INFORMED CONSENT FORM
AND
AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

Sponsor / Study Title:	**National Institutes of Health (NIH)/Division of Microbiology and Infectious Diseases (DMID) / "A Phase 4 Study of a 3-Day vs. 7-Day Regimen of Doxycycline for the Treatment of Chlamydial Infection"**
Protocol Number:	**22-0019**
Principal Investigator:	**«PiFullName»**
Telephone:	**«IcfPhoneNumber»**
Address:	**«PiLocations»**

Key Information about This Research

You are being invited to be part of a research study, please read this form carefully. This form gives you information to help you decide whether to be in the study. Being in the study is voluntary.

Why is this study being done?

Doxycycline is the recommended US Food and Drug Administration (FDA) approved treatment for chlamydia (CT) in most places. This research study is studying if a 3-day course of doxycycline works as well as the recommended 7-day course of treatment for chlamydia.

This study is funded by the National Institutes of Health (NIH), National Institute of Allergy and Infectious Diseases (NIAID), Division of Microbiology and Infectious Diseases (DMID), Infectious Diseases Clinical Research Consortium (IDCRC) and is being conducted at 5 study sites in the USA and 2 study sites in Kenya. About 664 total participants will be enrolled.

Do you have to be in the study?

You are being invited to be part of a research study because you are in general good health, 16 years old or older and have been diagnosed with CT. Participation is voluntary and if you choose not to take part, you will still receive the standard of care treatment for CT.

What do I have to do if I choose to participate in this study?

You will be in the study for about 29 days. You will be randomly assigned by chance (like the flip of a coin) to a 3-day regimen of doxycycline or a 7-day regimen of doxycycline. You will receive pills to take twice each day for 7 days. Neither you nor the investigators study team will know whether all of the pills include the study drug or only the pills for the first 3 days. You will have

a 50% (1 in 2) chance of receiving either regimen, and you will not know which regimen you received.

You will have at least 2 study visits. These include 1-2 screening visits, enrollment visit and 1 final study visit. The final study visit will occur 28 days after you receive the study drug. If necessary, there may be an unscheduled visit to check on you. During the study visits, you will be asked questions and complete questionnaires about your medical and medication history and sexual behaviors. You will also have swabs collected from your rectum (butt) and/or vagina, or be asked to give a urine sample. A study clinician may also do a physical exam.

How is this study going to help you?
If you are in the study, you may benefit from additional clinical care and testing provided in the study. You will also be helping the researchers answer the study question.

What are the risks or discomforts I should know about before making a decision?
All studies have some risks. The primary risk in this study is the possibility that your CT infection may worsen if the 3-day study treatment does not work as well as the 7-day study treatment. If your infection has not cleared by day 29, you will receive the standard-of-care treatment for CT.

All participants will have a rectal (butt) swab collected. This is a swab (like a Q-tip or cotton bud) inserted into your rectum. These samples will either be self-collected (collected by you) or collected by a clinician. Insertion of the swab into the rectum may cause brief discomfort. Some participants will also collect a vaginal swab (like a Q-tip or cotton bud). These samples will either be self-collected (collected by you) or collected by a clinician. Insertion of the swab into the vagina may also cause brief discomfort. Answering questions about your medical history or sexual behaviors may make you feel uncomfortable, but you can skip any questions you do not wish to answer. Other risks include loss of privacy, and breach of confidentiality. A full list of expected risks, their frequency and severity are detailed in the "Potential risks and discomforts" section below.

Costs
You WILL NOT have to pay for any of the research tests, study procedures and study product. There is more information in the cost section below.

What Should You do Next?
The remaining sections describe more about the research study. You are encouraged to ask any questions and discuss this study with family, friends, and anyone you choose. Take your time to ask the study doctor or study staff as many questions about the study as you would like. The study doctor or study staff can explain words or information that you do not understand.

Reading this form and talking to the study doctor or study staff may help you decide whether to take part or not. If you decide to take part in this study, you will be asked to sign and date this consent form. A copy of this signed and dated consent will be given to you to keep. Signing and

dating this consent form shows that you understand your involvement in the study, the risks of participating and that you agree to take part in the study.

