Children's Hospital of Philadelphia

Informed Consent and HIPAA Authorization Form

Study Title: Optimizing Vancomycin Therapy in Children II

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You, or your child, may be eligible to take part in a research study. This form gives you important information about the study. It describes the purpose of this research study, and the risks and possible benefits of participating.

In the sections that follow, the word "we" means the study doctor and other research staff. If you are a parent or legal guardian who is giving permission for a child, please note that the word "you" refers to your child.

Study Overview

You are being asked to take part in this observational research study because you are 1-17 years of age and you are prescribed intravenous (IV) vancomycin (a type of antibiotic) while hospitalized at CHOP. This is a commonly used antibiotic in the intensive care unit, but it can be hard to give the right amount of it to very sick children when their illnesses are complicated. This is a research study to learn more about how well we can predict vancomycin drug levels over time in critically ill children.

Your participation will take place during your hospital stay at CHOP, and there will be several study visits over the span of 2 to 5 days, during which you will be asked to:

- Have daily blood draws;
- Provide daily urine samples.

The main risks of this study are from the blood draws. These include fainting, infection, and catheter complication.

You will not benefit directly from participating in this study. Dosing of vancomycin will be determined by your clinical team.

If there is anything in this form you do not understand, please ask questions. Please take your time. You do not have to take part in this study if you do not want to. If you take part, you can leave the study at any time. If you do not choose to take part in this study, you can discuss treatment options with your doctor. You may also be eligible for a different research study.

Please see below for additional details about the study.

What are the study procedures?

Some of the procedures in this study will be repeated several times. Tests that are part of your regular, routine medical care will continue to be performed. Additional tests may be

performed if any of your initial test results are not normal. The study involves the following tests and procedures.

Blood tests: We need to collect blood at each study visit to measure vancomycin levels and Cystatin C (a test to look at kidney function). No genetic testing (and therefore no whole genome sequencing) is being conducted as part of this study. We will collect no more than 1 teaspoon of blood on each day of study participation. Altogether during the entire study, we will collect no more than 2 teaspoons of blood. This will be drawn when blood is being collected for clinical care, when possible. We will do our best to collect the samples at the same time as a clinical blood test. We will try not to stick you more than once. Some of the vancomycin level results will be shared with your doctors, but not all of them to avoid confusion with clinically performed tests. All of the Cystatin C test results will be shared with your doctors.

Urine samples: We need to collect urine at each study visit to measure NGAL (a protein in urine). This will be collected from a catheter if you already have one, or using cotton balls, a urine bag or urine cup. The results of the urine NGAL tests will not be shared with your doctors.

Weight: If you don't have a recent weight in your medical record, we may measure your weight.

Medical record review: We will review your medical record to gather information about your medical history and conditions, treatments you had, health and infection status, medications received, results of clinical tests (such as results of X-rays, blood tests, CT scans, etc.) that have been performed recently (in the past 90 days) or are performed while you are in the hospital, and other information about your hospital stay. We will also collect information about your age, race, gender and ethnicity.

Visit Schedule

During each day of study participation you will have blood and urine samples collected. If you are already having blood drawn for clinical care, we will do our best to collect the research samples at that time too. The urine samples can be collected anytime during the day. The study will last at least 2 days and up to 5 days, depending on when you are having your vancomycin levels tested for clinical care.

What will be done with my data and specimens during this study?

During the study, we will collect blood and urine samples from you. We will use results of research tests performed on the blood (cystatin C) and urine (NGAL) to try to predict vancomycin levels you will achieve using math models we have developed. By agreeing to participate in the study, you agree to give these samples to CHOP for research purposes.

Will I receive any results from the tests done as part of this study?

Results of vancomycin tests and Cystatin C tests that could be important for your clinical care will be shared with your doctors. We will not share other results with you.

What are the risks of this study?

Taking part in a research study involves inconveniences and risks. The main risks of taking part in this study are discussed below.

