# Participant Information and Consent form

**Study title: B-cell lymphoma 6 protein (BCL6) as a potential biomarker for endometriosis: can it be used to predict endometriosis' presence and/or severity?**

**Principal investigator: Dr Alison Bryant-Smith**
AGES Accredited Training Program trainee, Centre for Advanced Reproductive Endosurgery (CARE)

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You are invited to take part in this study, which is called 'B-cell lymphoma 6 protein (BCL6) as a potential biomarker for endometriosis: can it be used to predict endometriosis' presence and/or severity'? You have been invited because you are planning to have keyhole surgery with one of the following gynaecologists: A/Prof Alan Lam, A/Prof George Condous, or Dr Jessica Lowe. This Participant Information and Consent Form tells you about the research project. It explains the processes involved in taking part. Knowing what is involved will help you decide if you want to take part in the research.

**Please read this information carefully. Ask questions about anything that you don't understand, or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend, or local health worker.**

**Participation in this research is voluntary. If you don't wish to take part, you don't have to.**

If you decide you want to take part in the research project, you will be asked to sign the consent section. By signing it, you are telling us that you:

- Understand what you have read
- Consent to take part in the research project
- Consent to be involved in the research described
- Consent to the use of your personal and health information as described

You will be given a copy of this Participant Information and Consent form to keep.

**What is the purpose of the study?**

This research is trying to find a way of screening for a condition called 'endometriosis', using samples of the lining of the womb (an 'endometrial biopsy'), rather than keyhole surgery. This research has been initiated by the Principal Investigator, Dr Alison Bryant-Smith.

<u>Purpose of this study</u>

Endometriosis is a common condition, affecting approximately 10% (1 in 10) of women of reproductive age. Endometriosis leads to a build-up of old period blood collecting around a woman's internal organs (e.g. ovaries, Fallopian tubes, womb). Endometriosis can cause problems such as: severe period pain, difficulty falling pregnant, and pain during sex.

Currently, the best way to diagnose endometriosis is by having keyhole surgery. Imaging (e.g. ultrasound or 'MRI') is helpful in severe endometriosis, however keyhole surgery remains the only way to diagnose mild endometriosis. There are currently no less invasive ways to diagnose or screen for endometriosis, such as blood tests.

Some researchers overseas have found that taking a tiny sample of tissue from the lining of a woman's womb can be helpful: measuring the level of a substance called 'B-cell lymphoma 6 protein' (or 'BCL6') in this tissue can help predict whether or not endometriosis is present at keyhole surgery.

Our current research project aims to determine if there is a link between how abnormal a woman's BCL6 result is, and how bad her endometriosis is.

Selection

All women aged 18 – 50 years old who are planning to have keyhole surgery with A/Prof Alan Lam, A/Prof George Condous, or Dr Jessica Lowe will be invited to participate. Participants need to have a regular menstrual cycle (i.e. no shorter than 21 days, and no longer than 35 days).

**What will my participation in the study involve?**

You have been invited to participate in this research because you have been offered keyhole surgery ('laparoscopy') with A/Prof Alan Lam, A/Prof George Condous, or Dr Jessca Lowe.

You will be asked to complete a questionnaire regarding possible symptoms of endometriosis. This validated questionnaire is called the 'Endometriosis Health Profile Questionnaire', or 'EHP-30'. This takes approximately five minutes to complete.

As you were not originally planning to have a sample of the lining of your womb taken as part of your procedure, this would be an additional part of your operation, done only for these research purposes, after you have been anaesthetised. The potential risks of having this sample taken are outlined below.

Once the endometrial biopsy sample has been collected, we will send one part of the biopsy tissue to the laboratory for the usual analysis, and another part of the tissue to a different laboratory to measure the BCL6 level. During your operation, your surgeon will classify how bad your endometriosis is, by looking closely at all your pelvic organs with our keyhole surgery camera.

