OREGON HEALTH & SCIENCE UNIVERSITY

IRB#: 19379

MED. REC. NO. _____
NAME _____
BIRTHDATE _____

CLINICAL RESEARCH CONSENT AND AUTHORIZATION SUMMARY OF KEY INFORMATION ABOUT THIS STUDY

TITLE: A Phase IV Open-Label Pharmacokinetic Study of Minocycline for Injection Following a Single Infusion in Critically-Ill Adults (ACUMIN)

PRINCIPAL INVESTIGATOR: Dr. Akram Khan (503) 494-1620

You are being asked to join a research study. This consent form contains important information to help you decide if you want to join the study or not.

PURPOSE:
The purpose of this study is to learn more about a drug called minocycline (study drug) in treating suspected bacterial infections. Minocycline will be referred to as the "study drug" throughout this form. We are hoping to learn more about the pharmacokinetics (PK) of the study drug. PK is a type of testing that measures the amount of the drug in your blood and tells the researchers how much time it takes for the drug to be absorbed into your body and how long it stays in your body after it has been absorbed.

DURATION:
The total duration of your participation is about 48 hours (2 days) after you are enrolled in the study. Your Investigator or study team may ask for you to participate in a follow-up visit.

PROCEDURES:
If you decide to participate, the study will involve:

- You will receive a single dose of the study drug through an intravenous infusion (IV)
- Investigator and study team will review your medical history and medications
- Assessments including physical exams and vital signs
- Blood and urine samples will be collected 7 times over the course of 48 hours. One sample will be collected prior to study drug administration and then at 1 hour, 4 hour, 12 hour, 24 hour, 36 hour, and 48 hours after you receive the study drug.

CO1450

- Investigator may ask you to participate in a follow-up examination after you complete the 48 hours study duration

RISKS:
The most common risks of the study drug are:

- Watery diarrhea
- Bloody stools
- Stomach Cramps
- Unusual headaches
- Blurred vision
- Fever
- Rash
- Joint pain
- Feeling very tired

BENEFITS:
You will not directly benefit from being in this research study. This study may help doctors and scientists learn things about the study drug that could help others in the future.

ALTERNATIVES:
You may choose not to participate in this study, and may receive standard treatment which may include other types of antibiotics for your infection.

This is a voluntary research study. You do not have to join the study. Even if you decide to join now, you can change your mind later. Please ask the Investigator if you have any questions about the study or about this consent form.

END OF CONSENT SUMMARY

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Clinical Research Consent and Authorization Form

TITLE: A Phase IV Open-Label Pharmacokinetic Study of Minocycline for Injection Following a Single Infusion in Critically-Ill Adults (ACUMIN)

PRINCIPAL INVESTIGATOR: Akram Khan, MD 503-494-1620

WHO IS PAYING FOR THE STUDY?:
The study is being conducted by the Antibiotic Resistance Leadership Group (coordinated by Duke University), which is funded by a grant from the National Institutes of Health (NIH). Portions of Dr. Akram Khan's salary and the doctor's research staff's salaries are being paid by the NIH grant.

The investigators, NIH, Duke University, Rempex Pharmaceuticals, Inc. Melinta Therapeutics Inc., and the FDA have the right to stop the study at any time.

WHO IS PROVIDING SUPPORT FOR THE STUDY?:
Rempex Pharmaceuticals, Inc., a wholly owned subsidiary of Melinta Therapeutics, Inc., will be responsible for providing the study drug.

WHY IS THIS STUDY BEING DONE?:

You have been invited to be in this research study because you have a known or suspected infection for which you are receiving intravenous antibiotics and are requiring intensive care.

This study is being done to learn more about the study drug, minocycline. The study drug is used to treat infections such as urinary tract infections, respiratory infections, and skin infections suspected to be caused by bacteria. The original IV formulation of minocycline was approved in the US on 26 October 1972. Rempex Pharmaceuticals, INC., has developed a new form of minocycline, which was approved by the FDA in 2015.

The purpose of this study is to examine the pharmacokinetics (PK) of the study drug. PK is a type of testing that measures the amount of the drug in your blood and tells the researchers how much time it takes for the drug to be absorbed into your body and how long it stays in your body after it has been absorbed. This study will require 7 blood draws over 48 hours. The blood for these blood draws will be used to determine the amount of study drug in your body and how long the study stays in the body after absorbed.

CO1450

Previous research studies with the study drug included healthy volunteers. This study will include patients who are in the intensive care unit or will be admitted to the intensive care unit. This research is important to doctors like yours because it can help your doctors understand how to use minocycline in the type of ill patients that are in this study.

