PILOT PARTUM TRIAL CONSENT FORM

TITLE: A pilot study assessing the feasibility of a randomized controlled trial evaluating aspirin in postpartum women at risk of developing venous thromboembolism

SPONSOR: University of Calgary

PRINCIPAL INVESTIGATOR: Dr. Leslie Skeith, Telephone: 403-944-5246

RESEARCH COORDINATOR: Alexandra Garven, Telephone: 403-220-7631

This consent form is only part of the informed consent process. It should give you the basic idea of what the research is about and what your participation will involve. If you would like more detail about something mentioned here, or information not included here, please ask. Take the time to read this carefully and to understand all information given to you. You will receive a copy of this form for your records.

BACKGROUND

You are being asked to take part in this research trial because you are pregnant or postpartum and have known risk factors for blood clots. Some women are at risk for developing blood clots in the legs or lungs (thrombosis) after they deliver a baby (postpartum). A blood clot can form in the lungs, which can be serious. The risk of blood clots is highest in the first 6 weeks following delivery. While we know what the risk factors are for getting a blood clot after delivery, we still don't know what the best way is to prevent blood clots.

Previous research studies (trials) tried to see if using daily injectable blood thinners after delivery could prevent blood clots. These trials were not successful because taking daily injectable blood thinners at home was not very popular. Many women who deliver babies and have modest risk factors for blood clots may be given injectable blood thinners while they are in hospital, but they usually do not go home on injectable blood thinners.

The PARTUM trial asks if aspirin is a safe and effective option for preventing blood clots in women who have risk factors for blood clots after delivery. Aspirin helps to prevent blood clots in people after hip and knee surgery. It is an attractive choice after delivery because it is safe with breastfeeding. We are studying whether aspirin will help to prevent blood clots in postpartum women who have risk factors for blood clots.

WHAT IS THE PURPOSE OF THIS PILOT TRIAL?

A pilot trial is a smaller trial that is done before a large, expensive trial. The purpose of our pilot PARTUM trial is to show that a larger international trial is possible. We will collect information about blood clots and bleeding that will be used in our larger trial. Our larger trial will be able to answer if aspirin does safely prevent blood clots in postpartum women. This will allow us to better care for postpartum women who are at risk of blood clots.

We estimate that 384 participants will be in our pilot PARTUM trial in 8 centres across Canada and Europe, with 48 participants from Calgary.

WHAT WOULD I HAVE TO DO?

If you choose to take part, following the birth of your baby you will be given either low dose aspirin or placebo pills (sugar pills) to take every day for 6 weeks. Before you leave the hospital, we will give you a bottle of the study medication (aspirin or placebo). No blood work or imaging tests are needed for this trial.

If your doctor thinks you are at a high risk for developing blood clots and they recommend that you go home on injectable blood thinners, or you need aspirin for other reasons, then you will not be eligible to participate in this trial.

Neither you nor your doctor will know what treatment you receive (double blinded). A computer system is used to randomly put each participant into either the aspirin or placebo group. The doctors and research team do not get to choose or know which medication you will be given. You will not know if you are taking aspirin or placebo. If an emergency arises and your doctor needs the information, they will be able to know if you have been given aspirin or placebo.

After 6 weeks of taking the medication every day, we will see you at a visit. You have the option of this doing visit in person, over the telephone or by a video call. The questions will be about symptoms of blood clots, bleeding and possible side effects, and will take 15 minutes or less to answer. We will ask you similar questions at 3 months by a telephone call. We are available

over the telephone or in person if you have any questions or new symptoms that come up any time within the 3-month trial duration.

We will provide you with a drug diary to record taking the study drug daily and any NSAID (nonsteroidal anti-inflammatory drug) use. At the 6-week visit we will ask for your dairy and your study drug bottle to be returned. The 6-week visit may be in person or alternatively may be completed by phone or video call. If you chose to complete the 6-week visit by phone or video call, then we will provide you with a pre-paid envelope to mail the empty study drug bottle back.

WHAT ARE THE RISKS?