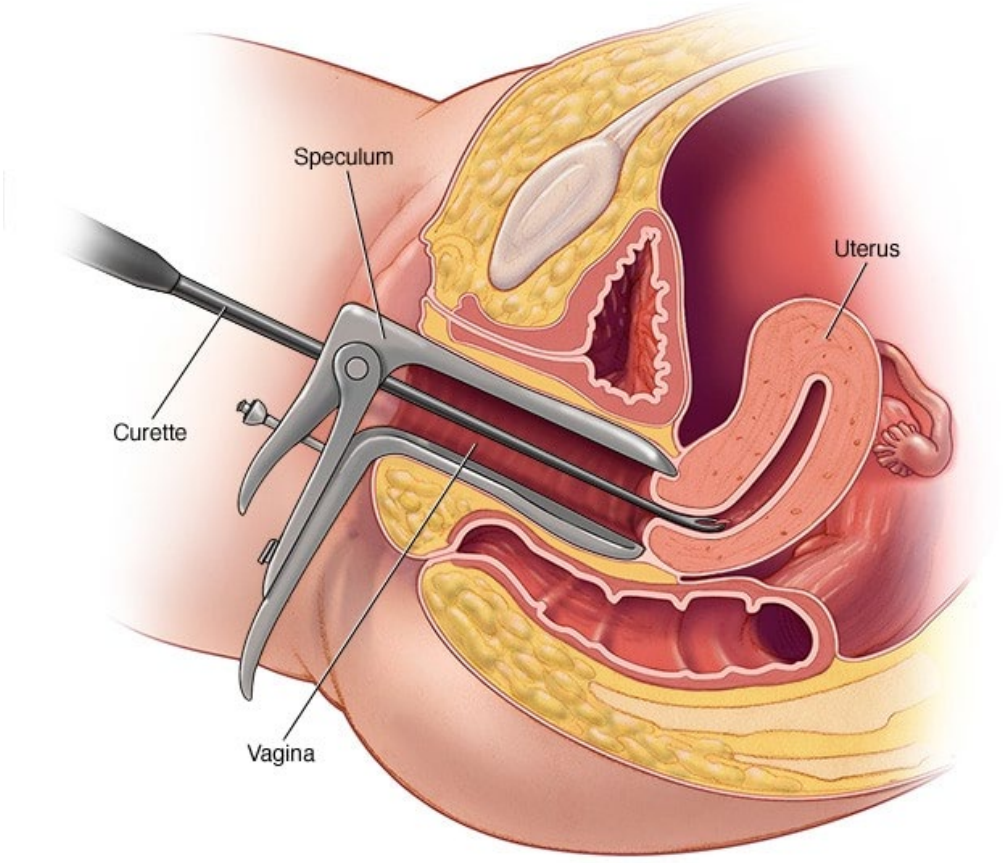
Endometrial biopsy procedure

As part of your planned operation, you will be given a general anaesthetic (i.e. you won't feel or remember anything during the operation). If you agree to participate in this research, in addition to your planned keyhole surgery, an endometrial biopsy will be taken.

To take a sample of the layer of cells lining the inside of your womb, your surgeon will perform a simple procedure known as 'dilatation and curettage'. An instrument called a 'speculum' is inserted into the vagina, to allow us to see your cervix (the opening to the womb) (please see diagram below). The cervix muscle is dilated temporarily using rods called 'dilators'. A sample of the

endometrium (the lining of the womb) is then scraped off, using a spoon-shaped instrument called a 'curette'. (This is like using a spatula to scrape the last bit of cake mix out of a mixing bowl when baking.) This procedure takes approximately 1-2 minutes.

The diagram below shows how an endometrial biopsy is taken, using the 'curettage' technique. This will be performed while you are anaesthetised ('asleep').






After the endometrial biopsy tissue has been sent to the pathology laboratory, it will be analysed to assess the BCL6 level. The pathology company then routinely stores all pathology slides and paraffin block for ten years. After this point, ???

Data collection

In addition to your answers for the 'EHP-30' questionnaire, and the endometrial biopsy sample, your surgeon will assess how bad your endometriosis (if you have any) is, during your keyhole surgery. This would be done during all laparoscopies in any case, whether or not you participate in this research. We use the standard endometriosis classification system, which is called the 'revised American Society of Reproductive Medicine' classification system for endometriosis. This involves looking closely at your pelvic organs using the the keyhole surgery camera, and classifying any endometriosis present by its location, size and depth.