Risks of blood tests:
Risks associated with blood draws include infection or catheter complication. To minimize these risks, we will try, whenever possible, to draw blood for the research study when you are having blood drawn for clinical purposes. If you have an IV placed for a blood draw, this may cause some pain, bleeding or bruising at the spot where the needle enters your body. Rarely, taking blood may cause fainting or infection. If you have blood collected from a fingerstick or heelstick, this may be bit uncomfortable and may cause some soreness and bruising. Very rarely, the site can become infected.

Risks associated with measurement of weight:
There are no physical risks but you might experience momentary embarrassment or discomfort.

Risks associated with collection of urine:
There are no physical risks but you might experience momentary embarrassment or discomfort. The test is similar to those performed as part of routine medical care.

Risks associated with medical record review:
As with any study that involves collection of data, there is a possibility that confidentiality will be breached. Every precaution will be taken to ensure confidentiality. At the time of participation, each participant will be assigned a study identification number. This number will be used on data collection forms, research blood and urine samples. A database will be maintained that will link each participant's name and CHOP medical record number to the study identification number for future reference and communication. The database that contains your name and medical record number is password protected with dual authentication and will be stored on CHOP servers behind the CHOP firewall to ensure that only the CHOP study team can access it.

Urine samples may be temporarily labeled with your patient sticker and stored on the hospital floor overnight. This patient sticker will be destroyed by our study team the next day and replaced with a study label. Vancomycin levels and Cystatin C tests will be labeled with your patient sticker as per routine clinical care.

Are there any benefits to taking part in this study?

There will be no direct benefit to you from taking part in this study. The knowledge gained from this study may help doctors determine how best to treat children with IV vancomycin in the future.

Do you need to give your consent in order to participate?

If you decide to participate in this study, you must sign this form. A copy will be given to you to keep as a record.

What are your responsibilities?

Please consider the study time commitments and responsibilities as a research subject when making your decision about participating in this study.

What happens if you decide not to take part in this study?

Participation in this study is voluntary. You do not have to take part in order to receive care at CHOP.

If you decide not to take part or if you change your mind later there will be no penalties or loss of any benefits to which you are otherwise entitled.

Can you stop your participation in the study early?

You can stop being in the study at any time. You do not have to give a reason.

Can the study doctor take you out of the study early?

The study doctor may take you off of the study if you are unable to provide blood or urine samples, or if you stop being prescribed vancomycin.

What about privacy, authorization for use of Personal Health Information (PHI) and confidentiality?

As part of this research, health information about you will be collected. This will include information from medical records, physical examinations, urine and blood tests. Information related to your medical care at CHOP will go in your medical record. This could include physical exams, or blood and urine tests done in the clinical lab. Medical records are available to CHOP staff. Staff will view your records only when required as part of their job. Staff are required to keep your information private. Information that could identify you will not be shared with anyone - unless you provide your written consent, or it is required or allowed by law. Laboratory test results will appear in your medical record with the exception of research-only vancomycin levels, which are performed only for this research study. We will do our best to keep your personal information private and confidential. However, we cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law.

The results of this study may be shown at meetings and published in journals to inform other doctors and health professionals. We will keep your identity private in any publication or presentation.

Several people and organizations may review or receive your identifiable information. They will need this information to conduct the research, to assure the quality of the data, or to analyze the data or samples. These groups include:

- Members of the research team and other authorized staff at CHOP;
- People from agencies and organizations that perform independent accreditation and/or oversight of research; such as the Department of Health and Human Services, Office for Human Research Protections;

- InsightRx, Inc. will receive deidentified data for software development;
- The National Institutes of Health who is sponsoring this research.

By law, CHOP is required to protect your health information. The research staff will only allow access to your health information to the groups listed above. By signing this document, you are authorizing CHOP to use and/or release your health information for this research. Some of the organizations listed above may not be required to protect your information under Federal privacy laws. If permitted by law, they may be allowed to share it with others without your permission.

There is no set time for destroying the information that will be collected for this study.

Your permission to use and share the information and data from this study will continue until the research study ends and will not expire. Researchers continue to analyze data for many years and it is not possible to know when they will be completely done.

Certificate of Confidentiality (CoC)

A Certificate of Confidentiality (CoC) from the National Institutes of Health (NIH) covers this research. A CoC helps protect your identifiable information and biological samples.