Purpose of this Research Study

Chlamydia is the most common STI (sexually transmitted infection) in the world. There is a treatment for chlamydia (an antibiotic called doxycycline) that is safe and works well to treat chlamydia. People who are diagnosed with chlamydia are asked to take doxycycline twice a day for 7 days. It is possible that people can take doxycycline for less than 7 days to clear the infection. In this study we are trying to figure out if taking doxycycline for 3 days works as well as taking doxycycline for 7 days. You are being asked to take part in this study to help us answer this question. If the researchers find out that 3 days of study treatment works as well as 7 days of study treatment, it might help more people finish their treatment.

This is a blinded, randomized, placebo-controlled, non-inferiority trial. Blinded means that you and the study staff members that will be working with you during the study will not know which study treatment you were assigned to until after the study is over for all participants. Randomized means that the assignment of participants to either the 3-day or 7-day will be random (assigned by chance). A "Placebo" has no active drug but looks the same as the study drug. Placebo-controlled means that some participants will receive either 7 days of doxycycline or 3 days of doxycycline and 4 days of pills that look the same but do not contain any active drug. Non-inferiority means that we are trying to figure out whether the new regimen is "no worse than" the standard treatment.

What will happen during the study?

To qualify for this study, you must:

- Have a positive test result for CT and have not yet been treated.
- Be at least 16 years of age or older with valid contact information
- Be willing and able to understand and provide written informed consent before initiation of any study procedures
- Be willing to complete a 7-day study drug regimen
- Be willing to abstain from condomless anal or vaginal sex during the trial
- Be willing and able to comply with planned study procedures for all study visits

Screening/Enrollment/Baseline/Visit 1 (Day 1):

Screening, enrollment, and assignment of study treatment will happen at the baseline visit/Visit 1. During the screening, the study staff will talk with you to check if you are eligible to enroll in this study. Before any study-related tests and processes are performed, you will be asked to read, sign, and date this consent document.

The following screening test and processes will be performed to decide if you qualify to take part in this study:

- We will collect demographic information from you. This includes information like your age and race.

- We will collect contact information for follow-up and study visit reminders.
- We will collect information about your targeted medical history, sexual and STI history, sexual behaviors, therapies, medications.
- The study clinician may conduct an exam of your butt, groin area, and stomach.
- If you are a woman and able to be pregnant, we will collect a urine sample from you (ask you to pee in a cup) to do a pregnancy test. We will also ask you some questions about when your last menstrual period was.

If you qualify to take part in the study, the following will happen:

- We will ask all participants to provide some samples. These samples will either be self-collected (collected by you) or collected by a clinician. If you are a woman, we will collect 2 vaginal samples and 2 rectal samples. If you are a man, we will collect a urine sample (ask you to pee in a cup) and 3 rectal samples. Getting the rectal samples involves inserting a small swab (like a Q-tip or cotton bud) into your butt. Getting the vaginal samples involves inserting a small swab (like a Q-tip or cotton bud) into your vagina. These samples will be tested for CT in the laboratory.
- If there are leftover samples, these may be frozen and stored for secondary research.
- Identifiers (such as barcodes, your name, and study number) might be removed from your data or samples and could be used for future research studies or sent to another investigator for other research studies without additional informed consent. You will have the opportunity to decide if you want to give consent to store your data and samples with codes, to be used for secondary research. You can read more about this in the section "Secondary Research Using Identifiable Data and Samples" below.
- You will be given a study drug adherence log and asked to mark each day that you take the study drug. You will also be asked to return the log at your follow-up visit.

Study Treatment:

You will receive pills to take by mouth twice daily for 7 days. You will be randomly assigned by chance (like the flip of a coin) to receive either:

1) 3 days of doxycycline (100 mg doxycycline by mouth twice daily) plus 4 days of placebo (1 placebo tablet by mouth twice daily) (these are pills that look like the study drug but do not contain any active drug)
   OR
2) 7 days of doxycycline (100 mg doxycycline by mouth twice daily).