Information and blood samples will be discarded 6 years after study closure. Your information and samples will not be stored and used for future research.

About 67 people at approximately 13 hospitals in the United States will take part in this study. Approximately 5 people at OHSU will participate in the study.

HOW LONG WILL I BE IN THIS STUDY?

The total duration of your participation is about 2 days after you are enrolled in the study. The investigator may ask for you to participate in a follow-up visit.

WHAT EXAMS, TESTS AND PROCEDURES ARE INVOLVED IN THIS STUDY?

If you decide to participate in the study, you will receive a single dose of the study drug through an intravenous infusion (IV) over the course of 60 minutes. You will have 7 blood draws over the course of 48 hours. You may be asked questions about how you are feeling to check to see if you experienced any side effects from the study drug. Weight, vitals, blood and urine will be collected during the study. You will also be asked questions about your medical history and medications. These procedures are outlined in the table below.

	Screening	After Enrollment (Hour 0)	Hour 1	Hour 4	Hour 12	Hour 24	Hour 36	Hour 48
Consent Discussion, Screening tests and Medical History	X							
Blood draw (1 Tablespoon)	X	X	X	X	X	X	X	X
Urine Collection	X							
Weight measurement		X				X		X
Vitals measured	X	X	X			X		X
Check current medications	X	X	X	X	X	X	X	X
Study Drug Infusion		X						
Doctor Assessment	X	X	X	X	X	X	X	X

You may also be asked to participate in a follow-up visit in addition to the procedures outlined in the table above.

Throughout your participation, additional blood samples may be drawn if the investigator considers it necessary for monitoring your health. Every effort will be made to get the study blood samples at the same time you have your hospital blood samples taken or to have blood withdrawn from one of your catheters (the tube that is inserted in one of your blood vessels), but there is a possibility that you may need to have a separate needle stick in order to get the study blood samples.

Screening:
If you agree to be in this study, you will be asked to sign this consent form. If you agree to participate in this research study and sign this consent form, the investigator and study staff will collect the following information about you to determine if you are able to take part in this study. This helps to ensure that participants are appropriate candidates. If you already have information in your medical records from your hospital visit, for example, height, a urine sample, and blood tests, they may be used in place of some of the screening procedures below. During this visit, the following will occur:

- Information about your age, gender, race and ethnicity will be collected.
- Your height and vital signs (like blood pressure, heart rate, breathing rate, and temperature) will be measured.
- You will have a physical exam which will focus on any places on your body that are causing any problems.
- Approximately 12mL of your blood (about Approximately1 tablespoon) will be collected. This blood will be used to perform common blood laboratory tests, for example to see how well your liver and kidneys are working.
- If you are a female with child bearing potential, a pregnancy test will be run as well. If you are pregnant, you will not be eligible to be enrolled in the study.
- You will be asked to provide a urine sample (Approximately ½ cup).
- Your medical history and recent medications will be reviewed for up to 2 weeks prior to enrolling in this study.

After Enrollment (Hour 0):
The following procedures will be completed after screening:

Prior to receiving the study drug:
- Approximately 6mL of blood (about 1.5 teaspoons) will be collected to measure the levels of study drug in your body
- Your weight and vital signs will be measured
- We will look at the medications you are receiving.
- Approximately 7mL of blood (about 1.5 teaspoons) will be collected. This blood will be used to check your magnesium level and how well your kidneys are working (creatinine). Other common lab tests (called hematology, blood chemistry, and liver function test) will also be conducted if the most recent results were collected more than 8 hours before you received the study drug.

You will then receive a single dose of the study drug through an IV. This will take about 60 minutes to complete.
- Your investigator will check to see if you experienced any serious side effects from the study drug.

At 1hr after the infusion was started (Hour 1):
- Approximately 6mL of blood (about 1.5 teaspoons) will be collected to measure the levels of study drug in your body.

- Approximately 5mL of blood (about 1 teaspoon) will be collected to measure your creatinine levels.
- Your vital signs will be measured.
- We will look at the medications and kidney treatments you are receiving.
- The investigator will check to see if you experienced any serious side effects from the study drug.

At 4hrs and 12hrs after the infusion was started (Hour 4 and Hour 12):

- Approximately 6mL of blood (about 1.5 teaspoons) will be collected at each time point to measure the levels of the study drug in your body.
- Approximately 5mL of blood (about 1.5 teaspoons) will be collected to measure your creatinine levels.
- We will look at the medications and kidney treatments you are receiving.
- Your doctor will check to see if you experienced any serious side effects from the study drug.

