INFORMED CONSENT FORM

STUDY TITLE: A prospective, observational study to evaluate the clinical utility circulating synuclein gamma (SNCG) and B-cell lymphoma-6 (BCL6) levels as potential biomarkers for endometriosis

Principal Investigator: Dr. Robert Casper, TRIO Fertility

Research Coordinator: Yasaman Sadeghi, TRIO Fertility

Sponsor: SYNG Pharmaceuticals Inc.

Study Site: TRIO Fertility

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1. INTRODUCTION

You are being invited to participate in a research study. This form provides detailed information about the study so you can decide whether to participate. Please read it carefully and ask any questions before agreeing to join. Participation is entirely voluntary, and you may withdraw at any time without affecting your medical care.

2. PURPOSE OF THE STUDY

Endometriosis is a condition in which tissue similar to the lining of the uterus grows outside the uterus, often causing pain and infertility. Currently, endometriosis can only be definitively diagnosed through invasive procedures like laparoscopy and biopsy.

The purpose of this study is to investigate whether the proteins **Synuclein Gamma (SNCG)** and **B-Cell Lymphoma 6 (BCL6)**, measurable in blood and menstrual fluid, can serve as non-invasive biomarkers to diagnose or monitor endometriosis.

3. STUDY PROCEDURES

If you agree to participate, the following procedures will be performed:

A. Screening and Enrollment

- You will be evaluated to determine if you meet the eligibility criteria (see Section 4).
- If eligible, you will be provided detailed verbal and written information about the study and asked to sign this consent form.

B. Sample Collection

1. **Peripheral Blood Sample**
    - 10 mL of blood will be collected from a vein in your arm using a sterile needle and collection vial (VACUTAINER).
2. **Menstrual Blood Sample**
    - Using a provided reusable menstrual cup (DIVA), you will collect approximately 5 mL of menstrual blood on the 1st or 2nd day of your menstrual cycle.
    - If collected at home, a designated research team member will pick up the sample the same day (local participants only).
    - Menstrual blood will be processed to separate supernatant and stored in 1 mL aliquots at -80°C until analysis.
3. **Follow-up Samples for Endometriosis Group**
    - If you are in the endometriosis group and undergo treatment (medical or surgical), additional blood and menstrual samples will be collected at 3 months and 6 months post-treatment to assess changes in SNCG and BCL6 levels.

4. ELIGIBILITY CRITERIA

Endometriosis Group (n=50):

- Women aged 18–45 with active endometriosis confirmed by ultrasound, MRI, or laparoscopy.

Exclusion:

- Women <18 or >45 years
- Pregnant women
- Women currently undergoing gonadotropin stimulation
- History of cancer (uterine, ovarian, colon, pancreatic, breast, or other) or chronic illness

Control Group (n=50):

- Women aged 18–45 without endometriosis or other gynecological issues

Exclusion:

- Women <18 or >45 years
- Pregnant women

- History of any disease including cancer or chronic illness

5. LABORATORY ANALYSIS

- Serum and menstrual fluid samples will be analyzed using **EndoID ELISA kits** specific for SNCG and BCL6.
- ELISA involves adding your samples to pre-coated plates, incubating with detection antibodies, and measuring the color change that corresponds to protein concentration.
- All procedures follow standard laboratory safety and quality control protocols.

6. RISKS and DISCOMFORTS

Physical Risks:

- **Blood Draw:** May cause minor pain, bruising, swelling, or very rarely infection.
- **Menstrual Blood Collection:** Minimal discomfort, possible inconvenience or messiness.
- **Laboratory Risks:** No direct physical risks. All samples will be handled with standard precautions.

Privacy and Confidentiality Risks:

- Although your samples and data will be coded and stored securely, there is a small risk of loss of confidentiality if data were accidentally accessed by unauthorized individuals.
- The information collected in this study (protein levels and basic demographic data) is not considered highly sensitive and does not include genetic or identifying medical data. Therefore, the risk of harm from a confidentiality breach is considered minimal.