Low dose aspirin is well tolerated. Side effects of aspirin at low doses include nausea, stomach upset and a small increased risk of bruising or bleeding, including gastrointestinal (stomach and intestines) bleeding. There is the potential that aspirin could make your lochia (vaginal bleeding after birth) heavier. Aspirin can trigger asthma, bronchospasm (tightening of the muscles that line the airways) or allergic reactions, especially in those already at risk (people who have asthma, hay fever, nasal polyps or chronic lung disease). You may not benefit from the medication so you could be at a small risk of developing a blood clot.

There is a risk of a privacy or confidentiality breach, but we will take every precaution to protect your personal information. We will only collect and use the minimal amount of information needed to answer our research questions.

ARE THERE ANY RISKS WITH BREAST FEEDING?

Expert guidelines recommend that low doses of aspirin can safely be taken daily during breastfeeding, but that higher doses of aspirin should be avoided. Your study medication will either be a low dose of aspirin (81 mg) or placebo (sugar pill) and we recommend taking only one pill of the study medication a day. Low dose aspirin is safe to babies who are being breastfed.

In a research trial of women who took low dose aspirin (81 mg) daily, there was no aspirin detected in breast milk. Only a small amount of the break-down products of aspirin was detected in breast milk and that amount was below the level considered safe for breastfed infants. In a research trial of postpartum women who were taking low doses of aspirin, there were no negative effects seen in their breastfed babies.

WILL I BENEFIT IF I TAKE PART?

If you agree to take part in this trial there may or may not be a direct benefit to you. Your chance of developing a blood clot after delivery of your baby may improve during the trial but there is no guarantee that this research will help you. The information we get from this trial may help us to provide better treatments in the future for women at risk of blood clots after delivering a baby.
If you decide to take part in this trial you will be given information to help you be aware of the signs and symptoms of a blood clot. This information as well as discussions with the research team could help you to detect potential blood clots. You will be given contact information for the research team so that you can reach out at any time to ask questions. The research team and doctors are available to discuss any concerns or symptoms you are experiencing.

DO I HAVE TO TAKE PART?

Your participation in this trial is voluntary. The alternative to this trial is not to take part. There is currently no standard or approved treatment available, however you can talk to your doctor about two different options available. The options include going home on no preventative medication for blood clots or on injectable blood thinners.

It will not affect your medical care if you decide not to be in this trial, or to be in the trial now, and then change your mind later. If your health changes, then your doctor may also withdraw you from the trial at any time.

If you withdraw your consent, the research team will no longer collect your personal or health information.

If new information becomes available that might affect your participation in the trial, then you will be informed as soon as possible.

WILL I BE PAID FOR PARTICIPATING, OR DO I HAVE TO PAY FOR ANYTHING?

You will not receive any money for participating in the trial. We will reimburse you for your parking at the 6-week trial visit, if you choose to attend this visit in person.

WILL MY RECORDS BE KEPT PRIVATE?

We will protect your confidentiality.

- All information collected during your participation in this trial will be given a unique trial number, and will not contain information that identifies you, such as your name, address, etc.
- The link between your unique trial number and your name and contact information will be stored securely and separate from your trial records and will not leave an Alberta Health Services facility.
- Any documents leaving an Alberta Health Services facility will contain only your unique trial number. This includes publications or presentations resulting from this trial.
- Information that identifies you will be released only if it is required by law.
- Research records will be kept for 25 years by law, after this time they will be destroyed.

If you agree to join this trial, we may need to access your personal health records. Any personal health information that we get from these records will be only what is needed for the trial. This may include accessing records with Alberta Health Services, Alberta Health and/or your electronic health record in Netcare, the provincial electronic health record system.

A description of this clinical trial will be available on www.clinicaltrials.gov. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

Authorized representatives from the University of Calgary, the Conjoint Health Research Ethics Board and Health Canada may look at your medical records that include your personal information for quality assurance purposes.

Data collected during your time in this research trial will have your personal information removed. This data will be held in a database for future use for the larger PARTUM research trial. Any future use of this research data is required to undergo review by a Research Ethics Board.

IF I SUFFER A RESEARCH-RELATED INJURY, WILL I BE COMPENSATED?

In the event that you suffer injury as a result of taking part in this trial, no compensation will be provided to you by the University of Calgary, Alberta Health Services or the Researchers. You still have all your legal rights. Nothing in this consent form changes your right to seek damages.

