## INFORMATION AND CONSENT FORM

**RESEARCH ACTIVITY**

**TITLE: Development of Endometriosis Test Kit - Lateral Flow Device**

**RESEARCH TEAM:**

| Name | Role in Research | Affiliation | Email | Phone |
|---|---|---|---|---|
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You are invited to participate in a research study aimed at developing the first-of-its-kind rapid and non-invasive diagnostic kit for endometriosis (EndoID) because you are a person between the ages of 19 – 45 years and have been diagnosed with endometriosis by laparoscopy or you are a healthy control subject without endometriosis. Before agreeing to participate in this research and signing this Information and Consent form, please take the time to read, understand and consider the following information. We invite you to consult with any individual about your potential participation in this study. We also invite you to speak with the research team member who contacted you for any question you may have about the research.

SYNG Pharmaceuticals Inc. (SYNG Pharma) is an Ontario based biotechnology company, developing a new first-in-class diagnostic test and therapeutic for endometriosis.

**Research Activity and Purpose of the Study:**
Endometriosis is an immunologic condition that affects one in ten women. Despite being one of the most prevalent female reproductive disorders characterized by debilitating menstrual pain, discomfort during intercourse, abnormal vaginal bleeding, chronic pelvic pain and infertility, the disease remains misdiagnosed, misunderstood, and ineffectively treated. At present, the diagnosis of endometriosis can only be determined by laparoscopy and biopsy of endometrial lesions. There is no rapid diagnosis for endometriosis.

Synuclein gamma (SNCG) is a protein involved in cellular proliferation. Several studies have demonstrated that SNCG is correlated with poor outcomes of breast cancer, ovarian cancer, colon cancer and pancreatic cancer. Elevated SNCG levels have been observed in ovarian endothelial cells of endometriosis lesions. Based on these results, SYNG Pharma has developed antibodies that can bind to this protein. Another antibody has been also developed by the company to bind B-CELL LYMPHOMA-6 (BCL-6), a transcription factor that could be a promising biomarker of endometriosis. The goal of this project is to develop the first-of-its-kind rapid and non-invasive lateral flow-based diagnostic kit for endometriosis using these two antibodies.

The research project has 3 objectives which are as follows:
a) to evaluate the storage and preservation conditions of the samples - i.e., to evaluate the levels of SNCG1 and BCL-6 proteins in the samples under various temperature conditions (-20 °C, 4 °C, 20 °C) and time periods (1, 2, 4, 8, 24 h);
b) to detect and measure the concentrations of SNCG1 and BCL-6 between endometriosis and healthy participants. BCSG1 and BCL-6 levels in endometriosis participants will be compared to healthy participants using newly generated antibodies to these two potential molecular markers using an *in vitro* ELISA test (a colorimetric test to detect/measure the amount of a marker using a reaction with a specific antibody); and
c) to validate the proof of concept of the prototype (a lateral flow device).

Your sample could be used for one objective or could be separated into several parts to meet several objectives of the research project. The risks and benefits of your participation are explained below in the benefits and risks sections.

Participants who register and qualify for the research study will be asked to provide a menstrual effluent sample and a blood sample. Once received at the clinic in confidentiality, the biological samples will be transferred to the TAC-B lab at La Cité. They will be collected and refrigerated until processed for serum separation and then stored at -80°C before further analysis.

**Nature and Length of Participation:**
Your participation in the research study will consist of you providing both a menstrual effluent sample and a venous blood sample. Upon receipt of your completed registration form, the CSanté Medical Centre will call you to qualify you for the study. They will ask you whether you have endometriosis or not, and if you do, whether it was diagnosed by laparoscopy. To qualify for the study, you need to have endometriosis as diagnosed by laparoscopy or be a healthy control. You will be asked other questions as per the registration form, to qualify for the study including whether you are breastfeeding, pregnant or present with other health conditions.

To register for this study, you will be asked for your name, full mailing address, phone number and email address. The mailing address will be used to send the instruction booklet and kit to collect the menstrual effluent at home (this includes menstrual cup). The email address and/or phone number will be used to contact you if necessary.

If you qualify for the study, you will be asked to call the clinic on the first day of your period to book an appointment on a day between day 2-5 of your period to deposit your menstrual effluent sample (at least 10 mL) and provide a blood sample (10 mL). We ask that you wear the menstrual cup from the night before your appointment. At your appointment, a medical professional (nurse or doctor) will provide you with a receptacle into which to transfer your menstrual effluent sample and they will also draw your blood

sample The appointment with CSanté should last about 30 minutes. The medical professional will go through this Information and Consent Form and be able to answer any questions you may have. It is at this time that you will be asked to sign the Information and Consent Form. Your samples will be collected in coded tubes. Once the samples are provided to the clinic in total confidentiality and you have left the clinic, a member from the research project from TAC-B will collect the samples and store them appropriately.