Neither you nor the investigators will know whether all of the pills include the study drug or only the pills for the first 3 days. You will have a 50% (1 in 2) chance of receiving either regimen study treatment. This is a double-blind study, which means neither you nor the Investigators will know to which of these study groups you are assigned.

Unscheduled Visits

You may be asked to come back to the study site at other times if needed, for example, if you have a symptoms or illness that should be evaluated before the next scheduled visit. The study

doctor will decide what activities will be needed after reviewing any symptoms that you are having.

Final Study Visit (Day 29):
At the final study visit the following will happen:

- We will collect information about your focused medical history, sexual and STI history, sexual behaviors, therapies, medications.
- We will ask you questions about how much study drug you took and review the study drug adherence log.
- We will ask all participants to provide some samples. These samples will either be self-collected (collected by you) or collected by a clinician. In addition to the samples described below, we may collect additional samples as needed for clinical (non-research) testing.
- If you are a woman, we will collect 2 vaginal samples and 2 rectal samples.
- If you are a man, we will collect a urine sample (ask you to pee in a cup) and 3 rectal samples.
- Getting the rectal samples involves inserting a small swab (like a Q-tip or cotton bud) into your butt.
- Getting the vaginal samples involves inserting a small swab (like a Q-tip or cotton bud) into your vagina.
- We will physically examine your butt, groin area, and stomach depending on your symptoms.

We will test your samples for CT. If your samples test positive for CT, we will contact you to let you know about your results, will provide you with treatment or will arrange for you to get treatment for CT. Where applicable, we will also report this positive test result to the local health department, as required by state law. If you do not test positive for CT we will not contact you with the test results. The test we use to determine whether you have chlamydia might also tell us if you have another STI. If your test comes back positive for another STI, we will let you know the result and you will be provided with treatment by the study staff or referred for treatment.

If there are leftover samples, these may be frozen and stored for secondary research. You will have the opportunity to decide if you want to give your samples for secondary research. You can read more about how to in the section "Secondary Research" below.

Expectations
If you take part in this study, you will be expected to:

- Follow the instructions you are given.
- Take the study drug as directed.
- Come to the study site for all study visits.
- Tell us about any changes in your health or the way you feel.
- Tell us if you want to stop taking part in this study at any time.

Potential Risks and Discomforts

The primary risk in the study is if the 3-day study treatment is less effective than the 7-day study treatment. There is a potential risk for the infection to persist due to shorter duration of treatment. If your infection has not cleared by day 29, you will receive the standard of care treatment for CT.

Doxycycline is an approved drug for the treatment of chlamydia and is generally well-tolerated. Potential side effects could include:

- Nausea, vomiting, diarrhea or abdominal pain
- Difficulty swallowing (pill esophagitis)
- Sensitivity to sunlight (easier to sunburn)
- Skin rash
- Other possible but rare side effects include: intracranial hypertension, blood cell disorders, pericarditis (heart inflammation) or a rare, potentially life-threatening and severe allergic skin reaction (Stevens-Johnson syndrome)

Other risks may include:

- The collection of study swabs from the rectum and vagina may result in temporary physical discomfort.
- The questionnaires used in this study may ask sensitive questions about your medical history and your sexual history. These questions may make you uncomfortable and may cause you some stress. You do not need to answer any questions that you are not comfortable with.
- Participation in research may involve a loss of privacy. Your records will be kept as confidential as possible under the law. Individual identity will not be used in any reports or publications resulting from this trial. Reporting sexual abuse or assault if you are under 18 years of age is required by law and will become part of your medical record, but not your research record.

There is a risk of loss of confidentiality of your information. You will read more about the protection of your information later in this consent form. Please ask us if you would like to know more about how your information will be protected while you are in this study.

Unforeseen Risks

There may be risks and discomforts we do not know about right now. It is possible that we will learn new information on the risks and discomforts of being in this study. If this happens, the study clinician will tell you about them. Then you can decide if you want to continue to be in this study or not.

Alternatives to Participating in This Study

You do not have to be in this study to receive treatment for chlamydia. Please talk to the study doctor about your options before you decide whether or not you will take part in this study.

