RA-2022-015

THE QUEEN'S MEDICAL CENTER
HONOLULU, HAWAII

INFORMED CONSENT TO TAKE PART IN A CLINICAL RESEARCH STUDY

Title of Study: *Exploring the effects of an intravaginal lactic acid gel on the vaginal microbiome*

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Sponsor:
University of Hawaii Foundation, Sharma Fund
1314 South King Street, Suite B
Honolulu, HI 96814

SUMMARY of KEY INFORMATION

- You are being asked to take part in a research study because you have been diagnosed with either bacterial vaginosis or yeast infections two or more times this year. This consent form has important information to help you decide if you want to join the study or not. Taking part in this is voluntary.

- The purpose of the study is to learn if Phexxi, an intravaginal gel used for birth control, causes any changes to the vaginal microbiome. We believe that by influencing the vaginal microbiome (or normal bacteria that live in the vagina) with an acidic environment, we can help encourage the growth of more acid-producing bacteria in the vagina. These bacteria help to maintain balance in the vagina, preventing the overgrowth of organisms such as yeast and other organisms. If Phexxi does help encourage more growth of these "good" bacteria, we may do future research to determine if this product can reduce the number of BV or yeast infections a patient experiences each year.

- Taking part in this includes 1 in-clinic visit over 60 days, which is today's visit

- This study involves filling out multiple surveys, as well as swabbing your vagina with a cotton swab at home three times over the course of 60 days. For the intervention, you will be inserting a gel into your vagina, using a prepackaged applicator that is similar to a tampon.

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- Potential Risks: While using this study medication, you are at risk for the following side effects. Not everyone who uses these products experiences any or all of these side effects, but they are possible. If you experience these side effects, you will be given medications to make them less serious and uncomfortable. You or your health insurance will be billed for these medications. Many side effects go away as soon as you stop the study medication, but, in some cases, the side effects may be serious and/or lasting.
    - Vaginal burning, itching

- Abnormal vaginal discharge
- Vaginal discomfort or pain
- More detailed information about the risks of this study can be found under the "Risks" section.

- Potential Benefits
  - We cannot promise any benefits from taking part in this study. However, possible benefits may include a decrease in the number of yeast infections or episodes of bacterial vaginosis you have per year.

- Cost for Participation

  - There is no cost to you to participate in this study.However, if you develop side effects from the study drug while taking part in this study and choose to seek medical treatment for them, you will be responsible for using your health insurance carrier to cover the costs of this medical treatment.
  - The study drugs, Phexxi, will be provided by the sponsor. There are some procedures/tests that will be done only because you are taking part in a research study; these will be paid for by the sponsor. If there will be other visits/procedures/tests that would normally be done even if you were not taking part in a research study; and these will be billed to you and your insurance company along with the usual co-pay/deductibles.

- Even if you decide to take part in this study now, you can decide to stop taking part at any time in the future.

- You will be told if there are any changes to the study in the future that might change your decision to take part.

END OF KEY INFORMATION SUMMARY

INFORMED CONSENT

You are being asked to take part in this research study *because you have been diagnosed with either bacterial vaginosis or yeast infections two or more times this year.* This is a research study that will seek to identify if a vaginal contraceptive called Phexxi can change the microbiome of the vagina.

Before you decide whether or not to take part in this study, you must understand the purpose, how it may help, any risks, and what you have to do. This process is called informed consent. The researcher(s) will talk with you about the study and the informed consent form. The consent also gives you information about what health information will be collected as part of the research study and how that information will be used or disclosed. Once you understand the study, and if you agree to take part, you will be asked to sign this consent form. If you sign this form you are agreeing to take part in this study and to allow the use and disclosure of your medical records and health information collected in connection with your part in this study. You will be given a **signed** copy to keep. If you do not sign this consent form, you will continue to receive care, but not as part of this study."

Before you learn about the study, it is important that you know the following:
- Taking part in this study is of your own free will.
- You may decide not to take part in the study or stop being in the study at any time without it making any difference to your care now or in the future, or to any benefits that you are allowed.

- If the study changes in any way which could make a difference to your taking part, you will be told about the changes and may be asked to sign a new consent form.

