PROMISE – PROGESTERONE IN RECURRENT MISCARRIAGE STUDY

Participant Information Sheet

We would like to invite you to take part in a research study. Whether you take part or not is entirely your choice. You do not have to take part, nor give a reason why you decide not to. Before you decide you need to understand why the research is being done and what it would involve for you. Please take time to read the following information carefully.

We want to see whether progesterone hormone pessaries reduce the chance of a miscarriage in women who have previously had three or more miscarriages. This study is called the PROMISE trial; "PRO" referring to Progesterone and "MISE" referring to Miscarriage.

- Part One of this information sheet tells you the purpose of this study and what will happen to you if you take part.
- Part Two of this information sheet gives you more detailed information about the conduct of the study.

Please ask us if there is anything that is not clear or if you would like more information.

PART ONE

What is the purpose of the study?

The purpose of this study is to find out whether treating women with history of recurrent miscarriage with progesterone, a natural pregnancy hormone, from the time of a positive pregnancy test until 12 weeks of pregnancy decreases their chance of miscarrying.

Why have I been invited?

You have been invited to take part in the study as you have a history of recurrent miscarriage for which no underlying cause has been found.

Do I have to take part?

No. It is up to you whether or not you take part. If you wish to take part, you will be given this information sheet to keep and will be asked to sign a consent form. You are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect your medical care or maternity care in any way.

What will happen to me if I take part?

If you decide to take part in the study, and have signed the consent form, you don't need to do anything until you become pregnant (and have a positive urine or blood pregnancy test). Once this happens, we want you to let the research nurse know, by telephone as soon as possible. The phone number to call is given on the last page of this information sheet. You will probably be about 4 weeks pregnant (four weeks from the last menstrual period) at this time. When the

research nurse receives your call, she will ask you some details about this pregnancy and recheck your clinical history to make sure you are still eligible to take part in the study.

If you remain eligible, the nurse will arrange the study pessaries to be dispensed to you. You will be asked to take two pessaries – either vaginally or rectally – twice daily (in the morning and at bedtime), from the time you receive them from us to 12 weeks of pregnancy (We will let you know when you need to stop taking the pessaries). These pessaries will either be progesterone or identical looking dummy pessaries. We do not know if progesterone will help reduce the risk of miscarriage at all, and that is why we need to compare women who take progesterone with others who take the dummy pessaries.

Whether you get the progesterone or dummy pessaries will be decided by a computer. The computer will allocate treatment randomly, like tossing a coin, to decide whether you should receive progesterone or dummy pessaries. You will have an equal chance of receiving progesterone or the dummy pessaries. You will not know which, and neither will the doctors, nurses or researchers looking after you (although they will be able to find out if they need to).

The research nurse will be able to get most of your pregnancy outcome data from your hospital notes. But she may need to contact you to complete the outcome data if these are not available in your or your baby's notes. We may ask you to come and see us so we can get all the information we need. We would also like your permission to follow up your baby's long-term health. At the conclusion of the study, we will let you know of the findings through your preferred method of contact.

What will I have to do?

All you have to do is to keep the pessaries in a safe place, and take two pessaries in the morning and two pessaries in the evening. It is not necessary to take the pessaries at exactly the same time every day. If you forget to take the pessaries, don't worry. If it has been less than six hours from when you would have normally taken it, please take the pessaries as soon as possible, and continue the rest of the pessaries as usual. If it has been more than six hours from when you would have normally taken the pessaries, please omit these pessaries, and take the next lot of pessaries at the usual time.

In the event of you losing the pessaries, please let us know, and we will get you a further supply of the same type of pessaries as soon as possible.

You will be given enough vaginal pessaries to last you until 12 weeks of pregnancy. Each packet will contain enough pessaries for four weeks (112 pessaries). At the end of each 4 weeks, please post back the packet, either empty or with any unused pessaries. You will be given free-post envelopes to post the packets back to your hospital. Your research nurse will contact you by telephone to make sure everything is okay if you do not return the packets. If you lose your envelopes, please use another and write the freepost address, making sure your study number is on the envelope. That way you won't need a stamp.

What is the drug being tested?

We are testing progesterone hormone pessaries (versus a dummy pessaries), at a dose of 400mg (two pessaries at 200mg each), twice daily. Progesterone is a naturally occurring female hormone. It is commonly used in IVF (test-tube baby) practice and to prevent preterm birth.

What are the other possible disadvantages and risks of taking part?

Side effects with progesterone pessaries are rare or minor. Previous studies on natural progesterone treatment did not report any serious side-effects to the mother or the baby. However, reported side effects of progesterone include fluid retention, bloating, headache, sleeplessness, diarrhoea and jaundice. We do not anticipate any problems for those taking part in this study. If you have any concerns, please contact the research nurse (details on the last page of this information sheet). If you become unwell, please contact your general practitioner, accident and emergency services, or ambulance services, as appropriate.

What are the possible benefits of taking part?

We do not know if the study will help you personally, but the information we will get may help improve the pregnancy outcome for women in the future.

How is progesterone administered?

