UHN Toronto General Toronto Western Princess Margaret Toronto Rehab

CONSENT FORM TO PARTICIPATE IN A RESEARCH STUDY

Study Title: **A randomized, double-blind, placebo-controlled phase 3 study: Efficacy and safety of the recombinant VPM1002 BCG vaccine in reducing SARS-CoV-2 infection rate and COVID-19 severity (COBRA)**

Investigator/Study Doctor: **Dr. Alexandre Zlotta**

Contact Information: **416-946-4501 x7510**

Emergency Contact: **416-357-0817**

Sponsor: **University Health Network**

Introduction:

You are being asked to take part in a research study. Please read the information about the study presented in this form. The form includes details on study's risks and benefits that you should know before you decide if you would like to take part. You should take as much time as you need to make your decision. You should ask the study doctor or study staff to explain anything that you do not understand and make sure that all of your questions have been answered before signing this consent form. Before you make your decision, feel free to talk about this study with anyone you wish, including your friends, family, and family doctor. Participation in this study is voluntary.

Background/Purpose:

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), commonly called Coronavirus or COVID-19 has affected large number of people across the globe leading to an increase in morbidity (disease) and mortality (death). Although people of any age can acquire Coronavirus or COVID-19, certain individuals are at a higher risk of infection with Coronavirus or COVID-19.

The people who are at high risk of contracting this disease include first-responders, public transport employees, health-care providers, and members of the police forces. They remain in their jobs and are faced with the challenge of having to enforce the law and provide services while often placed in difficult situations where social distancing is difficult, if not impossible. There is an urgent need to ensure the safety and health of staff and people performing tasks, which involve a high risk of spreading of COVID-19 infection.

Bacillus Calmette Guérin (BCG) vaccine is a known vaccine routinely given against tuberculosis (an infection caused by a mycobacteria that mainly affects the lungs). BCG vaccine is given routinely to all newborn babies as part of childhood immunization programs in a number of countries and is one of the most widely used vaccines in the

world. It has been seen from the previous studies that the BCG vaccine might also have the ability to improve the body's immune response (ability to fight off disease causing germs) and provide protection against unrelated pathogens (disease causing agents) like viral infections.

Serum Institute of India Pvt. Ltd. (SIIPL) has developed an investigational genetically modified BCG vaccine called VPM1002. Genetically modified means, the vaccine is artificially altered to produce desired features so that the vaccine could have a better safety and efficacy profile. Investigational means Health Canada has not approved the sale or use of the VPM1002 vaccine but they have approved its use in this research study.

We are doing this study to find out the effectiveness of VPM1002 vaccine in reducing the chance of getting the infection and reducing disease severity of coronavirus/COVID-19 infection.

Study Design:
A total of 3626 individuals will take part in this study over about one year.

If you decide to participate, you will be "randomized" into one of the treatment groups ("arms") described below. Randomization means that you will be put into a group by chance (like flipping a coin). There is no way to predict which group you will be assigned to. You will have an equal chance of being placed in either group. Neither you nor study staff can choose what group you will be in. You, your doctor and the study staff taking care of you will not know which treatment you will receive. However, if required, this information can be found out in an emergency situation. You will be told at the end of the study which group you were in.

There is an optional part of the study involving the collection of additional blood samples that is described in a separate consent form.

Experimental Treatment:
Arm A: If you are randomized to Arm A, you will receive *one* VPM1002 BCG vaccine injected into the skin of your upper arm.

Arm B: If you are randomized to Arm B, you will receive *one* injection of placebo (normal saline) into the skin of your upper arm.

You will be given the injection intradermally (within the layers of skin). After the vaccine administration, the study staff will observe you for a minimum of 30 minutes. Should you have any health concerns after receiving the injection, you will be given instructions on how to contact the doctor/study staff.

Study Visits and Procedures:
Initial Study Visit
Screening procedures, collection of a research sample, and administration of the vaccine will take place on the same day that you sign the consent form.

Screening procedures
After signing this Informed Consent Form, a member of the research team will collect information about your present and past health, including information about childhood or adult vaccinations, results of previous COVID-19 tests, as well as the names and reasons for any medications you are currently taking. A study coordinator will check your medical history and your current health status.

Research Sample Collection
Blood samples (approximately 1 tablespoons) will be taken by inserting a needle into a vein in your arm. These will be collected before vaccination and at the end of the study (7 months later).

Your samples will be studied to learn how to identify COVID-19, or to find out how the disease develops and progresses. Types of research that will be done on your samples will include:

Proteomics
Selected participant samples will be used in large-scale protein studies. The proteome is the entire set of proteins that is produced in the human body. These studies help identify and quantify the functional molecules of the cell and their interactions with each other.

Genetic or Genomic Research
Genetic or genomic research looks at your genes (the information stored within your body that makes you unique). Genes are of interest to researchers because genetic changes may determine how you respond to the vaccination or the COVID-19 disease.

