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# INFORMATION SHEET AND CONSENT FORM

STUDY TITLE: A Canadian, Pilot, Open Label Study to Evaluate the Efficacy and Safety of the Bacterial Vaccine, Uromune® in Treating Recurrent Urinary Tract Infections in Women

STUDY NUMBER: Uromune® CAUR2018

STUDY DRUG: Uromune® Bacterial Vaccine

STUDY INVESTIGATOR: Dr. J. Curtis Nickel

ADDRESS: Centre for Applied Urological Research
Kingston, ON Canada
K7L 3J7

**Purpose of the Participant Information and Consent Form**
This Participant Information and Consent Form may contain words you do not understand. If there is anything that is not clear, or if you would like more information, please ask your study doctor or the study team.

The purpose of this form is to give you information about the research study and if you sign, it will give your consent to participate in the study. You are being invited to take part in the study. This form will give you information on why the study is being done and what will be involved if you decide to participate. You may refuse to take part now or you can withdraw from this study at any time and it will not impact your medical treatment or care. Please read this Participant Information and Consent Form and ask as many questions as you need to before making your decision.

## Introduction and Background

You are being invited to participate for this research study because you experience recurrent urinary tract infections (recUTIs). In most cases, UTIs are very common and can be easily treated with a course of antibiotics. Unfortunately, approximately 20-25% of women suffer from recurrent UTIs.

In this study, you will take the Uromune® vaccine once daily. Uromune® is currently in the pre-license phase development stage and is available in a number of countries (e.g. Europe and New Zealand) under various compassionate use programs. Uromune® is still an experimental drug (still being tested) for recurrent UTIs. Uromune® is being tested by Dr. J. Curtis Nickel (investigator of this study) and it will be supplied by Red Leaf Medical.

There is only one treatment group in this study and you will know that you are taking the Uromune® vaccine. This is called open-label treatment. You will take the study treatment daily for 3 months (90 days).

Throughout this study you will receive observational follow up. You will be seen in clinic at 3 and 12 months after treatment and contacted by phone at 6 and 9 months after treatment.

**Why is this study being done?**
This study is being done to help Dr. Nickel assess whether the bacterial vaccine, Uromune®, can prevent recurrent UTIs. This study will follow participants at 3, 6, 9 and 12 months to find out if participants have experienced a UTI or had any other problems with the vaccine.

This study is also being done to test the safety of Uromune®; meaning, how taking this vaccine may affect your health (this includes looking for possible side effects). The effects on your quality of life will also be tested.

**How many people will participate in this study?**
About 80 participants will be in this study.

**What will happen if I participate?**
If you decide to participate in this study, Dr. Nickel will do screening tests to find out if you qualify to be in the study.

If you qualify and agree to take part in this study, you will receive a bottle of the Uromune® vaccine at your baseline visit (day 1) and you will take it for 90 days.

You may stop taking the study drug at any time if you or Dr. Nickel feels that it is in your best interest.

After you stop study treatment you will continue to be followed by the study team at 3, 6, 9 and 12 months after the start of your treatment. Your total involvement in this study will last 12 months. This includes the treatment period and the follow up period.

## Study Activities

The study activities (procedures, tests and assessments) are listed below.

## Screening Period (approximately 90 minutes)

If you decide to participate in this study and sign this consent form, you will have the following screening procedures performed to find out if you are eligible to take part in this study:

- A complete medical history, including a review of your UTI history, any treatments you have had before for your UTIs and a review of your previous urine culture results;
- A physical examination and check of your current health;
- A midstream urine sample for urinalysis, bacterial culture and pregnancy test.
- Vital signs (blood pressure and heart rate), height and weight;
- A review of your current medications.

Dr. Nickel will look at your screening tests to find out if you can be in this study. All of these procedures must be completed within 4 weeks of starting study treatment.

If your urine culture comes back positive for a UTI, you will be put on antibiotics and, if you would like, may continue in the study once a negative urine result is obtained and all eligibility criteria are met.

## Treatment and Follow Up Period

If Dr. Nickel decides that you are eligible to be in this study, you will be given open-label treatment. This means that you and the study team will know that you are getting the Uromune® vaccine.

**Treatment with spray of study drug**

You will be given a spray bottle of the Uromune® vaccine once you have completed the screening process. You will be given enough treatment to last you the 3 month treatment period (90 days). You will take your first dose with the study team at your day 1 visit (baseline visit). You will take 2 sprays of Uromune®, once daily, under your tongue. After spraying the liquid under your tongue, you will need to hold it there for about 2 minutes without swallowing. Once the 2 minutes has passed you can swallow. This should be done before breakfast each day to avoid mixing your treatment with any food or drink.