SIGNATURES

Your signature on this form means that you have understood the information about your participation in the research project and agree to take part. In no way does this remove your legal rights nor release the investigators or involved institutions from their legal and professional responsibilities. You are free to withdraw from the trial at any time without affecting your health care. If you have further questions about this research, please contact:

Dr. Leslie Skeith (403) 944-5246

Alexandra Garven (research coordinator) (403) 220-7631

If you have any questions about your rights as a possible participant in this trial, please contact the Chair, Conjoint Health Research Ethics Board, University of Calgary at 403-220-7990.

Participant's Name	Signature and Date
Investigator/Delegate's Name	Signature and Date
Witness' Name	Signature and Date

☐ **Witness Signature Required?**

The University of Calgary Conjoint Health Research Ethics Board has approved this research trial.

A signed copy of this consent form has been given to you to keep for your records and reference.

Study Title: The Pilot PARTUM Trial
PI: Dr. Leslie Skeith
REB #: 19-1237

DOCUMENTATION OF CONSENT PROCESS

Participant Name: _____

Person obtaining consent initial each completed step in the process:

____ Participant agreed to speak with the research coordinator about the above referenced study.

____ Informed consent was discussed with participant.

____ Copy of the consent form was provided for participant and/or authorized representative review.

____ Participant and/or authorized representative was given adequate time to read the consent form and discuss the study with study investigators, family doctor, and/or family members.

____ All questions were answered. Participant and/or authorized representative was given time to discuss.

____ Participant and/or authorized representative agreed to participate and signed and dated the informed consent.

____ A copy of the consent form was provided to the participant and/or authorized representative upon conclusion of the consent process.

____ Consent has been signed prior to any study procedures being performed.

Comments:

_____

_____

_____

_____

_____

Consent process documented by:

_____	_____	_____
Name of person obtaining consent	Signature	Date

PARTUM

Participant Contact Sheet

Full Name: _____

MRN: _____

Phone Number: _____

Secondary Phone Number: _____

Email: _____

Preferred Method of Contact: Phone ☐ Email ☐

Address: _____

_____

_____

Baby's Name: _____

Baby's Sex: Male ☐ Female ☐

Emergency Contact

Full Name: _____

Relationship: _____

Phone Number: _____

Randomization Case Report Form

Randomization Details	
Date of randomization:	D D M M M Y Y Y Y
☐ **Randomization code obtained and matched with study medication**	
Medication randomization code (Drug ID):					

Study Medication	
Date of subject's first dose:	D D M M M Y Y Y Y
Time of subject's first dose:	H H M M

Delegate's Name

Delegate's Signature

D D M M M Y Y Y Y
Date

Confirmation of Eligibility

Screening No. ☐☐☐

Inclusion Criteria	YES	NO
At risk for thromboembolism for at least <u>ONE</u> of the following reasons:		
1. **Known inherited thrombophilia** (diagnosed prior to enrolment) ☐ Heterozygous factor V Leiden ☐ Heterozygous prothrombin gene variant ☐ Protein C deficiency ☐ Protein S deficiency	☐	☐
2. **Antepartum immobilization (strict bedrest) for ≥7 days at any time during pregnancy**	☐	☐
<u>OR</u> At risk for thromboembolism for any <u>TWO</u> of the following reasons:		
3. **Pre-pregnancy BMI ≥30 kg/m²**	☐	☐
4 **Smoking ≥5 cigarettes/day pre-pregnancy**	☐	☐
5. **Previous clinical history of superficial vein thrombosis**	☐	☐
6. **Pre-eclampsia** *(blood pressure ≥140 and/or 90 mmHg on at least one occasion <u>and</u> proteinuria of ≥0.3 grams/24 hours or ≥30 mg/mmol in a random urine sample)*	☐	☐
7. **Current pregnancy ending in stillbirth** *(pregnancy loss >20 weeks gestation)*	☐	☐
8. **Emergency cesarean delivery** *(emergency = not previously planned)*	☐	☐
9. **Small-for-gestational-age infant at time of delivery** *(<3rd percentile adjusted for gestational age and sex)*	☐	☐
10. **Postpartum infection** (*temperature ≥38.3°C <u>and</u> elevated WBC <u>or</u> neutrophil count <u>or</u> positive blood cultures)*	☐	☐
11. **Postpartum hemorrhage** *(>1000 mL of blood loss, regardless of delivery mode)*	☐	☐