Follow-up

Your follow-up consultations will be similar, whether or not you participate in this research. Our clinic nurse will call you approximately 1 week after your operation, to see how you are recovering, and clarify whether you have suffered any complications of the surgery. The clinic nurse will call you again at approximately four weeks after your operation, to ask if you have suffered any complications of the surgery. The Principal Investigator will also call you at approximately four weeks after your operation, to explain what stage of endometriosis was found (if any), and the results of the BCL6 test that was done on the sample of your endometrial lining.

**What are the possible benefits and risks of this study?**

If this research can help develop a way to diagnose the presence and severity of endometriosis using only an endometrial biopsy, there would be significant benefits to many other women in future. For example: women who may have endometriosis based on their symptoms could have an endometrial biopsy taken (while awake, in a clinic room). The result may help guide whether or not she would benefit from laparoscopic surgery. It may also help to guide whether keyhole surgery or *in vitro* fertilisation (IVF) is the next best step.

There will be no clear benefits to you from your participation in this research.

In terms of the potential risks to you if you choose to participate: the potential complications of having an endometrial biopsy done include:

- Uterine perforation (small hole in the muscle of the uterus) (approximately 1 in 300 women)
- Formation of scar tissue inside the cavity of the uterus (approximately 1 in 60 women)
- Injury to the cervix (neck of the womb) (approximately 1 in 25 women)
- Infection (approximately 1 in 20 women)
- Blood loss > 100mLs (approximately 1 in 10 women)

By and large, having an endometrial biopsy performed is a very safe procedure.

The potential implications of the above possible complications and their management include:

(1) Uterine perforation: collection of blood tests for full blood count; injury to bladder or bowel (1 in 15 patients who have a uterine perforation); intra-abdominal bleeding (1 in 6 patients who have a uterine perforation); need for open surgery (very rare)[21]
(2) Formation of scar tissue inside the cavity of the uterus: lighter periods (4 in 5 women with intra-uterine scarring); decreased fertility (1 in 8 women with intra-uterine adhesions); cyclical pelvic pain (1 in 30 women with intra-uterine adhesions); recurrent pregnancy loss (1 in 8 women with intra-uterine adhesions). Management of the above issues involves hysteroscopy (a procedure performed under general anaesthetic to visualise the lining of the uterus with a small video camera), and resection of the intra-uterine adhesions (separating the intra-uterine scarring, using electrosurgical devices).[22]
(3) Injury to the cervix: repair of any cervical injury is performed immediately, using absorbable stitches.

(4) Infection: mild infection (the majority) are treated with tablet antibiotics; severe infections (very rare) require admission to hospital and intravenous antibiotics.
(5) Blood loss > 100mLs: observation; collection of blood tests for full blood count; administration of medications to help control the bleeding; in the cases of very rare major haemorrhage (> 1000mLs), open surgery may be needed

The above potential complications of dilatation and curettage can be compared with the potential risks of keyhole surgery, which include:

- Conversion to an open operation ('laparotomy') (approximately 1 in 70 women)
- Injury to urinary tract (bladder or ureters) (approximately 1 in 100 women)
- Injury to major (big) blood vessel (approximately 1 in 200 women)
- Injury to minor (small) blood vessel (approximately 1 in 350 women)
- Later development of a hernia through one of the scars (approximately 1 in 500 women)
- Injury to gastrointestinal tract (stomach or bowels) (approximately 1 in 1000 women)

**Who pays for the study?**

Participants who agree to take part will not incur any out-of-pocket costs or significant inconvenience above normal care. Funding for this study has been sought from the Australasian Gynaecological Endoscopy and Surgery society.

**What happens if I suffer injury or complications as a result of the study?**
If you suffer any injuries or complications as a result of this study, you should contact the study doctor as soon as possible, who will assist you in arranging appropriate medical treatment. You may have a right to take legal action to obtain compensation for any injuries or complications resulting from the study. Compensation may be available if your injury or complication is caused by the drugs or procedures, or by the negligence of any of the parties involved in the study. If you receive compensation that includes an amount for medical expenses, you will be required to pay for your medical treatment from those compensation monies.
If you are not eligible for compensation for your injury or complication under the law, but are eligible for Medicare, then you can receive any medical treatment required for your injury or complication free of charge as a public patient in any Australian public hospital.
If applicable The parties to this study agree to follow the Medicines Australia Guidelines for Compensation for Injury Resulting from Participation in an Industry-Sponsored Clinical Trial. These Guidelines allow for some claims for compensation to be settled without the need for legal action to be taken. The fact that the parties have agreed to abide by these guidelines in respect of the clinical trial does not affect your rights to pursue a legal remedy in respect of any injury you may suffer as a result of participation. You can obtain a copy of these Guidelines from the Secretary of the Human Research Ethics Committee.