Store the study treatment in its original packaging to protect it from the light. You will need to keep your study treatment in the fridge and it should be kept between 2 to 8 degrees Celsius. It is important not to freeze the product.

Please keep the study drug bottle once you have completed your treatment. Bring the drug bottle, labels and unused spray to the clinic with you at your 3 month clinic visit so the study staff can check them.

**Missed doses of study drug**
It is very important that you tell the study staff if you miss any doses or take the wrong number of sprays. If you forget to take your dose at the regular time, you can take it as soon as you remember that day. However, if you forget to take your dose for the whole day, just take your usual dose at your regular time the next day. Do **NOT** try to make up for a missed dose by taking a double dose or an extra dose the next day.

**Day 1 (Baseline Visit-approximately 60 minutes)**
The following activities will be part of day 1:

- A midstream urine sample for urinalysis, bacterial culture and pregnancy test;
- A questionnaire about your quality of life and satisfaction;
- A review of your current medications;
- Instructions on how to fill out the treatment period diary;
- If you meet all of the requirements, you will receive your bottle of study drug, which is the Uromune® vaccine. You will be instructed to take 2 sprays under your tongue once daily for 90 days. You will hold the liquid under your tongue for 2 minutes without swallowing. After the 2 minutes you can swallow. You will receive enough study treatment to last you the entire 3 months.

**Month 3 (approximately 30 minutes)**
You will come to the clinic 3 months after you start treatment for the following:

- Questionnaires about your quality of life and overall satisfaction with the study drug;
- A midstream urine sample for urinalysis, bacterial culture and pregnancy test;
- You will be asked to return your completed study treatment bottle;
- Your diary will be reviewed for compliance;
- A check of your health status, including a review of any symptoms or UTIs you have been having, as well as any treatment you may have received;
- A review of any changes in medications;
- Instructions on how to complete your post treatment diary.

**Months 6 and 9 (approximately 15 minutes)**
You will receive a phone call at month 6 and 9 after starting study treatment and you will be asked about the following:

- A check to see if you have been filling out your symptom diary.
- A check on your health status, including a review of any symptoms or UTIs you have had, as well as any treatment you may have received;
- A review of any changes in medications.

**Month 12 (approximately 60 minutes)**
You will be asked to return to the clinic 12 months after starting study treatment for your end of study visit. During this visit, you can expect to go through the following:

- Questionnaires about your quality of life and overall satisfaction with the study drug;
- A midstream urine sample for urinalysis, bacterial culture and pregnancy test;
- Your diary will be reviewed for compliance;
- You will be asked about any changes in your health and any changes in your medications;
- A review of your UTI history including any symptoms and treatments you have had.

**Unscheduled Study Visits (time dependent on issue)**
In addition of the regularly scheduled study visits, the study team may call you to check on your health or ask you to come in for an unscheduled study visit if you need it (for example, to check on a side effect). This may include the following:

- A midstream urine sample for urinalysis, bacterial culture and pregnancy test;
- Your diary will be reviewed for compliance;
- You will be asked about any changes in your health and any changes in your medications;
- A review of your UTI history including any symptoms and treatments you have had.

If at any point you need to seek medical attention for any symptoms you are experiencing, please first attempt to contact your study coordinator, Kerri-Lynn Kelly at 613-548-6033. During evenings, weekends, or in the event that your study coordinator is unavailable please seek medical attention elsewhere and bring your consent form with you so that you can get proper documentation of your urine test results (i.e. documented culture and sensitivity).

## Procedure Instructions

**Midstream Urine Sample Instructions**
To perform the midstream urine specimen collection, hold the labial folds open and clean the urinary opening with the provided cleaning towelette. Begin urinating into the toilet and then bring the open specimen bottle into the urinary stream to collect the "midstream urine". You can stop collecting when the specimen cup is about halfway to two thirds of the way full. Once you are finished, place the lid back on the specimen cup and firmly tighten it.

**Treatment Period Diary**

You will receive a treatment period diary during your baseline visit. This will be the diary you will complete during the 90 days you are taking study treatment. At the end of every week you are required to complete your diary for that week. You will be asked to fill out whether or not you took your study treatment each day of the week. You will also be asked about any symptoms you experienced. You will complete this diary every week while you are on treatment. At your 3 month clinic visit, you will bring your diary with you to give to the study team.