Voluntary Participation and Early Withdrawal from the Study

Your decision to take part in this study is voluntary. You may choose to not participate or you may withdraw from the study for any reason without penalty or loss of benefits to which you are otherwise entitled and without any effect on your future medical care. Whether or not you choose to take part in this study has no impact on the care you receive in this study site today or in the future. You can decide to stop your study participation at any point. That said, we will continue to use any information from your participation in this study up to the point you withdraw from the study. If you do decide to stop your study participation, we will ask you to please notify the study staff about this.

The Investigator or the sponsor can stop your participation at any time without your consent for the following reasons:

- If it appears to be medically harmful to you;
- If you fail to follow directions for participating in the study;
- If it is discovered that you do not meet the study requirements;
- If the study is canceled; or
- For administrative reasons.

If you leave the study for any reason, the Investigator may ask you to have some end-of-study tests for your safety.

New Findings

Any new important information that is discovered during the study and which may influence your willingness to continue participation in the study will be provided to you.

Benefits

You may not get direct benefit from being in this study. You may benefit from additional clinical care and testing provided in the study. Society will benefit from knowledge of effective treatment for CT and whether fewer days of antibiotics may be as effective as 7 days.

Compensation for Participation

«Compensation»

You will be paid up to a total of $xxx if you complete this study. You will be paid for the visits you complete according to the following schedule:

- $xxx for Visit 1 (enrollment)
- $xxx for the final follow-up visit (day 29)
- $xxx if you are asked to come for an extra (unscheduled) visit

You will be paid following each completed visit. If you have any questions about your compensation for participation, please contact the study staff.

Costs

There will be no charge to you for the research tests, procedures, and study product while taking part in this study. Procedures and treatment for clinical care may be billed to your insurance or third party.

Research-Related Injury

If you become ill or are injured while you are in the study, get the medical care that you need right away. You should inform the healthcare professional treating you that you are taking part in this study. If you tell the study staff that you think you have been injured then they will help you get the care you need. If you experience a research-related illness or injury, you and/or your medical hospital insurance carrier will be responsible for the cost of treatment.

In general, no long-term medical care or financial compensation for research-related injuries will be provided by the NIH or the Federal Government. By signing and dating this document, you will not lose any of your legal rights or release anyone involved in the research from responsibility for mistakes.

Certificate of Confidentiality

To help us protect your privacy, we have a Certificate of Confidentiality (Certificate) from the NIH. Study staff cannot provide to any person not connected with the research your name, or any materials that have identifiable, sensitive information about you, unless permitted by a legal exception, such as state and national laws that require reporting of some contagious diseases. The most important protection provided by the Certificate is that the study staff cannot be forced to provide any of your identifiable, sensitive information, in any Federal, State, or local civil, criminal, administrative, legislative, or other proceeding, such as if there is a court subpoena, without your permission.

The study staff will use the Certificate to resist any demands for information that would identify you.

Your information protected by the Certificate may still be disclosed or used when the information:

1. is disclosed to people connected with the research; for example, information may be used for auditing or program evaluation internally by the NIH; or
2. is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the FDA. This does not include disclosure for use during legal proceedings as noted above;
3. is necessary for your medical treatment and you have consented to this disclosure;
4. is for other scientific research as allowed by applicable federal regulations;
5. is disclosed with your consent.

The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing and dating below you

consent to those disclosures. As previously noted, reporting sexual abuse or assault if you are under 18 years of age is required by law and will become part of your medical record, but not your research record.

Confidentiality

Paper documents containing personal information about you will be kept in locked file cabinets. Computerized information will be kept in password-restricted files. Information from this study will be placed into a research database. A study number, rather than your name, will be used on study records. Only people who are involved in the conduct, oversight, or auditing of this study will be allowed access.

By signing and dating this consent form you are giving permission for representatives of the NIH, NIAID, the Office for Human Research Protections (OHRP), and the Advarra IRB (a group of people who review research studies to protect the rights and welfare of research participants), as well as the study clinician and other employees of the study site involved with this research study, to inspect sections of your medical and research records related to this study. While every effort will be made to protect the confidentiality of your information, absolute confidentiality cannot be guaranteed.

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.