Exclusion Criteria		YES	NO
1.	**More than 48 hours since delivery of the placenta at the time of randomization**	☐	☐
2.	**Received more than 2 doses of LMWH since delivery of the placenta**	☐	☐
3.	**Need for postpartum LMWH prophylaxis or systemic anticoagulation as judged by the local investigator. May include but is not limited to the conditions below. If yes, please specify:** ☐ Documented history of provoked or unprovoked VTE ☐ Mechanical heart valve(s) ☐ Known antiphospholipid syndrome (APS) ☐ Known high-risk inherited thrombophilia ☐ Antithrombin deficiency ☐ Homozygous factor V Leiden ☐ Homozygous prothrombin gene mutation ☐ Compound heterozygosity factor V Leiden and prothrombin gene mutation ☐ More than 1 thrombophilia: any combination of 2 or more: factor V Leiden, prothrombin gene mutation, protein C deficiency, protein S deficiency, antithrombin deficiency ☐ Other: _____	☐	☐
4.	**Need for postpartum ASA as judged by the local investigator. May include but is not limited to:** ☐ Documented history of myocardial infarction ☐ Documented history of ischemic stroke or transient ischemic attack (TIA) ☐ Other: _____	☐	☐
5.	**History of known ASA allergy**	☐	☐
6.	**Documented history of a gastrointestinal ulcer**	☐	☐
7.	**Known platelet count <50 x 10^9/L at any time during the current pregnancy or postpartum**	☐	☐
8.	**Active bleeding at any site, excluding normal vaginal bleeding, at the time of randomization**	☐	☐
9.	**Most recent known hemoglobin ≤70 g/L documented during the current pregnancy or postpartum**	☐	☐
10.	**Known severe hypertension (SBP >200 mmHg and/or DBP >120 mmHg) during the current pregnancy or postpartum**	☐	☐
11.	**<18 years of age**	☐	☐
12.	**Unable to give or refused consent**	☐	☐

Eligibility Criteria		YES	NO
1.	**All eligibility criteria have been met and the subject will be enrolled into the study**	☐	☐
2.	**Version date of the consent form signed by subject:**	D D M M M Y Y Y Y	

Please review with the Investigator/Co-Investigator prior to randomization:

I _____ (Investigator/Co-Investigator) confirm that I have reviewed all relevant reports, results and annotations and find the potential subject to meet all eligibility criteria. This subject may be randomized to the pilot PARTUM trial.

_____ D D M M M Y Y Y Y

Investigator/Co-Investigator Signature Date

Baseline Assessment Case Report Form

A. Demographic Data

1. Date of baseline visit: ☐☐☐☐☐☐☐☐ (D D M M M Y Y Y Y)

2. Age at randomization: ☐☐ Years

3. Race/Ethnicity (may choose more than one):
- ☐ White/Caucasian
- ☐ Black/African Heritage
- ☐ Indigenous
- ☐ Asian/South East Asian
- ☐ Hispanic/Latino
- ☐ Pacific Islander

4. Height and weight prior to this pregnancy (can be reported by the subject):
Pre-pregnancy weight: _____ ☐ kg ☐ lbs
Height: _____ ☐ cm ☐ feet/inches
Pre-pregnancy BMI: _____ (kg/m^2)
If pre-pregnancy weight unknown, use subject's reported weight in 1st trimester

5. Current maternal weight (can be reported by the subject): _____ ☐ kg ☐ lbs

6. Smoking history:
Current smoker? ☐ Yes ☐ No
Number of cigarettes per day (average over past year): ☐☐
Previous smoker? ☐ Yes ☐ No
If yes, quit date: ☐☐☐☐☐☐☐ (M M M Y Y Y Y)
Number of cigarettes per day (average over year prior to quitting): ☐☐