**Post Treatment Period Diary**
At your 3 month clinic visit, you will receive your post treatment diary. You will not have to fill out this diary every week. Instead, you will only fill out this diary when you experience a symptom. You will be asked to record the date you felt the symptom and about any medical attention or treatment you had. The study team will ask you about your diary at the 6 and 9 month phone calls to see how you have been feeling. At your 12 month clinic visit you will bring your diary in for the study team.

## Other Study Information

**Can I take other medications while I am in this study?**
You should not take prophylactic (continuous low dose) or post-coital (short-term dose after sexual activity) antibiotics while you are taking Uromune®. This is so we can accurately tell if Uromune® is effective or not. All other medications and over the counter remedies are allowed.

It is very important to tell Dr. Nickel about all of the medicines you take, including prescription and over-the counter medications, herbal remedies, vitamins, and any new medicines prescribed by another doctor, including your family doctor.

You should speak with Dr. Nickel before starting any other medical treatment.

You must not take any other experimental drug while you are taking part in this study.

**How long will I be in this study?**
You will be in this study for 12 months. Your treatment will be taken during the first 3 months of this 12 month period. Dr. Nickel may take you out of the study at any time for any of these reasons:

- You begin some other therapy;
- You experience adverse (bad) side effects from the treatment;
- You begin a different research study;
- You do not follow the study requirements;
- The study is stopped;
- Thinks it is in your best interest.

If your treatment is stopped for any reason, you will continue with your follow up visits after you are off study treatment. These visits are important to find out the effects of the study treatment.

**Can I stop being in this study?**
Your participation in this study is completely voluntary and you can decide to stop being in this study at any time. If you decide that you want to stop being in this study, it is important that you tell Dr. Nickel or the study team so that they can continue to follow you for any side effects. Dr. Nickel can also discuss other treatment options with you at this time.

You must return your bottle of study treatment to the clinic when you stop study treatment.

**What risks or side effects can I expect?**
Any research study has some risks, which may include things that may make you feel unwell, uncomfortable or harm you. You might experience negative effects related to the study drug while taking part in the study. Participants will be watched carefully throughout this study for any side effects. Side effects may range from mild to severe. Your study doctor may give you medications to help lessen any side effects.

This study treatment may have unknown or unexpected side effects. Because this study treatment is still an investigational drug, it is possible that you may have a reaction that is currently unknown or not expected. All drugs have the potential to cause an allergic reaction that could be life threatening or result in death if not treated properly. If you experience signs of an allergic reaction such as hives, difficulty breathing, or swelling of your face, lips, tongue or throat, you should seek emergency medical attention.

Talk to Dr. Nickel if you have any side effects while taking the study drug.

The following section describes the rare, mild side effects that may occur with the use of Uromune®.

Since 2010, more than 17,000 treatments of Uromune® have been given in several countries. No major side effects have been experienced by any of the participants. The adverse reactions that have been reported are as follows:

- Itchy, small, red, raised rash during the last few days on both legs and the left knee. Sparse itchy areas on the lower back, chest, behind and below the ears;
- Severe skin rash to the face and neck at the start of treatment and after restarting treatment several times a month later;
- Itching and pain in the joints.

The following are adverse reactions that could occur when you initially spray Uromune® into your mouth:

- Mild heat sensation in the mouth;
- Itching in the mouth;
- Swelling in the mouth;
- Skin rash;
- Gastrointestinal discomfort;
- Mucosal inflammatory reaction;
- Difficulty breathing;
- Allergic skin reaction.

During this study, if there are any new findings, Dr. Nickel will let you know about any new side effects that may occur with the use of the Uromune® vaccine.

It is very important that you tell Dr. Nickel or the study team about any new symptoms or changes in your health, or any health concerns you may have.

**Pregnancy Risk/ Use of Birth Control:**

- The effects of the study drug on the unborn child or nursing infant are not known. For this reason, you should not be in the study if you are pregnant, planning to become pregnant, or breast feeding a child. If you are of child-bearing potential, you must avoid pregnancy during this study. You and your partner must use a medically acceptable method of birth control from the time of your screening visit to your final follow up visit of the study. These include hormonal contraception (i.e. estrogen, and/or progesterone or preparations that contain a combination of these hormones), non-hormonal intrauterine device or double barrier method (i.e. condom with foam or vaginal spermicidal suppository, or diaphragm with spermicide) or vasectomy of sole sexual partner. Complete abstinence alone can be used as a method of contraception. Dr. Nickel or the study team can talk to you about these birth control methods. If you become pregnant, during the study you must immediately notify the study team or Dr. Nickel. If you become pregnant, the study drug will be stopped immediately. You will continue to be monitored to obtain information on your general health and the outcome your pregnancy (including the health of your baby) until 30 days after you are no longer pregnant. Dr. Nickel will request information about the outcome of your pregnancy.