A CoC protects your private information from all legal proceedings. Unless you consent, information from this research study that identifies you will not be shared outside this research.

- No one can be forced to share your identifiable information or biological samples for a lawsuit.
- Your information can't be used as evidence even if there is a court subpoena.

If you consent, your information or biological samples could be shared for:

- Other scientific research;
- Your medical treatment.

The CoC does not prevent some disclosures.

- The researchers can't refuse requests for information from those funding this research. The NIH may need information to assess this project.
- You can still share information about yourself. You can also freely discuss your involvement in this research.
- The researchers must disclose things required by law. This includes suspected child abuse and neglect, harm to self or others, or communicable diseases.

Can you change your mind about the use of personal information?

You may change your mind and withdraw your permission to use and disclose your health information at any time. To take back your permission, it is preferred that you inform the investigator in writing.

Dr. Kevin Downes
The Children's Hospital of Philadelphia

Division of Infectious Diseases
Roberts Center for Pediatric Research
2716 South Street, Rm 10360
Philadelphia, PA 19146

In the letter, state that you changed your mind and do not want any more of your health information collected. The personal information that has been collected already will be used if necessary for the research. No new information will be collected. If you withdraw your permission to use your personal health information, you will be withdrawn from the study.

Financial Information

While you are in this study, the cost of your usual medical care – procedures, medications and doctor visits – will continue to be billed to you or your insurance.

Will there be any additional costs?

There will be no additional costs to you by taking part in this study. All tests collected for this study will be paid for by the research team and the National Institutes of Health (NIH).

Will you be paid for taking part in this study?

Your parent or guardian will receive $20 for your time and effort for taking part in this study. This will be given to you after all blood samples have been collected. This amount will be provided in the form of a bank card to the child at the completion of the study. Payment will be provided using a bank card, therefore the bank will have access to identifiable information. The bank will not have access to any medical information.
Who is funding this research study?

The National Institutes of Health is providing funding for this study.
Please ask Dr. Kevin Downes if you have any questions about how this study is funded.

Conflicts of Interest

Dr. Downes and CHOP have intellectual property/a patent pending on math (pharmacokinetic) models for vancomycin, which are being evaluated in this study. If the study shows that a model may be useful for dosing vancomycin, Dr. Downes and CHOP may gain financial benefit if the research is successful.

What if you have questions about the study?

If you have questions about this study or how your samples/data are going to be used, call the study doctor Dr. Kevin Downes at 215-590-4024. You may also talk to your own doctor if you have questions or concerns.

The Institutional Review Board (IRB) at The Children's Hospital of Philadelphia has reviewed and approved this study. The IRB looks at research studies like these and makes sure research subjects' rights and welfare are protected. If you have questions about your rights or if you have a complaint, you can call the IRB Office at 215-590-2830.

Optional Consent for Use of Identifiable Data and Specimens for Future Research

As part of the study, we will collect data and urine samples. We may wish to use and share this information or samples in a future study about biomarkers or antibiotics.

Research could occur at CHOP, or at outside institutions, which could include for profit companies. The information and samples will be given a unique code and may include information that can identify you. Information that can identify you or the urine samples may be kept permanently in a computer database at CHOP.

We may not ask for your consent before using or sharing your identifiable specimens or data. You will not receive any results or financial benefit from the future research done on your specimens or data. We may share your identifiable specimens or data with outside researchers who will use them for future research.

If you leave the study, you can ask to have the data collected about you removed or the samples destroyed. You can also ask us to remove information that identifies you from the data or samples. This may not be possible if your samples and data have already been shared.

Please indicate whether you will allow the identifiable data and samples to be used for future research by putting your initials next to one of the following choices:

_____ (initials) **NO**, my identifiable data and specimens may not be used for future research. They may be used for this study only.

