibiotics may also allow the bacteria to become resistant.

All children who are in this study will have the benefit of a clinician monitoring the symptoms on a daily basis. If your child's clinical score is worsening or not improving as expected they can be evaluated



without delay and treated with rescue antibiotics. You will have 24-hour access to the study physicians who will arrange a study visit, usually within 24 hours, if indicated.

Side-by-side Risks and Benefits of Treatment with Antibiotics or No Treatment	
Treatment with Antibiotics	No Treatment
Every time doctors prescribe an antibiotic, there is a chance that bacteria or germs may change so that the antibiotic no longer kills them. We call this a “resistant” germ. Then, your child may not respond to antibiotics when needed for a more serious infection. In addition, resistant germs may spread to other family members, neighbors and playmates.	“Resistance” to antibiotics does not happen when taking placebo.
Augmentin, like many other antibiotics, may cause side effects (diarrhea or diaper rash being the most common) or allergic reactions.	Placebo may rarely cause an allergic reaction, but in general does not have the side effects of an active medication.
If your child is having pain from of a sinus infection (headache or face pain) an antibiotic does not relieve pain, although pain may go away faster if the infection is caused by a bacteria and if the bacteria is treated with an antibiotic. Tylenol can be given for pain.	If your child is having pain from a sinus infection (nasal congestion, headache or face pain) the placebo will not relieve pain. Tylenol can be given for pain.
Augmentin is approved by the FDA for treatment of sinus infections.	“Watchful waiting” is an option accepted by many physicians for children with an uncertain diagnosis and in children non-severe disease whose symptoms may be caused by a viral infection.
If your child is given Augmentin, the sinus infection may be treated and the symptoms may respond to antibiotic treatment.	If your child is given placebo, their symptoms may eventually get better without any antibiotics.
Symptoms of the sinus infection may improve hours sooner with antibiotic treatment.	Symptoms of the sinus may continue or worsen and require treatment with antibiotics.

May I refuse to give my permission for the use of my child’s medical information for the purpose of this research study?

Your permission 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 permission, your child will not be allowed to be in this study.

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

Antibiotics may be prescribed to some children who present with symptoms similar to your child’s symptoms. Usual medical care includes an antibiotic prescription or, following your child for changes in symptoms (“watchful waiting”). This is where antibiotics are not prescribed initially but the child is followed and if the child gets worse, then an antibiotic prescription is provided. This is done because many children have a viral infection and not a bacterial infection and therefore do not need an antibiotic. If your child improves without an antibiotic, then it is assumed that the infection was due to a virus. Participation in this study is 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 UPMC hospital or affiliated health care provider of the University of Pittsburgh.

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 the conduct of this research. Before putting your child in this study or at any time during the study you may discuss your child’s care with your child’s pediatrician or family doctor, another



doctor at that practice, or a physician or health care provider 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 Institute of Allergy and Infectious Diseases, which is part of the National Institutes of Health (NIH). 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.

What costs will be associated with permitting my child to participate in this research?

You will not be charged for any study procedures while your child is a participant in this study. If your child's sinus infection does not get better, we may stop the study medication and give your child a prescription for another antibiotic. The cost of this rescue medication would not be covered by the research study. If your child develops a yeast diaper rash, we will prescribe an antifungal cream. You or your insurance company will be charged for any procedures or treatment performed for your child's routine medical care.

To help cover any expenses such as transportation or time off from work, we will provide a WePay card: \$30 at study entry; \$5 for each day the symptom diary is completed (maximum is \$55 for 11 entries) and \$50 for the end of study visit and for returning the tablet if one is lent to the family for diary entries.

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 permission. 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. 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. 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 study identification number and initials. Only the study staff will be able to link the code number to your child's name. The NIH 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 will not result in specific research related health information being placed in the Children's Hospital of Pittsburgh medical chart, outpatient chart, or research record. A letter will be sent to your child's primary care provider with information about study participation and the letter



may be added to your medical records. It will include a phone number for your care provider to contact the study if needed.

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. Each computer has a password only available to the study staff. 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 UPMC hospitals or other affiliated health care providers may have access to identifiable information (which may include your child's identifiable medical information) related to your participation in this research study for the purposes of (1) fulfilling orders, made by the investigators, for hospital and health care services (e.g. laboratory tests, diagnostic procedures) associated with research study participation; (2) addressing correct payment for tests and procedures ordered by the investigators; and/or (3) for internal hospital operations (i.e. quality assurance).

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. Authorized representatives of the NIH and the Office for Human Research Protections (OHRP) 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 are required under Pennsylvania law to report any suspicion of child abuse to child protection services. If the investigators learn that your child or someone related 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 (antibiotics or placebo). The study doctor will be able to find out which study medication your child is taking if he/she needs to know for safety reasons. After the study is finished and the results have been studied, we will send you a letter that tells you which study medication your child received.

May I stop my child's participation in this study and may I withdraw my permission 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 did not complete the study medication, he/she may still need additional medication for the sinus infection or 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 or the Office for Human Research Protections, 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 permission for the use of your child's medical information for the purpose of this research study. Of course, if you withdraw your permission 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 permission, you should notify your child's study doctor in writing along with the date of your decision. Your decision to withdraw your permission 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, UPMC 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. Shaikh and his study staff will be permitted to use your child's identifiable health information and nasal swab specimen indefinitely. Any information shared with those who are not members of the research team will be in de-identified form.

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

If you believe that the research procedures have resulted in an injury to you, immediately contact the Principal Investigator who is listed on the first page of this form. Emergency medical treatment for injuries solely and directly related to your participation in this research study will be provided to you by the hospitals of UPMC. Your insurance provider may be billed for the costs of this emergency treatment, but none of those costs will be charged directly to you. If your research-related injury requires medical care beyond this emergency treatment, you will be responsible for the costs of this follow-up care. At this time, there is no plan for any additional financial compensation.

Could I be contacted for future research studies?

The investigators may contact you in the future if we have new research questions. You are under no obligation to participate in future research studies.



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 Subject Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668). Dr. Shaikh 412-692-SNOT (7668) 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)

"I understand that, as a minor (age less than 18 years), the above named child is not permitted to participate in this research study without my consent. Therefore, by signing this form I give my consent for my child to participate in this research study and provide my authorization to share their medical records with the research team.

Parent's Name (print)

Relationship to Participant (Child)

Parent's Signature

Date

Child Assent (to be used with children who are developmentally able to sign)

This research has been explained to me in age appropriate language, and I agree to participate.

Signature of Child-Subject

Date

Printed Name of Child-Subject

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.

Printed Name of Investigator

Role in Research Study

Signature of Investigator

Date

Time