Talk with Dr. Nickel if you have questions or concerns about risks and side effects.

**What are the possible benefits of participating?**

You may or may not receive any direct benefit from participating in this study. Your symptoms may or may not get better. However, you, and future patients may still benefit from this research because the results from this study may help to develop a new treatment for you and others with recurrent UTIs.

**What other choices do I have if I do not take part in this study?**
You do not have to take part in this study to receive treatment for your recurrent UTI.
Your other choices may include the following:

- Getting other treatments or care for your recurrent UTIs without being in this study.
- Having no treatment.

Please talk to Dr. Nickel about your choices before deciding if you will take part in this study. Your medical care will not be impacted by your decision to participate in this study or not.

**What are the costs of participating in this study?**
Dr. Nickel will provide the study treatment to you free of charge while you are in the study. You will not be charged for any study related procedures and will not receive any payment for participating in this study.

**Participant responsibilities**
You are required to follow all of the instructions given to you by Dr. Nickel, the study team and as outlined in this information and consent form.

If you are currently in another research study, you cannot participate in this study. Additionally, while you are in this study, you cannot participate in another clinical trial.

It is important for you to read the instructions on your study drug bottle and to take it as instructed. You must return your completed study treatment bottle at your 3 month clinic visit. You need to attend all of your scheduled study visits including the follow up phone calls.

You are required to complete your treatment period diary every week during your 3 month (90 day) treatment period. You also need to complete your post treatment diary every time you experience a symptom from the 3 month clinic visit to the 12 month clinic visit.

**Will my medical information be kept confidential?**
Your identity and all information obtained during the course of this study are considered confidential. Dr. Nickel, the study team, Queen's University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board, study monitor, auditors and inspectors from regulatory authorities (Health Canada) will have direct

access to your original medical records in order to verify study procedures and data. By signing this consent form, you are authorizing for this to happen.

You will be provided with a unique study number so your identity is not known. All personal identifying information such as your name or address will be removed and entered into a database located at the Centre for Applied Urological Research.

Dr. Nickel is responsible for keeping a code list which makes it possible to link your unique study number to your name. This will be kept in a safe place to ensure that in case of emergency, you can be identified and contacted. The code list will be kept until the last marketing application has been received.

All your study data will be protected in accordance with local privacy laws. Your confidentiality will be protected to the extent permitted by law.

The study analysis, our interpretation of our results and the final publication will be published or submitted to medical journals but the identifiable study information and data will remain at our centre. You will not be mentioned in a way that would let people find out who you are. By signing this consent form, you are giving your permission for the use of your data described above.

Your permission has no expiration date, but you may take back your permission at any time by notifying the study doctor to ask that your information stop being used. At that time, no new information will be added, but information that is already in use will continue to be used. You have the right to ask to see the data that has been collected about you.

If you decide to stop taking part in the study, please tell Dr. Nickel so that no new data will be collected.

If you agree, Dr. Nickel may inform your family doctor about your study participation and request medical information about you.

Health Canada Regulations require your data be stored for 25 year. All study data will stored at the Centre for Applied Urological Research for this time period and then it will be destroyed by research personnel.

The results of this study will be published and used to make informed clinical decisions for developing this new medication. You will not be identified in any report or publication. Please talk to your study doctor if you want the results to be made available to you.

**What will happen to any samples you give?**
Urine samples will only be used for standard laboratory tests and will not be kept after the end of your participation in the study.

**What happens when the study stops?**
Dr. Nickel may stop this study at any time, if it is considered necessary. If this study is stopped the reason will be explained to you and you may be asked to stop taking study treatment and to continue with your scheduled follow up visits.

Dr. Nickel may also withdraw you if it is found to be in your best interest.

You may also decide to stop participating in this study at any time, for any reason without penalty or impact to your current or future medical care. If you wish to stop participating in the study, you must inform Dr. Nickel. If you discontinue participation, you will be required to return to see Dr. Nickel for a final visit and check-up. It is important for your health and safety to have this last visit. Dr. Nickel will talk to you about any potential medical issues that may arise and discuss alternative treatments for your condition.