For this study, people who are between the ages of 19 – 45 years and suffering from endometriosis diagnosed only by laparoscopy, or are healthy controls subjects without endometriosis, will be included. . People with endometriosis during stimulation with gonadotropins, or current or prior history of uterine, ovarian, colon, pancreatic or breast cancer, will be excluded. Individuals who present with any other medical problem (hormonal, metabolic, immunologic) will be excluded.

The menstrual effluent and venous blood samples you will provide will be number coded at the site of collection; thus, there will be no link between you and the samples you provided once they enter the biological sample and data collection phase. The alphanumeric codes ENDO-001 and CTRL-001 will be used for participants in the test and control groups, respectively. Only the Principal Investigator will have access to this information, which will be protected by lock and key. Strictly only members from the research study will handle your coded biological samples. Your biological samples will be stored either in the fridge (for fresh, unprocessed samples) or freezer (for samples that have undergone the first step of the process). The data from your biological samples (for example, your levels of BCL-6 protein) will also be stored in coded format to protect your identity. Therefore, the participant's identifying information will not be disclosed. The project team members will have access to the biological material and biological data, but only in coded format. Only the principal investigator will have access to personal information. The biological samples will be stored for 7 years after which they will be destroyed by autoclaving. The data will be also stored for the same time and then deleted.

All the information and the biological material collected during this project will be kept strictly confidential within the limits established by the law. To safeguard your identifying information and the confidentiality of the data, you will only be identified using a code. The data collected will be kept in the principal investigator's office, at La Cité, under lock and key and on a code-protected computer. The principal investigator and members of the research team will use the research data collected for the sole purpose of this research. There will be no sample transfer to Syng Pharmaceuticals. Raw data will be transferred to Syng Pharmaceuticals using encrypted communication.

Syng Pharmaceuticals will co-fund the study and will assist in the analysis of the results during the project. The data collected and the research results will only be used to meet the objectives of the study. All samples and data or research results are identified by a code so there will be no linkage between the samples, data, results and identity of the participants.

Only the levels of the two proteins in menstrual fluid and venous blood would be studied to meet the objectives of the research project. No other tests (genetic or other) or other diagnosis would be performed on the collected samples.

**Benefits:**
You will receive no personal benefits from your participation in the current research project. No economic benefit resulting from the commercialization of the test will be paid to the participants. However, the

knowledge gained from your participation will help to improve the accuracy of diagnosing endometriosis in the future.

For those participants whose sample will be used for objective a), your participation will allow the research study to evaluate the limitations of the storage conditions. With this evaluation, we can well standardize the methodology for the study. Several articles have already established certain storage protocols so we wanted to confirm them, and to delve deeper which would be beneficial in advancing our knowledge within our research but also to other research in similar fields.

For those participants whose sample will be used for objective b), your participation will demonstrate proof of principle that the levels of the proteins of interest named above are higher in samples from participants with endometriosis than those from healthy participants. This proof of validation will bring us closer to generating a proof of concept for the endometriosis test.

Finally, for those participants whose sample will be used to address objective c) (proof of concept for a lateral device), your sample will bring us closer to commercializing a rapid screening device for endometriosis which will make diagnosis of this disease more accessible to the general population.

As such, appreciable benefits are afforded from the participants' menstrual effluent and blood samples whether they are used to address a, b, or c only, or for objectives a & b, b & c, or a & b.

**Risks:**
The risks listed below are applicable regardless of whether your sample is used to meet objective a, b and/or c.

Menstrual cups are small, flexible receptacles that are inserted into the vaginal canal to catch menstrual blood. They are an alternative to sanitary pads, period underwear, or tampons during menstruation and are generally regarded as safe within the medical community. The risks are considered minimal and unlikely to occur when the cup is used as recommended. The current research project involves minimal risks of irritation, bacterial infection and toxic shock syndrome (TSS).

To reduce these risks, we ask that you wash your hands thoroughly with warm water and antibacterial soap before removing or inserting your cup and apply a small amount of water or water-based lube to the outside of the cup to aid insertion.

Risks associated with blood drawing may include pain, bruising, light-headedness, fainting, blood clots, and bleeding at the blood drawing site. Occasionally, there can be swelling around the area where the needle enters the body. There is also a small risk of infection.