PURPOSE OF THE STUDY

This research study is being done to:

1) Find out if Phexxi, an intravaginal gel used for birth control, causes any changes to the vaginal microbiome.
2) Find out if Phexxi can decrease symptoms of bacterial vaginosis or yeast infections

PROCEDURES

Screening

We will confirm if you have had at least two instances of BV or yeast infections in the last 12 months, and that you meet our other study criteria. If you are interested in participating, we will then complete this consent form.

Study Treatment

1. Everyone within the study receives the same treatment
2. You will receive a collection kit, instructions, and 8 pre-filled inserters with the study medication after completing this informed consent process.
3. Your first sample will be collected at least 10 days after the last day of your period. If you have been treated with an antibiotic or antifungal medication, we also ask that you wait at least 10 days after completing the medication before collecting your first swab.
4. Following the instructions provided, you will collect this first sample (your "baseline" sample) and then return to us using the pre-paid envelope within 24 hours of collecting the sample. Once we receive your baseline sample and surveys, we will send you your first $10 payment for your time.
5. After you have mailed us your baseline sample, you are ready to start the study medication. Instructions will be sent with the inserters. You should use 1 inserter 2 times per week. To help you remember to use the inserter, we ask that you use the product on the same days of the week, every week (for example, if you start on Monday and Thursday, continue using the product every Monday and Thursday). For the four weeks you are using the study drug, you will be asked to complete a symptom diary on every day you use Phexxi, as well as other days where events which could affect your vaginal microbiome, such as menses and intercourse, occur. There will also be room on this diary for you to record any symptoms you feel after using Phexxi.
6. After 4 weeks, you will have used all of the inserters. At this point, we would like you to perform a second vaginal swab, 30 days after your first dose of Phexxi. Once you have collected the sample, we ask that you send the sample in the pre-addressed envelope to our lab within 24 hours. We will also email you a survey to fill out at this point.
7. Throughout the time you are using the study drug, you will be asked to keep a diary log of your symptoms, as well as any significant events, such as intercourse, menses, or other medications taken.
8. 30 days after inserting the last dose of the study medication, we will ask you to collect a third, final swab. Once you have collected the sample, we ask that you send the sample in the pre-addressed envelope to our lab within 24 hours. We will also email you a survey to fill out at this point. Once you have completed this, you will be done with the study. You will receive your second $10 payment at this time. , as well as the results of your microbiome if you would like them. **Please note,**

that genetic sequencing will only be performed on the vaginal bacteria that is collected from the swab, not on your personal genetic material. If you would like help interpreting the results of your microbiome analysis, you may contact Dr. Manayan at the email address below.

Follow-up Visits

After completing the 30 day final swab and survey, there are no further study-related activities.

Length of Time in this Study

If you agree to take part in this study, your involvement will last approximately 60 days.. You will also be asked to self-collect and send vaginal swabs to our labs 3 times: once before starting the study medication, once after completion, and once 30 days after completion. You will also be asked to fill out 3 surveys. One at the beginning before treatment starts, one at the end of use of the investigational product and a final survey at the end of the study. You will receive the results of your microbiome at the end of your study participation.

Stopping Your Part in the Study Before the End (Withdrawal or Early Termination)

You can decide to stop taking part in the study at any time without any penalty or loss of benefits to which you are allowed. The following procedures will need to be completed if you stop taking part before the study ends: You must do this in writing. Write to Dr. Manayan and let her know that you are withdrawing from the research study. Her email address is fprch@queens.org.

If you withdraw your permission:

- We will not collect additional information about you or your samples for this research study, except when the law allows us to do so.
- We are unable to take back anything we have already done or any information we have already shared with your permission.
- We may continue using and sharing the information obtained from you prior to your withdrawal if it is necessary for the soundness of the overall research.
- We will keep our records of the care that we provided to you as long as the law requires.

The research team may use the following sources of health information:

- Your medical demographic information, your medical history as it relates to the research study, questionnaires, and your provided samples, for the duration of the study, and for any related publications or follow-up studies

RISKS

While on the study, you are at risk for the following side effects. Not every person will experience any or all of these side effects, but they are possible. Should you develop side effects, you may request treatment from the study team or from your primary provider.. Many side effects will go away after the study medication is stopped but, in some cases, the side effects may be serious and/or lasting. If you

develop any of these side effects, please contact the research team immediately. Additionally, if you seek medical care for your symptoms, it will be your responsibility to use your medical insurance or self-payment to cover the cost of medical care.