_____ (initials) **YES**, my identifiable data and specimens may be used for other future research studies.

Consent to Take Part in this Research Study and Authorization to Use and Disclose Health Information for the Research

The research study and consent form have been explained to you by:

Person Obtaining Consent	Signature of Person Obtaining Consent
	Date

By signing this form, you are indicating that you have had your questions answered, you agree to take part in this research study and you are legally authorized to consent to your child's participation. You are also authorizing the use of your/your child's health information as discussed above. If you don't agree to the collection, use and sharing of health information, you cannot participate in this study. **NOTE:** *A foster parent is not legally authorized to consent for a foster child's participation.*

Name of Subject	
Signature of Subject (18 years or older)	Date
Name of Authorized Representative (if different than subject)	Relation to subject: ☐ Parent ☐ Legal Guardian
Signature of Authorized Representative	Date

Documentation of Verbal Consent to Take Part in this Research Study and Authorization to Use and Disclose Health Information for the Research

Name of Subject

The research study and consent form was explained to:

Person Providing Consent

Relation to subject:
☐ Parent ☐ Legal Guardian

The person who provided consent confirmed that all of their questions had been answered and they agreed to their/their child's participation in this research study.

They confirmed that they were legally authorized to consent to their child's participation.

They agreed to let CHOP use and share their child's health information.

Person Obtaining Consent

Signature of Person Obtaining Consent

Date

Child Assent to Take Part in this Research Study

For children capable of providing assent:

I have explained this study and the procedures involved to _____ in terms he/she could understand and that he/she freely assented to take part in this study.

_____
Person Obtaining Assent

_____ _____
Signature of Person Obtaining Assent Date

This study has been explained to me and I agree to take part.

_____ _____
Signature of Subject (optional) Date

For children unable to assent:

I certify that _____ was not capable of understanding the procedures involved in the study sufficiently to assent to study participation.

Reason: _____

_____
Person Responsible for Obtaining Assent

_____ _____
Signature of Person Responsible Date

STUDY SUMMARY SIGNATURE PAGES

For Subjects with Limited English Proficiency

Consent to Take Part in this Research Study and Authorization to Disclose Health Information

Name of Subject

Name of Authorized Representative (if different than subject)

Relation to subject:
☐ Parent ☐ Legal Guardian

The research study and consent form have been explained to the subject or parent/legal guardian.

By signing this form, you are indicating that you have answered the subject's or parent's/legal guardian's questions, they have agreed to take part in this research study and they are legally authorized to consent to their or their child's participation. They have also agreed to let CHOP use and share their or their child's health information as explained above. If they don't agree to the collection, use and sharing of their or their child's health information, they cannot participate in this study.

Person Obtaining Consent

Signature of Person Obtaining Consent

Date:

Witness/Interpreter

By signing this form, you are indicating that

- The information in the Summary Document as well as any additional information conveyed by the person obtaining consent was presented to the subject in a language preferred by and understandable to the subject; and
- The subject's questions were interpreted and the responses of the person obtaining consent were presented in a language preferred by and understandable to the subject.
- At the conclusion of the consent conference, the subject was asked in a language preferred by and understandable to the subject if s/he understood the information in the Summary Document as well as any additional information conveyed by the person obtaining consent (including responses to the subject's questions) and responded affirmatively.

Name of Witness/Interpreter

Signature of Witness/Interpreter

Date:

Child Assent to Take Part in this Research Study

For Subjects with Limited English Proficiency

For children capable of providing assent:

I have explained this study and the procedures involved to _____ in terms he/she could understand and that he/she freely assented to take part in this study.

_____
Person Obtaining Assent

_____ _____
Signature of Person Obtaining Assent Date

Witness/Interpreter

By signing this form, you are indicating that

- The information in the Summary Document as well as any additional information conveyed by the person obtaining assent was presented to the subject in a language preferred by and understandable to the subject; and
- The subject's questions were interpreted and the responses of the person obtaining assent were presented in a language preferred by and understandable to the subject.
- At the conclusion of the consent conference, the subject was asked in a language preferred by and understandable to the subject if s/he understood the information in the Summary Document as well as any additional information conveyed by the person obtaining assent (including responses to the subject's questions) and responded affirmatively.

_____ _____
Name of Witness/Interpreter Signature of Witness/Interpreter

Date: _____