7. POTENTIAL BENEFITS

- There may be no direct benefit to you.
- The study may contribute to earlier, less invasive diagnosis of endometriosis in the future, potentially improving care for other patients.

8. DATA CONFIDENTIALITY

- Each participant will be assigned a unique study code. Your name or any other identifying information will not appear on samples or data files. Publications or presentations will use only summarized, anonymous data.

- All electronic and paper study records will be stored securely at TRIO Fertility, 655 Bay Street, Suite 1100, Toronto, Ontario M5G 2K4, in locked cabinets and password-protected servers accessible only to authorized study personnel.
- Only the Principal Investigator and designated research team members will have access to the coded data.
- Data may be reviewed by authorized representatives of ethics or regulatory bodies (for example, the Research Ethics Board or Health Canada) for monitoring or auditing purposes, but these reviewers are also bound by confidentiality agreements.
- No information that could identify you will be released outside the research team unless required by law.

9. VOLUNTARY PARTICIPATION and WITHDRAWAL

- You may withdraw at any time without penalty.
- If you withdraw, collected samples may still be used for analysis unless you request destruction.

10. STORAGE of SAMPLES and FUTURE USE

- Your blood and menstrual fluid samples will be stored at -80°C at TRIO Fertility (655 Bay Street, Suite 1100, Toronto, Ontario M5G 2K4) until all planned analyses for this study are completed.
- Samples and associated data will be retained for five (5) years after study completion to allow for verification of study results and regulatory review if required.
- Only the Principal Investigator and authorized members of the research team will have direct access to the stored samples for processing and analysis. If required for auditing or monitoring purposes, authorized representatives of the Research Ethics Board or regulatory authorities may review storage procedures, but they will not have access to any identifying information.
- After this period, all remaining biological materials will be securely destroyed using standard laboratory biohazard disposal procedures.
- Samples will not be used for research unrelated to this study without additional consent.

11. INCIDENTAL FINDINGS

- This study measures specific proteins (Synuclein Gamma and BCL6) in blood and menstrual fluid. These tests are for research purposes only and are not intended for clinical diagnosis.
- It is unlikely that the analyses will reveal any unexpected medical information about your health.
- However, in the rare event that a result of potential clinical significance is identified, the Principal Investigator will review the finding and determine whether it is considered a material incidental finding under TCPS 2 guidelines.
- If so, you will be contacted and given the option to receive this information and to discuss it with your healthcare provider.
- You may also choose, by initialing below, whether you wish to be informed of such findings should they occur:

  ☐ Yes, I wish to be informed of any clinically relevant incidental findings.

  ☐ No, I do not wish to be informed of any incidental findings.

12.COMPENSATION

- No financial compensation will be provided.

13. DURATION of PARTICIPATION

- Participation includes initial sample collection and, for endometriosis patients, follow-up collections at 3- and 6-months post-treatment.
- Total participation may range from a single visit (control group) to multiple visits over six months (endometriosis group).

14. CONTACTS

For questions about the study or research-related concerns, contact:

- **Dr. R. Casper** – 416-506-0804 x3228
- **Yasaman Sadeghi** – 416-506-0804 x2268

15. ETHICS OVERSIGHT AND CONTACT INFORMATION

This study has been reviewed by Veritas Independent Review Board (IRB). If you have any questions about your rights as a research participant or the Investigator's responsibilities, you may contact the Manager of Veritas IRB 24 hours per day and 7 days per week at 514-337-0442 or toll-free at 1-866-384-4221. An IRB is a group of scientific and non-scientific individuals who perform the initial and ongoing ethical review of the research study with the subject's rights and welfare in mind. If you have any study-related comments, complaints or concerns, you should first contact the study investigator. Please call the IRB if you need to speak to a person independent from the Investigator and the research staff, and/or if the Investigator and the research staff could not be reached.

16. Consent Statement

I have read and understood the information provided. I have had the opportunity to ask questions and have received satisfactory answers. I voluntarily agree to participate in this study, and I know that I may leave the study at any time.

Print Study Participant's Name	Signature	Date

Witness's Name	Signature	Date

For the research team only:

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

Print Name of Person Obtaining Consent	Signature	Date