**What are my rights?**

Participation in this research is completely voluntary: you are free to decline to participate, or withdraw from the study at any time. You do not need to provide a reason. Choosing not to

participate, or withdrawing from the study, will not affect the care or treatment you receive from our team.

As a participant in this research, you have a right to access all information collected about you for the purposes of the study.

By signing the consent form, you consent to the research team collecting and using personal information about you for the research project. Any information obtained in connection with this research project that can identify you will remain confidential. All information collected about you will be stored in a secure Excel spreadsheet, which is password-protected, and only accessible by investigators on the study. No identifiable information about any research participants will be published or provided to anyone outside of this research.

It is anticipated that the results of this research project will be published and/or presented in a variety of ways. In any publication and/or presentation, information will be provided in such a way that you cannot be identified.

**What happens after the study, or if I change my mind?**

De-identified data collected about you will be stored electronically for 15 years, and then destroyed. When the research is completed, you will receive information about results of the study in a brief publication sent to the email address you provide to us.

If you change your mind, and decide not to participate in the study, please contact the Principal Investigator (whose contact details are listed below). If you have not yet had your surgery, your original surgery will be undertaken, without any additional components that were only needed because of your participation in this research. If you have already had your operation, any data relating to your involvement will be removed from the data to be analysed if possible. (This step is only possible up to the point of completion of data collection. Once the results from all participants start being analysed, it will not be possible to remove your data from other participants' data.)

You are welcome to decline involvement in the study: doing so will not have any impact on how the team of surgeons, nurses, and anaesthetists treat you.

**Who has reviewed the research project?**

All research in Australia involving humans is reviewed by an independent group of people called Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by the Northern Sydney Local Health District HREC. This project will be carried out according to the *National Statement on Ethical Conduct in Human Research*. This statement has been developed to protect the interests of people who agree to participate in human research studies.

**Who do I contact for more information if I have concerns?**

This research is being led by clinicians from the Centre for Advanced Reproductive Endosurgery: A/Prof Alan Lam and Dr Alison Bryant-Smith. Other clinicians involved in this study include A/Prof

George Condous, Dr Jessica Lowe, pathologists from Douglass Hanly Moir pathology company, and an infertility specialist (Dr Alison Gee).

If you have any questions, concerns or complaints about the research at any stage, you can contact:

Principal investigator Alison Bryant-Smith at alison.bryant-smith@sydneycare.com.au or

(02) 9966 9121.

Associate Investigator Alan Lam at alanlam@sydneycare.com.au or (02) 9966 9121.

If you would like to talk to someone who is independent of this research, you can contact the Human Research and Ethics Committee (HREC) that approved this study on:

Phone: (02) 9926 4590

Email: NSLHD-Research@health.nsw.gov.au

The Northern Sydney Local Health District HREC approved this study. If you would like to contact the HREC with any feedback or concerns, please quote reference number 2020/ETH02388.

# Consent form

**Study title: B-cell lymphoma 6 protein (BCL6) as a potential biomarker for endometriosis: can it be used to predict endometriosis' presence and/or severity?**

**Principal investigator: Dr Alison Bryant-Smith** MBBS/BA MPH MSurgEd MRCOG FRANZCOG
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**Declaration by Participant**

I have read the Patient Information Sheet (or someone has read it to me in a language that I understand).

I understand the purposes, procedures, and risks of the research described in the project.

My surgeon will be: A/Prof Alan Lam ☐

A/Prof George Condous ☐

Dr Jessica Lowe ☐

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I freely agree to participate in this research project as described, and understand that I am free to withdraw at any time during the project without affecting my future care.

I understand that I will be given a signed copy of this document to keep.

Name of Participant (please print): _____

Signature: _____ Date: _____ / _____ / _____

**Declaration by Researcher / associate**

I have given a verbal explanation of the research project, its procedures and risks, and I believe that the participant has understood that explanation.

Name of Researcher (please print): _____

Signature: _____ Date: _____ / _____ / _____