At 24hrs after the infusion was started (Hour 24):

- Approximately 6mL of blood (about 1.5 teaspoons) will be collected to measure the levels of the study drug in your body
- Approximately 7mL of blood (about 1.5 teaspoons) will be collected. This blood will be used to perform common blood laboratory tests, for example to see how well your kidneys are working.
- Your vital signs and your weight will be measured.
- We will look at the medications and kidney treatments you are receiving.
- Your doctor will check to see if you experienced any serious side effects from the study drug.

At 36hrs after the infusion was started (Hour 36):

- Approximately 6mL of blood (about 1.5 teaspoons) will be collected to measure the levels of the study drug in your body.
- Approximately 5mL of blood (about 1.5 teaspoons) will be collected to measure your creatinine levels.
- We will look at the medications and kidney treatments you are receiving.
- Your doctor will follow-up on any serious side effects from the study drug.

At 48hrs after the infusion was started (Hour 48):

- Approximately 6mL of blood (about 1.5 teaspoons) will be collected to measure the levels of the study drug in your body
- Approximately 7mL of blood (about 1.5 teaspoons) will be collected. This blood will be used to perform common blood laboratory tests, for example to see how well your liver and kidneys are working.
- Your vital signs and your weight will be measured.
- We will look at the medications and kidney treatments you are receiving.
- Your doctor will follow-up on any serious side effects from the study drug.

Follow up (as required by the Investigator):

A follow up visit may be required beyond your expected participation. Follow-up visits are conducted based on a decision by your Doctor and include follow up on any serious side effects from the study drug.

The investigator will determine what study procedures are completed during the follow up visit and may include:

- Measuring vital signs and conducting a physical exam.

- Looking at the medications you are receiving and have taken since your last visit.
- Drawing approximately 7mL of blood (about 1.5 teaspoons) and about 1/2 a cup of urine to perform laboratory tests (blood, urine, etc.) as required by your investigator.
- Follow-up on any serious side effects from the study drug that you may have experienced.

Your blood samples will not be stored and used for future research.

WILL I RECEIVE RESULTS FROM THE STUDY?

The information that will be collected could be a part of your medical record filed at Oregon Health & Science University. To maintain the integrity of this research study, you generally will not have access to your Protected Health Information related to this research until the study is complete. At the conclusion of the research and at your request, you generally will have access to your health information that Oregon Health & Science University maintains in a designated record set, which means a set of data that includes medical or billing records or other records used in whole or in part by your doctors or other health care providers at Oregon Health & Science University to make decisions about you. Access to your health information in a designated record set is described in the Notice of Privacy Practices provided to you by Oregon Health & Science University. If it is necessary for your care, your health information will be provided to you or your doctor.

WHAT RISKS CAN I EXPECT FROM TAKING PART IN THIS STUDY?:

We know that the study drug can have side effects. The following side effects have been reported in some participants taking the study drug.

The most common risks of the study drug are:

- Watery diarrhea
- Bloody stools
- Stomach Cramps
- Unusual headaches
- Blurred vision
- Fever
- Rash
- Joint pain
- Feeling very tired

The study drug may also cause:

- Central nervous system effects. Symptoms include light-headedness, dizziness, and a spinning feeling (vertigo). You should not drive or operate machines if you have these symptoms.
- Sun sensitivity (photosensitivity). You may get a worse sunburn with the study drug. Avoid sun exposure and the use of sunlamps or tanning beds. Protect your skin while out in the sunlight. Stop the study drug and call your doctor if your skin turns red.

Serious side effects with the study drug are rare. You should discuss these with the Investigator, and you may choose to talk with your regular health care provider, too. As with any treatment, all side effects cannot be totally predicted, and unforeseeable complications may occur.

Severe Allergic Reactions:

Rarely, infusion reactions and severe allergic reactions can be life-threatening or fatal. The study doctors will slow down or stop the IV infusion if you develop symptoms.

Potential Drug Interactions:

There are several drugs (prescription and non-prescription) that may cause problems when taken with the study drug. The investigator will carefully review all of the drugs you are taking before giving you the study drug. If any other health care provider prescribes any new drug(s) for you while you are in this study, please tell the investigator before you take the new drug. You could also have that provider talk to the investigator before prescribing the new drug. Do not take any new over-the-counter drugs while you are in this study unless you first check with the investigator.

Pregnancy/risk to fetus (For Women):
If you are nursing an infant or you are pregnant now, you must not be in the study. This study may involve risks to an embryo, fetus, or nursing infant that are currently unknown. If you are sexually active and could become pregnant, you and your male partner(s) must use birth control that works well or you must not have sex. The investigator will talk to you about the types of birth control that are acceptable. You will have to do this the whole time you are in this study. If you become pregnant during the research study, please tell the investigator and your doctor immediately. If you become pregnant, the study drug will be stopped immediately and we will request to monitor your pregnancy until the baby is born.