Both the progesterone and the placebo (inactive drug) are in the form of pessaries (capsules). We would ask you to give yourself two capsules twice a day ideally by placing them in the vagina – rather like using a tampon. Alternatively, you can use the capsules as suppositories – inserting them into the rectum.

What if there is a problem? What if something goes wrong?

If you have a complaint about the way you have been treated during the study or any other matter, you can make a complaint. There is more detailed information in Part Two of this leaflet.

Will my taking part in this study be kept confidential?

Yes. The study will follow ethical and legal practice and all the information about your participation in this study will be kept confidential. Details about this are included in Part Two of this leaflet.

This completes Part One of the information sheet.

If the information in Part One has interested you and you are considering participating, please read the additional information in Part Two before making any decision.

PART TWO

What if relevant new information becomes available?

Sometimes we get new information about the treatment being studied. If this happens, we will tell you and discuss whether you should continue in the study. If you decide not to carry on, we will make arrangements for your care to continue. If you decide to continue in the study we may ask you to sign an updated consent form.

If the study is stopped for any other reason, we will tell you and arrange your continuing care.

What will happen if I do not want to carry on with the study?

If you decide to take part and then change your mind you are free to withdraw at any time without giving a reason (although it would be useful to know why). Your treatment will not be affected in any way.

If you withdraw from the study, we will ask your permission to keep in touch with you to know the outcome of your pregnancy and to use such information in our analysis.

Keeping in contact

Until 12 weeks of pregnancy, you will be seen at your normal early pregnancy unit at regular intervals according to local policy. After this time, the research nurse will contact you by telephone at 20, 26, 34 and 38 weeks of pregnancy. The purpose of these telephone calls is to maintain contact and to enquire regarding the progress of your pregnancy. Such questions, which would have been routinely asked at your antenatal visits, may include specific enquires as to whether you have experienced any complications such as issues regarding blood pressure and growth of the baby. It is important to state that at all times the management of your pregnancy rests with the obstetricians and midwives at the hospital at which you have booked for antenatal care and delivery.

After delivery

After delivery, we will ask your permission to contact the hospital at which you delivered to obtain data on the outcome of your pregnancy (including any complications you may have had); the gestation at delivery; mode of delivery; baby's sex and birthweight and any complications the baby may have had after delivery.

What if there is a problem?

Complaints

If you have a concern about any aspect of this study, you should ask to speak to the local research nurse or doctor who will do their best to answer your questions (contact details can be found at the end of this information sheet). If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Details can be obtained from your hospital. You can contact the Patients Advisory and Liaison Service (PALS) or you can write to the Chief Executive of the hospital. You have the same rights whether or not you take part in this study.

Harm

Imperial College London holds insurance policies which apply to this study. If you experience harm as a result of taking part in this study, you may be eligible to claim compensation without having to prove that Imperial College is at fault. Adverse pregnancy outcomes (for example miscarriage or stillbirth) not directly related to study medication or conduct will not be eligible for compensation.

If you are harmed due to someone's negligence, then you may have grounds for a legal action. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been treated during the course of this study then you should immediately inform the Investigator (Mr Raj Rai, Imperial College London). The normal National Health Service complaints mechanisms are also available to you. If you are still not satisfied with the response, you may contact the Imperial College Clinical Research Governance Office.

Will my taking part in this study be kept confidential?

Yes. All information collected from you for the purposes of this study will be kept strictly confidential in the same way as your medical records. Any information used outside the hospital or university will have any identifying details removed so that your data remains completely anonymous. All information will be held securely and in strict confidence. You will not be identified in any publication of results from this study. Occasionally, inspections of clinical study data are undertaken to ensure that, for example, all participants have given consent to take part. But apart from this, only study organisers will have access to the data.

Involvement of your General Practitioner

We will inform your general practitioner of your participation in the study if you agree.

What will happen to the results of the research study?

When the results of the PROMISE study are known, we will inform you of the overall results of the study as well as which pessaries you were taking (through your preferred method of contact). We will also publish the results of the study in medical journal(s). We will make the information available on our website for the general public.

Who is organising the research?

The research is organised by Imperial College, London, UK, and managed and coordinated by the University of Birmingham, UK. No private or commercial companies are involved in the organisation or management of this study.

Who is funding the research?

The National Institute for Health Research (NIHR) has funded this study. The research nurses working on this project have their salaries paid by this organisation. The other nurses and doctors do not receive any payment if you help with this research.

Who has reviewed the study?

All research in the NHS is looked at by independent group of people, called a Research Ethics Committee to protect your safety, rights, wellbeing and dignity. This study has been reviewed and given favourable ethical opinion by West Midlands Research Ethics Committee.

Do you have any further questions?

Having read this leaflet and discussed with the research nurse or doctor, we hope that you will choose to take part in the PROMISE study. If you have any questions about the study now or later, please feel free to ask your nurse or doctor, or contact the research nurse at [research nurse name and contact details], or the trial manager at [redacted].

The UK Clinical Research Collaboration has produced a guide entitled, 'Understanding Clinical Trials'. This can be downloaded from their website: www.ukcrn.org.uk and could be useful if you require general information about research.

You will be given a copy of the information sheet and a signed consent form to keep.

Thank you for taking time to read this sheet and for considering taking part in the study.