Whom to Contact About This Study

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study such as:

- Whom to contact in the case of a research-related injury or illness;
- Payment or compensation for being in the study, if any;
- Your responsibilities as a research participant;
- Eligibility to participate in the study;
- The study doctor's or study site's decision to withdraw you from participation;
- Results of tests and/or procedures;

Please contact the study Principal Investigator at the telephone number listed on the first page of this consent document.

If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research subjects. If you have any questions about your rights as a research subject, contact:

- By **mail**:
  Study Subject Adviser
  Advarra IRB
  [redacted]
- or call **toll free**: [redacted]
- or by **email**: [redacted]

Please reference the following number when contacting the Study Subject Adviser: Pro00070076.

Secondary Research Using Identifiable Data and Samples

After all tests required for this study are done and if you say "Yes" below, we will save leftover samples for possible secondary research for sexually transmitted infections instead of throwing them away. Secondary research is research that is not part of this study but will be performed in the future. You will not be told about the secondary research and you will not be notified of any results from future research**.** Some examples of future research that may be done include tests to see if there are any byproducts of CT present in the sample.

Leftover samples saved for secondary research will be stored indefinitely by the Sponsor or at the institution where they were collected. Samples will be labeled with a barcode and an ID (not with your name, initials, or any other information that could easily identify you). The research staff will maintain a link, also called a code key, with your name that links to your ID code or barcode on your information or samples. This link is not shared with anyone outside this institution who receives your information or samples.

These samples saved for secondary research could be used for secondary research studies or distributed to another investigator for secondary research studies without additional informed consent. If these samples are tested in the future, the results may be published. You will not be identified in such publication. In other words, the publication will not have any information about you that would enable someone to determine your identity.

There are no benefits to you in the collection, storage and secondary research use of your samples. The results of any future research testing will be kept confidential in the same way as the results of other testing done for this study. The results of any future research will not be available to you or your regular doctor and will not be placed in your medical record.

You will not share in the commercial profit if your specimens provided for this study lead to a licensed product.

No human genetic testing will be done as part of this study.

You may change your mind about secondary research and withdraw consent for the storage and use of your coded samples or information at any time. You will need to contact the study clinician using the contact information listed on page 1 of this form. Research that has already begun using your samples cannot be withdrawn. For example, if some research with your samples and data has already been completed, the information from that research may still be used. Also, for example, if the samples and data have been shared already with other researchers, it might not be possible to withdraw the samples and data.

Please talk to the study staff if you have any questions about how your samples may be used.

Do you agree to allow your coded data and leftover samples to be stored and used for secondary research for sexually transmitted infections?

☐ Yes

☐ No

Please include your initials: Date:

CONSENT

I have read and understand the information in this informed consent document. I have had an opportunity to ask questions and all of my questions have been answered to my satisfaction. I voluntarily agree to take part in this study until I decide otherwise. I do not give up any of my legal rights by signing and dating this consent document. I will receive a copy of this signed and dated consent document.

_____
Subject's Printed Name

_____ _____ _____
Subject's Signature Date Time

_____
Printed Name of the Person Conducting the Consent Discussion

_____ _____ _____
Signature of the Person Conducting the Consent Discussion Date Time

WITNESS SIGNATURE FOR SUBJECTS WHO CANNOT READ

The study subject has shown that he/she is unable to read. The consent document has been read to the subject by a member of the study staff, discussed with the subject by a member of the study staff, and the subject has been given an opportunity to ask questions of the study staff.

_____
Printed Name of Impartial Witness

_____ _____
Signature of Impartial Witness Date Time

AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

Federal regulations give you certain rights related to your health information. These include the right to know who will be able to get the information and why they may be able to get it. The study doctor must get your authorization (permission) to use or give out any health information that might identify you (protected health information).

What information may be used and given to others?

If you choose to be in this study, the study doctor and study staff will get personal information about you. This will include information that might identify you, such as your name and address. The study staff will also get information about your health including:

- Past and present medical records. If you receive regular care at the study site, the study staff will periodically review your medical record to identify new health events, medications. The information reviewed will include study visit notes, hospitalization records, email exchanges with providers, laboratory results, medication prescriptions. If you receive regular care at the study site, we may ask you for a release of information to obtain your medical records if you have a new health event or if we need additional information about your health and medications
- Research records
- Records about phone calls made as part of this research
- Records about your study visits
- Information obtained during this research

Who may use and give out information about you?