B. Medical History

1. Has any related family members had a VTE?
☐ No ☐ First degree relative ☐ Second degree relative

2. Prior medical issues?
☐ **No prior medical issues** ☐ **Yes**, please check all that apply:
- ☐ Systemic lupus erythematosus (SLE, lupus)
- ☐ Sickle cell disease
- ☐ Inflammatory bowel disease
- ☐ Hypertension (prior to pregnancy)
- ☐ Type 1 diabetes (prior to pregnancy)
- ☐ Type 2 diabetes (prior to pregnancy)
- ☐ Known kidney disease: _____
- ☐ Known cardiac disease: _____

3. Previous history of superficial vein thrombosis? ☐ Yes ☐ No
If yes, confirmed by ultrasound? ☐ Yes ☐ No
If yes, pregnancy or postpartum related? ☐ Yes ☐ No
If yes, exogenous estrogen related? ☐ Yes ☐ No

4. **Previous history of varicose veins?** ☐ Yes ☐ No
(soft, dilated, large superficial veins)

C. Obstetrical History

1. **Parity:**

Number of pregnancies carried past 20 weeks gestation (including current pregnancy): ☐☐

2. **Prior cesarean delivery** (not including current pregnancy)? ☐ Yes ☐ No

3. **Did the subject have any complications during <u>PRIOR pregnancies</u>?**

☐ **No complications** ☐ **Yes <u>PRIOR</u> complications**, please check all that apply:

- ☐ Gestational hypertension
- ☐ Pre-eclampsia
  - Largest amount of proteinuria documented if known:
    - Urine protein / Cr ratio: _____ mg/mmol spot urine
    - **OR** 24-hour urine protein: _____ grams
- ☐ Eclampsia (seizures)
- ☐ HELLP syndrome
- ☐ Gestational diabetes
- ☐ Pregnancy loss
  - ☐ <10 weeks gestation Number of losses: ☐☐
  - ☐ 10-20 weeks gestation Number of losses: ☐☐
  - ☐ >20 weeks gestation Number of losses: ☐☐
  - ☐ Unknown timing Number of losses: ☐☐
- ☐ Intrauterine growth restriction or small-for gestational age
- ☐ Placental abruption
- ☐ Intrapartum infection (e.g. chorioamnionitis)
- ☐ Postpartum infection

D. Current Pregnancy

1. **Method of conception:**

☐ Spontaneous ☐ Ovulation induction with medical therapy

☐ Intrauterine insemination ☐ In vitro fertilisation (IVF) or Intracytoplasmic sperm injection

2. **Aspirin use in current pregnancy:** ☐ Yes ☐ No

If yes, dose per day: _____ mg

Gestational age when aspirin started: ☐☐ weeks + ☐ days

Date of last dose: D D M M M Y Y Y Y

3. Immobilization in current pregnancy:

Any type of bedrest at any point during pregnancy? ☐ Yes ☐ No

If yes, total days immobilized during this pregnancy: ☐☐

Bedrest at home? ☐ Yes ☐ No

Hospitalized for bedrest? ☐ Yes ☐ No

Type of bedrest (choose all that apply):

- ☐ Strict bedrest (>90% of time, bathroom privileges)
- ☐ Modified bedrest (Limited walking, restricted activities)

Reason for bedrest: _____

Number of episodes of bedrest: ☐☐

Gestational age at **start** of bedrest closest to delivery: ☐☐ weeks + ☐ days

Gestational age at **end** of bedrest closest to delivery: ☐☐ weeks + ☐ days

E. Delivery Details

1. Date of admission for labor/delivery: D D M M M Y Y Y Y

2. Date of delivery of infant: D D M M M Y Y Y Y

3. Date and time of delivery of placenta: D D M M M Y Y Y Y

H H M M

4. Gestational age at delivery: ☐☐ weeks + ☐ days

5. Singleton or multiple pregnancy: ☐ Single ☐ Multiple pregnancy

6. Type of Labor:

- ☐ Spontaneous labor
- ☐ Induction of labor, reason if known:_____
- ☐ No labor (e.g. scheduled cesarean delivery)

7. Mode of Delivery:

- ☐ Vaginal delivery
  - ☐ Unassisted vaginal delivery
  - ☐ Assisted vaginal delivery (forceps/vacuum)
- ☐ Manual removal of placenta following vaginal delivery
- ☐ Cesarean delivery
  - ☐ Scheduled/planned cesarean delivery
  - ☐ Unplanned or emergency cesarean delivery, reason if known:

_____

8. Was the placenta previa or abnormally invasive? ☐ Yes ☐ No

9. Did the subject receive neuraxial anesthesia? ☐ Yes ☐ No

10. Was the subject's active labor prolonged >24 hours? ☐ Yes ☐ No

11. Postpartum hemorrhage?

☐ Yes ☐ No ☐ Unknown

If yes, estimated blood loss: ☐☐☐☐ mL

Estimated blood loss measured by: ☐ Visual estimate
☐ Counting/weighing pads or bedding

12. Did the subject receive a red blood cell transfusion?

☐ Yes, number of units ☐☐ ☐ No

13. Did the subject have any complications during the <u>CURRENT</u> pregnancy?

☐ **No complications** ☐ **Yes CURRENT pregnancy complications ,** please check all that apply:

- ☐ Gestational hypertension
- ☐ Pre-eclampsia
  - Largest amount of proteinuria documented:
    - Urine protein / Cr ratio: _____ mg/mmol spot urine
    - **OR** 24-hour urine protein: _____ grams
- ☐ Eclampsia (seizures)
- ☐ HELLP syndrome
- ☐ Gestational diabetes
- ☐ Intrauterine growth restriction or small-for gestational age
- ☐ Placental abruption
- ☐ Intrapartum infection (e.g. chorioamnionitis)
- ☐ Postpartum infection

14. Laboratory results:

Last known hemoglobin count: _____ g/L ☐ Pre-delivery ☐ Postpartum

Date of result: D D M M M Y Y Y Y

Last known platelet count: _____ x 10^9/L ☐ Pre-delivery ☐ Postpartum

Date of result: D D M M M Y Y Y Y

COVID-19 status in the last 14 days?

☐ Positive result ☐ Negative result

☐ Pending result ☐ Unknown result/Not done

Date of test: D D M M M Y Y Y Y

If **pending**, indicate final result: ☐ Positive ☐ Negative

F. Infant Details

1. Current pregnancy: Infant sex and weight:

Infant	Live birth (Y/N)	Sex (M/F)	Weight (g)
A			
B			
C			

G. Immediate Postpartum Details

1. Date and time of first mobilization after delivery (as reported by subject):

Date and time: D D M M M Y Y Y Y

H H M M

2. Use of pneumatic compression devices, graduated compression or TED stockings since delivery?

☐ **Yes,** please specify the type used: ☐ No

☐ Pneumatic compression device Number of days used: ☐☐

☐ Graduated compression stockings Number of days used: ☐☐

☐ TED stockings (<20 mmHg) Number of days used: ☐☐

3. Has the subject received low-molecular-weight-heparin (LMWH) or unfractionated heparin (UFH) since delivery?

☐ **Yes,** please specify dose of LMWH or UFH: ☐ No

☐ Enoxaparin _____ mg ☐ Dalteparin _____ IU

☐ Tinzaparin _____ IU ☐ Nadroparin _____ IU/mg

☐ Unfractionated heparin _____ IU

Frequency of doses given: ☐ Q24H ☐ Q12H ☐ Q8H

Number of doses given since delivery: ☐ 1 ☐ 2

Date of last dose: D D M M M Y Y Y Y

Time of last dose: H H M M

4. Hospital discharge date: D D M M M Y Y Y Y

Delegate's Name

Delegate's Signature

D D M M M Y Y Y Y

Date

Concomitant Medication Form

NSAID Use Postpartum: ☐ Yes ☐ No

	NSAID Name	Average Dose & Frequency	Date Started (dd/mmm/yyyy)	Date Stopped (dd/mmm/yyyy) Or N/A for ongoing	Investigator / Delegate Initials and Date
Baseline visit					
6-week visit					
90-day visit					
Unscheduled					

Other Medication Use: ☐ Yes ☐ No If yes, please complete table. Includes prescriptions, vitamins, supplements, and over the counter medications.

Medication Name	Dose & Frequency	Date Started Postpartum (dd/mmm/yyyy)	Date Stopped (dd/mmm/yyyy) Or N/A for ongoing	Investigator / Delegate Initials and Date