If you are diagnosed with BV or a yeast infection by your doctor while a part of this study, please notify the research team.

PHEXXI side effects.

More likely (>10% of patients experience):

- Vaginal burning, itching

Less likely (<10% of patients experience):

- Urinary tract infections
- Vaginal discomfort or pain
- Abnormal vaginal discharge
- Burning with urination
- Yeast infection or bacterial vaginosis
- Allergic reactions – if you experience a rash, hives, or nausea and vomiting immediately after using Phexxi, please contact the research team. If you develop difficulty breathing immediately after using Phexxi, call 911 or seek emergency care at your nearest hospital.

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If you are hospitalized in a hospital or go to an Emergency Room where the study doctor does not work, whatever the reason is, you (or one of your relatives) should tell your study doctor as soon as possible. You must also tell the doctor treating you at the hospital or Emergency Room that you are taking part in a study and the name of the study drug, Phexxi.

Additionally, if you should happen to become pregnant while enrolled in the trial, the FDA-approved labeling of Phexxi stipulates that there is no available data with the use of Phexxi in pregnant humans or animals. This means that the effects of Phexxi to the fetus are unknown. This is the case with many drugs which have not been studied in pregnancy.

As this study is not using Phexxi for its contraceptive benefits, if you do not want to become pregnant, it is important to talk with your doctor about more reliable methods of birth control.

BENEFITS

Possible benefits to the participant:

There is a possibility you will experience no benefit from taking part in this study.

However, you may experience a decrease in the number of yeast infections or episodes of bacterial vaginosis you have per year.

Possible benefits to others:

The results of this research may help researchers to gain further understanding of the makeup of the vaginal microbiome, and how it may be influenced by medicines like Phexxi

OTHER TREATMENT

As this is a study that is not testing Phexxi for the purposes of treatment, there are technically no other treatment options available.

You may choose to not take part in this study without it making a difference in the care that you get now or in the future.

CONFIDENTIALITY

Federal Privacy Regulations provide safeguards for privacy, security, and authorized access to health information. The confidentiality of all study-related records will be kept according to all applicable laws. Information gained during this study and information known about you will be confidential (private) to the extent permitted by state and federal law. The results of this research may be presented at meetings or in publications; however, your identity will not be disclosed.

Your research records that are reviewed, stored and analyzed at Queen's Medical Center will be kept in a secured area in a secured, encrypted hard drive. Your samples collected for research purposes will be labeled with your research participant number and will be stored in the lab until they are processed and analyzed. The list that matches your name with the code number will be kept in a secured, encrypted hard drive. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

Your identifiers will be removed from the information obtained as part of this research study. This un-identifiable information may be used for future research studies or shared with another investigator for future research studies without additional informed consent from you. It will be kept on a secured, encrypted computer. Your information will be available to the principal investigator, Olivia Manayan, the Queens Medical Center Research and Institutional Review Committee, the Queens Medical Center Research Regulatory Office, and the research team, including QMC research assistants/associates, co-investigators, and data analysts.

- Safeguards are in place to protect your privacy
    - Your research records that are reviewed, stored, and analyzed at Queens Medical Center will be kept in a secured area in a secured, encrypted computer that only study staff have access to.
    - We will not put your name or any other identifying information on any of your data or samples. Instead, we will assign you a unique study identification number.
    - Your samples collected for research purposes will be labeled with your study ID number and will be stored in the lab until they are processed and analyzed.

- The list that matches your name with your study ID number will be kept in a secured encrypted computer.
- When we share results from the research publicly, there will be no identifiable information about any of the study participants.
- Any information about yourself that could identify you will not be stored with the final study data and will be destroyed when we are done with the research.
- This un-identifiable information may be used for future research studies or shared with another investigator for future research studies without additional consent from you.
- All email communication that will be sent to you will be from the Queen's centralized email service. All emails will be encrypted using the Queen's system.

Your vaginal swab specimens collected as part of the research will not be used or distributed for future research studies.

HIPAA AUTHORIZATION TO USE AND DISCLOSE YOUR PERSONAL HEALTH INFORMATION

We understand that information about you and your health is personal, and we are committed to protecting the privacy of that information. Because of this commitment, we must obtain your special authorization before we may use or disclose your protected health information (PHI) for the research purposed described below. If you sign this authorization, your entire research record and any medical records may be used and disclosed as described below for the purposes described in this form. The information collected about your health will be entered into a computer database and kept indefinitely.