Risks of Drawing Blood and Blood Testing:
We will draw blood from your arm. You may feel some pain when your blood is drawn. There is a small chance the needle will cause bleeding, a bruise, an infection, or fainting.

Risks of Study Drug Infusion:
The study drug is administered through an IV catheter which is a small, flexible hollow tube inserted into a vein in your arm. Typically the tube remains in your arm even after you have received the study drug. Inserting an IV requires a needle and can cause localized discomfort. During IV infusion you are unlikely to feel discomfort, but will be asked to keep your arm still remain in a resting position during dosing (approximately 1 hour). In some instances the vein may develop a small rupture causing the Study Drug to leak out of the vein. This is generally not dangerous, but can cause discomfort and bruising.

WHAT ARE MY CHOICES IF I DECIDE NOT TO TAKE PART IN THIS STUDY?

You may choose not to be in this study. You do not have to be in this study to receive treatment for your infection. If you do not participate in this study, you will continue to receive standard treatment for your condition. This may include the use of other antibiotics to treat your infection. Your investigator can let you know what alternative treatments are available.

WHO WILL SEE MY PERSONAL INFORMATION?

We will take steps to keep your personal information confidential, but we cannot guarantee total privacy. Our study records will be kept as confidential as possible. You will be assigned a code number, and your Protected Health Information will be associated with that number and not your name for this study to ensure confidentiality.

We will create and collect health information about you as described in the “WHY IS THIS STUDY BEING DONE?” and the “WHAT EXAMS, TESTS AND PROCEDURES ARE INVOLVED IN THIS STUDY?” sections of this form. Health information is private and is protected under federal law and Oregon law. By agreeing to be in this study, you are giving permission (also called authorization) for us to use and disclose your health information as described in this form.

The investigators, study staff, and others at OHSU may use the information we collect and create about you in order to conduct and oversee this research study.

We may release this information to others outside of OHSU who are involved in conducting or overseeing research, including:

- The funder of this study, National Institute of Health (NIH), and the funder's representatives
- The sponsor of this study, Division of Microbiology and Infectious Diseases (DMID) at National Institute of Allergy and Infectious Disease (NIAID) and its representatives
- The Office for Human Research Protections, a federal agency that oversees research involving humans
- Duke Clinical Research Institute, the research organization that is managing this study, and their collaborators
- The U.S. Food and Drug Administration (FDA) and the U.S. Department of Health and Human Services (DHHS)
- Rempex Pharmaceuticals, INC., and individuals associated with Rempex Pharmaceuticals, INC.

Those listed above may also be permitted to review and copy your records, including your medical records.

We will not release information about you to others not listed above, unless required or permitted by law. We will not use your name or your identity for publication or publicity purposes, unless we have your special permission.

To help us protect your privacy, we have obtained a Certificate of Confidentiality to protect your privacy even from people who try to get your information using a court order. One exception is if you agree that we can give out research information with your name on it. Another exception is information about child or elder abuse or neglect and harm to yourself or others or communicable disease reporting. Note that this doesn't prevent you from releasing the information yourself.

Under Oregon law, suspected child or elder abuse must be reported to appropriate authorities.

OHSU complies with Oregon state requirements for reporting certain diseases and conditions to local health departments.

When we send specimens or information outside of OHSU, they may no longer be protected under federal or Oregon law. In this case, your specimens or information could be used and re-released without your permission.

Your name, date of birth, and social security number may be provided to the study funder (or an organization acting on their behalf) so the funder can meet Medicare reporting requirements.

We may continue to use and disclose your information as described above indefinitely.

Some of the information collected and created in this study may be placed in your OHSU medical record. While the research is in progress, you may or may not have access to this information. After the study is complete, you will be able to access any study information that was added to your OHSU medical record. If you have questions about what study information you will be able to access, and when, ask the investigator.

WILL ANY OF MY INFORMATION OR SAMPLES FROM THIS STUDY BE USED FOR ANY COMMERCIAL PROFIT?

Samples and data about you or obtained from you in this research may be used for commercial purposes, such as making a discovery that could, in the future, be patented or licensed to a

company, which could result in a possible financial benefit to that company, OHSU, and its researchers. There are no plans to pay you if this happens. You will not have any property rights or ownership or financial interest in or arising from products or data that may result from your participation in this study. Further, you will have no responsibility or liability for any use that may be made of your samples or information.