Information about your health may be used and given to others by the study doctor, the study staff, and the research center, both during and after the study.

Who might get this information?

Your information may be given to the sponsor of this research. “Sponsor” includes any persons or companies that are working for or with the sponsor and any companies that are owned by the sponsor. The sponsor of this research study is the NIH and IDCRC. For this study, “sponsor” also includes FHI360 and ICON, agents for the sponsor.

Information about you and your health which might identify you may be given to:

- DMID
- NIAID
- IDCRC
- Department of Health and Human Services (DHHS) agencies
- The OHRP
- Additional governmental agencies in the United States or other countries
- Advarra IRB
- Your regular doctor (If you receive regular care at the study site)
- A public health authority that is authorized by law to collect or receive such information for the purpose of preventing or controlling disease, injury, or disability, and conducting public health surveillance, investigations, or interventions

If you sign and date this form, you allow the study doctor to share your records with your health care payer to resolve your claim if you are hurt because of being in this study. If this happens, the study doctor or the sponsor may share your records with their insurance carriers to resolve your insurance claim, and the study doctor may also request medical records from your other health care providers to learn more about your condition.

<u>Why will this information be used and/or given to others?</u>
Information about you and your health that might identify you may be given to others to carry out the research study. The sponsor will analyze and evaluate the results of the study. In addition, employees of the sponsor and its consultants will be visiting the study site. They will follow how the study is done, and they will be reviewing your information for this purpose. The information may be given to the DMID. It may also be given to other governmental agencies in the United States or other countries.

The information may also be used to meet the reporting requirements of governmental agencies. The Advarra IRB may also use records to check how researchers are doing the study, the study information, and participants' safety.

The results of this research may be published in scientific journals or presented at medical meetings, but your identity will not be disclosed.

Please note that the study doctor or study staff may share personal information about you if required by law. For example, if the study doctor or study staff suspects that you are going to harm someone or yourself. If you have questions about this, please ask the study doctor or study staff.

What if I decide not to give permission to use and give out my health information?

By signing and dating this authorization, you are giving permission to use and give out the health information listed above for the purposes described above. If you refuse to give permission, you will not be able to be in this research study.

May I review or copy the information obtained from me or created about me?

You have the right to review and copy your health information as held by the study doctor and study staff. However, if you decide to be in this study and sign and date this authorization form, you will not be allowed to look at or copy your information until after the research is completed.

May I withdraw or revoke (cancel) my permission?

Your permission to use and share health data about you will end in 50 years unless you revoke it (take it back) sooner.

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending a written notice to the study doctor at the address listed on the first page of this form. If you withdraw your permission, you will not be able to continue being in this study.

When you withdraw your permission, no new health information which might identify you will be gathered after that date. Information that has already been gathered may still be used and given to others. This would be done if it were necessary for the research to be reliable.

Is my health information protected after it has been given to others?

If you give permission to give your identifiable health information to one of the entities listed above, the information may no longer be protected. There is a risk that your information will be released to others without your permission.

If you agree to be in this study, you will receive a signed and dated copy of this consent form for your records.

STATEMENT OF AUTHORIZATION

I have read this form and its contents were explained. My questions have been answered. I voluntarily agree to allow study staff to collect, use and share my health data as specified in this form. I will receive a signed and dated copy of this form for my records. I am not giving up any of my legal rights by signing and dating this form.

_____
Printed Name of Subject

_____ _____
Signature of Subject Date Time

WITNESS SIGNATURE FOR SUBJECTS WHO CANNOT READ

The study subject has indicated that he/she is unable to read. This Authorization document has been read to the subject by a member of the study staff, discussed with the subject by a member of the study staff, and the subject has been given an opportunity to ask questions of the study staff.

_____
Printed Name of Impartial Witness

_____ _____
Signature of Impartial Witness Date Time