The purpose of this section is to make sure that you are properly told of how your PHI will be used or disclosed. Please read the information below carefully before signing this form.

USE AND DISCLOSURE (RELEASE) OF YOUR HEALTH INFORMATION/HIPAA AUTHORIZATION

By signing this form you are authorizing the collection, use and release of your personal health information in medical records and diagnostic imaging and any health information gathered about you as part of this study. Your information will only be used/disclosed as described in this consent form and as permitted by state and federal laws. Your personal health information is health information about you that could be used to identify you. This information may include information about AIDS or HIV infection, treatment for alcohol and/or drug abuse, or mental health or psychiatric services.

The purposes of releasing your protected health information are to collect the data needed to complete the research, to properly monitor (watch) how the study is done, and to answer research questions related to this study.

There is no expiration date to this authorization.

Who may receive, use or release information:
Your medical records and any health information related to this study may be used or released in connection with this research study to the following:

- *Olivia Manayan, MD MPH; Corrie Miller, DO; and Bliss Kaneshiro MD MPH* and her research staff for the purposes of conducting this research study.
- The Research and Institutional Review Committee of QMC and staff members of the Research Regulatory Office for purposes of overseeing the research study and making sure that your ethical rights are being protected.
- Providers and other healthcare staff of QMC involved in your care.

Who may receive the information by the above groups:

The individuals or groups named above may release your medical records, this consent form and the information about you created by this study to:

- The sponsor of this study and their designees
- Federal, state and local agencies having oversight over this research, such as The Office for Human Research Protections in the U.S. Department of Health and Human Services, Food and Drug Administration, the National Institutes of Health,
- Representatives directed by QMC Research Department for audits to make sure studies are done as required.
- Staff in billing-related departments and insurance companies for billing purposes

There is a possibility that your information may be released again by the sponsor of the study or governmental agencies described above and no longer covered by federal privacy rules.

Right to Withdraw or Stop Taking Part in the Study

You may refuse to sign this authorization. If you refuse to sign the authorization, you will not be able to take part in this study. If you choose not to be in the study, or choose to withdraw from the study, or if you refuse to sign the authorization, it will not make a difference in your usual treatment, or your payment, and it will not change your eligibility for any health plan or health plan benefits that you are allowed.

If you decide to end your taking part in the study or you are removed from the study by the researcher (study doctor), you may revoke (take away) your authorization. In order to take away this authorization, you must send a letter/notice to the researcher in charge of this study. Send the written notice to the researcher to the address listed on the original consent form.

If you take away your authorization, your part in the study will end and the study staff will stop collecting medical information from you and about you. The researchers and sponsor will continue to use information that has already been collected, but no new information about you will be collected unless the information is about an adverse event (a bad side effect) related to the study or to keep the scientific integrity of the study. If an adverse event happens, we may need to review your entire medical record.

Access to Your Information

As is usually the case, you may see the information in your medical record; however, the records and information related only to the study that are kept separately will not be available to you until the study is finished. If you wish to review your study records after the completion for the study, you should request this from the study doctor.

END OF HIPAA AUTHORZATION SECTION

PAYMENTS TO YOU FOR TAKING PART IN THE STUDY

If you receive more than $600 per year for taking part in one or more research studies, you may be required to pay taxes on that money. This does not include any payments you receive to pay you back for expenses like parking fees. You may receive an Internal Revenue Service (IRS) Form 1099 if you receive more than $600 in one year for taking part in one or more research studies.

COSTS

There is no cost to you for participation in this study. However, if you develop side effects from the study drug while taking part in this study and choose to seek medical treatment for them, you will be responsible for using your health insurance carrier to cover the costs of this medical treatment.

Ask your doctor if you are unsure what your financial obligations are during the study.

FINANCIAL DISCLOSURE

The University of Hawaii Foundation Sharma Fund will pay for some of the costs associated with carrying out this study. Olivia Manayan is an employee of The Queen's Medical Center and will not financially benefit directly from being the principal investigator for this study or for carrying out this study on behalf of The Queen's Medical Center.