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?

Some of the services or items in this study are part of the regular treatment for your condition. These would be performed or used even if you were not in this study. The costs for these services or items will be billed to your insurance. You will be responsible for any costs your insurance does not cover. If you have any questions about these costs, or what out-of-pocket expenses you may be responsible for, contact your insurance company. If you are uninsured, you will be responsible for these costs.

You will not be billed for the costs of any services or procedures that are required by the study but are not considered part of your regular treatment.

WHAT HAPPENS IF I AM INJURED BECAUSE I TOOK PART IN THIS STUDY?:

If you believe you have been injured or harmed as a result of participating in this research and require treatment, contact Akram Khan, MD at 503-494-1620.

If you are injured or harmed by the study drug, you will be treated. OHSU and the NIH do not offer any financial compensation or payment for the cost of treatment if you are injured or harmed as a result of participating in this research. Therefore, any medical treatment you need may be billed to you or your insurance. However, you are not prevented from seeking to collect compensation for injury related to negligence on the part of those involved in the research. Oregon law (Oregon Tort Claims Act (ORS 30.260 through 30.300)) may limit the dollar amount that you may recover from OHSU or its caregivers and researchers for a claim relating to care or research at OHSU, and the time you have to bring a claim.

If you have questions on this subject, please call the OHSU Research Integrity Office at (503) 494-7887.

This federally funded study also does not have the ability to provide compensation for research-related injury. If you are injured or become ill from taking part in this study, it is important to tell the investigator. Emergency treatment may be available but you or your insurance company will be charged for this treatment.

WHERE CAN I GET MORE INFORMATION?

If you have any questions, concerns, or complaints regarding this study now or in the future, contact Dr. Akram Khan (503) 494-1620 or other members of the study team at (503) 494-6994.

This research has been approved and is overseen by an Institutional Review Board (“IRB”), a committee that protects the rights and welfare of research subjects. You may talk to the IRB at (503) 494-7887 or irb@ohsu.edu if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research subject.
- You want to get more information or provide input about this research.

You may also submit a report to the OHSU Integrity Hotline online at https://secure.ethicspoint.com/domain/media/en/gui/18915/index.html or by calling toll-free (877)

733-8313 (anonymous and available 24 hours a day, 7 days a week).

DO I HAVE TO TAKE PART IN THIS STUDY?

Your participation in this study is voluntary. You do not have to join this or any research study. You do not have to allow the use and disclosure of your health information in the study, but if you do not, you cannot be in the study.

Your health care provider may be one of the investigators of this research study and, as an investigator, is interested in both your clinical welfare and in the conduct of this study. Before entering this study or at any time during the research, you may ask for a second opinion about your care from another doctor who is in no way involved in this project. You do not have to be in any research study offered by your physician.

IF I DECIDE TO TAKE PART IN THIS STUDY, CAN I STOP LATER?

If you do join the study and later change your mind, you have the right to quit at any time. This includes the right to withdraw your authorization to use and disclose your health information. If you choose not to join any or all parts of this study, or if you withdraw early from any or all parts of the study, there will be no penalty or loss of benefits to which you are otherwise entitled, including being able to receive health care services or insurance coverage for services. Talk to the investigator if you want to withdraw from the study. If you withdraw from the study, we may contact you about the reason that you withdrew.

If you no longer want your health information to be used and disclosed as described in this form, you must send a written request or email stating that you are revoking your authorization to:

Akram Khan, MD
khana@ohsu.edu
3181 Sam Jackson Park Road
Portland, OR 97239
United States
503-494-1620

Your request will be effective as of the date we receive it. However, health information collected before your request is received may continue to be used and disclosed to the extent that we have already acted based on your authorization.

The data and samples we will collect from you will be provided to the funder. It will be stored with a coded identifier to protect your privacy. Once provided to the funder, we will not be able to destroy your samples or data if you decide in the future you do not wish to participate in the research.

You may be removed from the study if you have an unexpected reaction to the study drug or do not follow the study instructions or the entire study has been stopped.

We will give you any new information during the course of this research study that might change the way you feel about being in the study.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. law. This web site will not include information that can identify you. At most, the web site will include a summary of the results. You can search this web site at any time.

SIGNATURES:

Your signature below indicates that you have read this entire form and that you agree to be in this study.

We will give you a copy of this signed form.

Subject Name (Print)		Subject Signature	Date	Time
Name of Legally Authorized Representative (Print)	Relationship to Patient	Signature of Legally Authorize Representative	Date	Time
Name of Person Obtaining Consent (Print)		Signature of Person Obtaining Consent	Date	Time