**Funding**
The investigator, Dr. J. Curtis Nickel at The Centre for Applied Urological Research has designed this clinical trial however, is not being paid to do this research. There is no funding associated with this study. Uromune® is being provided free of charge for this study by Red Leaf Medical.

**Compensation**
It is important that you tell your study doctor, Dr. J. Curtis Nickel if you become ill or think that you have been injured as a direct result of being in this study. You can tell the doctor in person or call him at 613-548-2497 or the research coordinator Ms. Kerri-Lynn Kelly, RN at 613-548-6033.

If you are injured as a direct result of the study drug or by the required study procedures performed during your participation in this research study you will receive medical care, at no cost to you, through to resolution of your injury. No other compensation is available. Every effort will be made to prevent physical injury that could result from this research.

It is important to note that by signing this consent form you will not waive any of your legal rights nor release the Investigator from his legal and professional responsibilities.

**What are my rights if I am in this study?**
Taking part in this study is completely voluntary. You may choose to participate or not. If you do decide to participate in this study, you may leave this study at any time with no penalty to you and you will not lose any of your regular benefits. Your future medical care will not be affected.

If there are any new findings or changes to this study that may affect your health or your decision to continue, these will be discussed with you. If you decided to continue in the study after receiving this new information you may be asked to sign a new consent form.

By signing this consent form, you do not lose any of your legal rights to seek payment in the event of an injury resulting from this study.

**Who has reviewed the study?**
This study has been reviewed for ethical compliance by the Queen's University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board. This REB is responsible for protecting research patients' safety, rights, wellbeing and dignity.

**Who can answer my questions about this study?**
You can talk to Dr.Nickel about any questions, concerns or complaints you have about the study, or if you feel that you have experienced a research-related injury or reaction to the study drug, or have a complaint about the research study.

Contact your study doctor Dr. J. Curtis Nickel at 613-548-2497 or your study coordinator, Kerri-Lynn Kelly, at 613-548-6033.

For ethics concerns, please contact the Queen's University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board. Call 1-844-535-2988 (toll free in North America) or email the HSREB chair, Dr. Albert Clark, at clarkaf@queensu.ca.

**Follow-up Contact:** Unresolved adverse events will be followed post-study until resolution as medically indicated. The site staff may contact you during regular business hours by phone with questions regarding your health.

## Consent to Take Part in the Uromune® Study

**STUDY TITLE:** A Canadian, Pilot, Open Label Study to Evaluate the Efficacy and Safety of the Bacterial Vaccine, Uromune® in Treating Recurrent Urinary Tract Infections in Women
**STUDY PROTOCOL:** Uromune® CAUR2018
**STUDY DRUG:** Uromune® vaccine
**INVESTIGATOR:** Dr. J Curtis Nickel

I confirm the following:

- ☐ The information regarding this study has been thoroughly explained to me.
- ☐ I have read and understand the information sheet for this study and have had enough time to make my decision.

- ☐ All of my questions have been answered to my satisfaction. I voluntarily agree to participate in this study, to follow the study procedures and to provide the information Dr.Nickel, and research team ask from me.
- ☐ I have been told that I am may choose to stop being a part of this study at any time for any reason and my medical care and legal rights will not be affected.
- ☐ I agree that my family doctor may be told about my taking part in this study and asked for medical information about me.
- ☐ I agree to my samples being taken and used as described in this information sheet.

In the event I become pregnant during the study I agree that Dr. Nickel will request follow-up information that may include access to my child's medical records.

- ☐ YES
- ☐ NO

By signing this document I agree to take part in this study, as set out in the information sheet and consent form, and authorize the release of my medical records and protected health information related to this study to the investigator, monitoring representatives, the Research Ethics Board, laboratories for testing bio-specimens (as available), Health Canada and other regulatory agencies as described throughout this document. I have been told that I will receive a signed and dated copy of this Consent and Authorization for my records.

By signing this document I agree to take part in this study, as set out in this information sheet and consent form.

| Participant Name | Participant signature | Date (DD/MM/YY) |
|---|---|---|
| Name of person obtaining consent | Signature of person obtaining consent | Date (DD/MM/YY) |

**Legally Authorized Representative (if applicable)**

| Name of legally accepted representative | Signature of participants legally accepted representative | Date (DD/MM/YY) |
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