Selected participant samples will be used to perform Whole Genome Sequencing (WGS) on your samples. WGS is a specific type of genetic research that determines the exact order of the base pairs (chemical letters) in your genetic make-up (the sequence of the genome). If your samples are used for this type of research, the researchers may discover information about inherited changes in your DNA that may put you and/or your biological relatives (e.g., your parents, children, sisters or brothers, etc.) at a higher or lower risk of developing serious disease and requiring more intense therapy. The research findings may not be important for your or your relatives current care but they may be important in the future.

Vaccine Administration
The vaccine or placebo will be injected into your upper arm. You will be asked to wait for a minimum of 30 minutes before leaving the study centre to ensure that you have not had any side effects.

<u>Follow-up Questionnaires</u>
You will be asked to register to an online web site developed solely for the purpose of this study. To ensure strict confidentiality, a unique user ID and password will be used to allow you to complete the questionnaires during the study.

A reminder text message will be sent to you requesting that you log into the online system and complete short follow-up health questionnaires every 2 weeks for a maximum of seven months. At one week following vaccination, you will be asked to submit a photograph of the injection site using the online system.

Any time you experience symptoms such as fever, cough, cold, breathlessness, sore throat, headache, tiredness etc. you should call your doctor. In the event that this occurs, or you experience any other discomfort/symptoms/illness, you will be asked to connect with the study team. If the follow-up questionnaire is not completed within the required period (i.e., 7 days), you will receive additional reminders via the mobile application/portal and also telephonic reminders from the study doctor/ study staff. In the event we cannot reach you, information will be retrieved from your alternative designated contacts and/or from the hospital, for information on any hospital admission, ICU admission or death.

In addition to the visit and biweekly questionnaires, study staff may ask you to visit the study center to assess your health status if deemed necessary.

At the end of the study, you will receive a notification by text message to complete the end-of-study questionnaire.

End of Study Visit

At approximately 6 months following vaccination, a study team member will contact you to arrange for the collection of the 2nd blood sample. This visit will take place approximately 7 months following vaccination.

Risks:

Taking part in this study has risks. Some of these risks we know about. There is also a possibility of risks that we do not know about and have not been seen in humans to date. Please call the study team if you have any side effects even if you do not think it has anything to do with this study.

The common events following receipt of a vaccine include those that occur at the injection site and symptoms that are more general. These common events are called ‘side effects’. BCG vaccination at first leaves a small blister, which looks like a mosquito bite. The blister may grow bigger into a small pimple or boil; rarely, the pimple may turn into a sore or a whitish fluid may come out of it. When the pimple dries out, a crust will form. This crust will peel off by itself once the pimple has healed. There may be a small scar left behind. It usually takes about 3 months for the pimple to heal. Every individual is different, so the time that it takes to heal will not always be the same. If you are worried about the time it takes for the pimple to heal, or about its size and how it looks, talk to the study staff; they will tell you what to expect and will listen to your concerns. If there is a problem, they will be able to help.

The other side effects may be swelling, redness or pain at the site of injection. Sometimes the vaccine can cause headache, fever, tiredness, muscle pain, joint pain, loss of appetite, nausea and vomiting.

Seldom, a swelling may also appear in the glands located in the armpit of the arm where you got the injection. You may feel uncomfortable when these swollen glands are touched. Swelling may also appear in other glands of the body, but this is not common. Even more unusual are the side effects such as bone or tissue infections.

Vaccines can cause allergic reactions soon after they are given. There is a very small chance that you may have a serious allergic reaction to the vaccine. Serious allergic reactions may cause a drop in blood pressure, difficulty breathing, or lumps on the skin. Less serious allergic reactions, such as a skin rash, which may or may not be itchy and swollen, may also occur within hours to days after receiving the vaccine. In the very rare chance of a serious allergic reaction within the 30 minutes that you are at the study centre, the nurse or physician who administered the vaccine will have immediate access to medicine to treat such a reaction. In the event that this occurs, you will be required to remain at the study centre until such time that the trained health care professional determines it is safe for you to leave.

Most of the time, these side effects cause minor discomfort. You should watch for these side effects and call the study team if you have significant discomfort or concerns. The study doctor will decide if you should be seen immediately.

Following vaccination, it is common to develop a positive response to the Mantoux test, a common skin test used to detect tuberculosis infection. If you receive a Mantoux test reaction of 10 mm or greater in the future, you should be screened by a physician for latent tuberculosis. Following your participation in this study, future tuberculosis tests may require a blood test or chest x-ray to distinguish between latent tuberculosis and a prior vaccination.

Since the study vaccine is experimental, there may be other risks that are unknown. You should get medical help and contact the study team if you have any of these symptoms at any time during the study.

Risks related to the injection and blood draws: Getting the vaccine injection and having blood collected for the blood tests may cause a feeling of pain for a short time at the site of the needle puncture. Bruising, infection, light-headedness and, very rarely, fainting may occur.

Benefits:
You may or may not directly benefit from being in this study. Information learned from this study may help people at risk of COVID-19 infection in the future.

Reminders and Responsibilities:
If you choose to participate, it should be with the intent to remain in the study for the entire duration. Please consider all aspects of the study and the time commitment as well before you provide consent for participation.