TREATMENT AND COMPENSATION FOR INJURY

If you have an injury or illness (get sick) as a result of being in this study, immediate emergency medical care and treatment which may be needed will be available at the usual charge either to you or your health insurance. The sponsor of the study, the study doctor, and The Queen's Medical Center do not have any funding (money) to pay for treating the injury or illness. Your insurance company may not pay for some (or all) of the treatment of the injury or illness as a result of being in this study. If your medical insurance does not pay for these medical costs, you alone will be in responsible for payment. There is no way of knowing what the costs will be. You should talk about the kind of insurance coverage you have with your doctor and insurance company before you decide to take part in this study. You can have financial counseling to go over your insurance coverage.

The sponsor, The Queen's Medical Center and the study researchers have not set aside any other kind of compensation (payment) for lost wages, or other damages or losses resulting from any injury that you may get from taking part in the study.

REMOVAL FROM THE STUDY

You take part in this study of your own free will. You may be taken off the study without your consent for any of the following reasons:

- Your condition gets worse;
- You do not keep your study visits or take the drugs as you are told;
- You have a bad side effect to the drugs;
- You get pregnant;
    - If you become pregnant, you will be taken off the study medication and continue onto follow-up.
- The study doctors do not think it is safe for you to continue to participate in the study

If you are taken off the study, you may be asked to return for follow-up visits, and to return any unused study drug

NEW FINDINGS

You will be told of any important new information learned during the study that may change your willingness to continue in this study. You may be asked to sign a new updated consent if this happens.

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.

WHO TO CONTACT

If you feel that you have been injured as a result of taking part in this study, *please call Olivia Manayan, at 808-375-3785 or email the study team at FPRCH@Queens.org*

If you have any questions about your treatment, your rights as a volunteer or any other matter relating to this study, you may call Olivia Manayan at omanayan@hawaii.edu and talk about any questions that you might have.

If you cannot get satisfactory answers to your questions or you have comments or complaints about your treatment in this study, you may contact:

Research & Institutional Review Committee
The Queen's Medical Center
1301 Punchbowl Street
Honolulu, HI 96813
Phone: (808) 691-4512

RA-2022-015

AGREEMENT TO TAKE PART AND CERTIFICATION **and**
AUTHORIZATION OF PROTECTED HEALTH INFORMATION –

I, or my legally authorize representative (the legal person who cares for me) have read and understand the description of this study such as the purpose and nature of this study, its expected length, the procedures to be done, reasonably known risks and discomforts, benefits to expect, other treatments I may have, release of my medical records, payment and medical treatment for injury, and removal without my consent for this research study.

I am taking part in this study of my own free will. I may withdraw (stop taking part) and/or withdraw my authorization for use and release of protected health information at any time after signing this consent form without it making a difference to my care now or in the future or any loss of benefits that I am allowed. My consent does not take away my legal rights in case of carelessness or negligence of anyone connected with this study. My signature means that I have read the information above or that it has been read to me, my questions have been satisfactorily answered, and at any time I have other questions, I can contact the researcher listed on the first page.

Specially Protected Health Information
I agree to the release of the following information should it be contained in my medical records: Acquired Immune Deficiency Syndrome (AIDS or HIV), alcohol and/or drug abuse treatment, or behavioral or mental health services.

cc: ***Signed copy*** of consent/authorization form to patient

Subject's Name (Print)	Subject's Signature	Date/ Time
Witness' Name (Print) (Witnessing Signature Only)	Witness' Signature **********	Date/ Time

The following two items are **optional**, and are not required for participation in the study:

__ (Initials) I would like a copy of my vaginal microbiome report emailed to me. I understand that this will be emailed as an attachment. This attachment will be sent via the Queen's encrypted email system
__ (Initials) I would like a member of the research team to go through the results of my vaginal microbiome report with me.
__(Initials) If I develop a yeast infection, BV, or a UTI while on this treatment, I consent to letting the research team inform my GYN doctor of this.

I have explained this research to the above subject. In my judgment the subject is voluntarily and knowingly giving informed consent and has the legal capacity to give informed consent to take part in this research study.

Investigator's Name (Print) (Individual obtaining Subject's consent)	Investigator's Signature	Date/ Time

(Investigator:

- Fax a copy of this signed page to Research Regulatory Office at 691-7897 within 24 hours of signing.
- Document in MR: study name, sponsor, and sponsor-assigned protocol number, consenting
- Scan/copy signed consent for MR)

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