Importantly, you are under no obligation to participate. You have the right to withdraw from the research study at any time without any prejudice to pre-existing rights. To do this, the participant can send an email to one of the project members. You will receive, throughout the research and in a timely manner, pertinent information relating to your decision to continue, or not, to participate in the research project. You have a right to request that data or biological material pertaining to you be withdrawn. The destruction of your sample by autoclaving (a way of destroying biological products with high temperature and pressure) will be performed. All the data from your samples would also be deleted from our files.

**Shutdown criteria, removal of data/samples, and actions taken in the event of "incidental findings''**

The researchers or the Research Ethics Board from La Cité can withdraw participants without their consent, if they do not respect the project guidelines for their participation or if there are administrative reasons for abandoning the project, especially for reasons of security or feasibility. Participants' samples and data can also be withdrawn without consent from the study if they do not strictly meet the inclusion/exclusion criteria. Strictly adhering to the inclusion/exclusion criteria will ensure that the representative populations with which we are basing our results are stringent and conclusive. Women that are pregnant, breastfeeding, menopausal or present with other medical conditions can skew the levels of the potential protein markers.

In case of discovery other than in relation to the objectives of the project (incidental findings), we have an obligation to contact the participant. Within the course of our research study, we aim to show a strong correlation with the levels of SNCG and BCL-6 and endometriosis, and little to none of these proteins in control patients. If we come across a participant in the control group that has an appreciable level of these two proteins, the participant will be advised by the Principal Investigator to visit their family doctor for a follow-up.

**Commercialization and Conflicts of Interest:**
There is a possibility that the research results will be published in a peer-reviewed journal. It is expected that the lateral-flow device developed in this study will be commercialized. If so, no economic benefit from the commercialization of the test will be paid to participants.

There are no real, perceived or potential conflicts of interest concerning: any member of the research team or their family, their institution, or the sponsors of the research project, or with the principal investigator's institution and the funding agency.

**Financial Compensation**:
Parking and public transportation expenses will be reimbursed – an amount of $5 will be provided for 1h of parking or $3.75 will be provided for public transportation.

**Compensation for damages and rights of the participant:** If, following your participation in this research, you experience any harm or damages, you do not waive any of your rights nor do you release the researchers, the funding agency or the institution from their legal or professional responsibilities.

**Disseminating research results:**
The research results will be disseminated, in the form of a short report, upon request. The research results may be published in scientific magazines or shared with other individuals during discussions of a scientific nature. However, any scientific publication or communication will not disclose any information that could identify the participant.

For purposes of monitoring and control, your research file shall be available for consultation by an individual authorized by the Research Ethics Board from La Cité or by an individual authorized by research funding agencies. All these individuals and organizations adhere to a confidentiality policy.

You have the right to consult your research file to verify the accuracy of the information collected as long as the researcher or the institution responsible for the project has the information. However, to preserve the scientific integrity of the research project, you will only have access to certain details once the study has been completed.

**Resource Person:** Should you have any questions regarding this research project, please contact Julien LeRoy at 613-742-2483, ext 2829 or by email at jleroy@lacitec.on.ca.

If you have any questions concerning your participation in this research, please communicate with La Cité's Research Ethics Board's secretariat by email at cer@lacitec.on.ca.

**Consent:**

Returning this completed questionnaire signifies that you agree to participate in this research project according to the conditions that have been set out. Please keep a copy of this document.

1. AGE: _____. If you are between 19 – 45 you are included in the study
2. I have endometriosis: YES ☐ NO ☐
3. If I answered YES to question 2, I confirm that the method of diagnosis was laparoscopy: YES ☐ NO☐
4. Are you pregnant or breast-feeding?: YES ☐ NO☐
5. I have another medical problem (hormonal, metabolic, immunologic): YES ☐ NO☐
6. Current or prior history of uterine, ovarian, colon, pancreatic or breast cancer: YES ☐ NO☐
7.

I have read this information and consent form.
I acknowledge that the nature of my participation in this research project has been clearly explained to me, that my questions have been answered and that I have received sufficient time to make a decision. I agree to participate in this research project according to the conditions that have been set out in the current form, of which I have a copy.

_____ _____

Name and signature of the research participant Date

I certify that I have explained to the participant the nature of their participation in the current research project, have answered all their questions relating to this and have clearly indicated that they are free to terminate their participation at any time without any consequences. I, with the research team, promise to respect the terms and conditions set out in the current information and consent form, and declare that I have provided the participant with a signed copy.

_____ _____

Name and signature of research project member Date