- Be willing to follow all the instructions given by the study team, including completing the follow up questionnaires and undergoing blood sample collections.
- Tell your study team about all medicines taken, even those taken without doctor's advice, as this information is important and some of these medicines may not be allowed in the study.
- You must inform your study team if you have any history of allergic disease or history of serious reaction to any vaccine or medicine administered earlier.
- Immediately inform your study team of any unusual side effects or medical problems which you may experience anytime during the study.

Alternatives to Being in the Study:

Currently there is no treatment or vaccine specifically for COVID-19, although treatment and vaccines are under study. A number of other clinical trials may be available at UHN or other institutions.

Confidentiality:

Your data will be shared as described in this consent form or as required by law. All personal information such as your name, address, phone number, OHIP number, and family physician's name will be removed from the data and will be replaced with a number. A list linking the number with your name will be kept by the study doctor in a secure place, separate from your file.

Personal Health Information

If you agree to join this study, the study doctor and his/her study team will look at your personal health information and collect only the information they need for the study. Personal health information is any information that could identify you and includes your:

- name,
- phone number,
- date of birth,
- new or existing medical records, that includes types, dates and results of medical tests or procedures.

The following people may come to the hospital to look at the study records and at your personal health information to check that the information collected for the study is correct and to make sure the study is following proper laws and guidelines:

- Representatives of the University Health Network (UHN) including the UHN Research Ethics Board
- Representatives of Health Canada or other regulatory bodies (groups of people who oversee research studies) outside of Canada, such as the United States Food and Drug Administration.

Study Information that Does Not Identify You

Some study information will be sent outside of the hospital. Any information about you that is sent out of the hospital will have a number and will not show any information that directly identifies you.

The study information may be shared with partner companies or with national and international regulatory agencies to help answer the study question, to get approval to sell VPM1002, to develop future studies on this product or for research related to this study.

You will not be named in any reports, publications, or presentations that may come from this study.
Your health information from this research project will be sent to other countries but your identifiers will be removed. They will not be able to identify you.

It is important to note that positive results for communicable diseases, including COVID-19, must be reported to the Medical Officer of Health (also known as the local public health unit), under the Health Protection and Promotion Act. Additionally, the Ontario government has passed a regulation authorizing first responders, such as police, firefighters and paramedics to access an individual's name, address, date of birth and whether the individual has had a positive test for COVID-19. This regulation may be enlarged or rescinded in the future as the COVID-19 situation changes.

Registration of Clinical Trial:
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.

Voluntary Participation:
Your participation in this study is voluntary. You may decide not to be in this study, or to be in the study now, and then change your mind later. You may leave the study at any time.

If you are a First Nations or an indigenous person who has contact with spiritual 'Elders', you may want to talk to them before you make a decision.

We will give you new information that is learned during the study that might affect your decision to stay in the study.

Withdrawal from the Study:
If you no longer want to participate in this research, you should tell the study team. The study team will ensure all data collection is completed.

Similarly, if you no longer want your samples to be used in this research, your study doctor will notify the sponsor who will ensure the samples are returned to the hospital from which they were obtained if needed, or destroyed. If tests have already been done on your sample(s), it will not be possible to withdraw those results. However, no further testing will be done.

Costs and Reimbursement:

There will be no cost for participation in this study. The study vaccine will be provided at no charge. You will not be paid for participating in this research study.

Rights as a Participant:
If you are harmed as a direct result of taking part in this study, all necessary medical treatment will be made available to you at no cost.

By signing this form, you do not give up any of your legal rights against the investigators or involved institutions for compensation, nor does this form relieve the investigators or involved institutions of their legal and professional responsibilities.

Conflict of Interest:
The drug manufacturers Verity Pharma is providing the study drugs free of charge for use in this study. They are, however, not the sponsor of this study and are not involved in the analysis or publication of the data. Dr. Neil Fleshner, one of the study co-investigators, is part of Verity Pharmaceuticals' Scientific Advisory Board. Dr. Fleshner is not directly involved in any recruitment or data collection for this study.

The researchers will not receive any direct benefit for conducting this study.

Researchers have an interest in completing this study. Their interests should not influence your decision to participate in this study.

If you would like additional information about the funding for this study, or about the role of the doctor in charge of this study, please speak to the study staff.

Commercialization:
It is possible that the research conducted using your samples and/or study data may eventually lead to the development of new diagnostic tests, new drugs or other commercial products. There are no plans to provide payment to you if this happens.

Questions about the Study:
If you have any questions, concerns or would like to speak to the study team for any reason, please call: *416-946-4501 x7510.*

If you have any questions about your rights as a research participant or have concerns about this study, call the Chair of the University Health Network Research Ethics Board (UHN REB) or the Research Ethics office number at 416-581-7849. The REB is a group of people who oversee the ethical conduct of research studies. The UHN REB is not part of the study team. Everything that you discuss will be kept confidential.

You will be given a signed copy of this consent form.

Consent:

This study has been explained to me and any questions I had have been answered. I know that I may leave the study at any time. I agree to the use of my information as described in this form. I agree to take part in this study.

Print Study Participant's Name	Signature	Date

My signature means that I have explained the study to the participant named above. I have answered all questions.

Print Name of Person Obtaining Consent	Signature	Date