RESEARCH PARTICIPANT INFORMATION SHEET

Safer pre-natal diagnosis using free DNA in maternal blood test

(also known as the IONA Study)

REC ref: 07/H0607/101

Principal Investigator: Mr Edward Johnstone

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We would like to invite you to take part in a research study into the possible diagnosis of Down’s Syndrome/chromosomal abnormalities, from a maternal blood sample. 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. Talk to others about the study if you wish.

Part 1 explains the purpose of the study and what will happen to you if you chose to take part.

Part 2 gives you more detailed information about the conduct of the study.

Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part. Please feel free to talk to your own doctor or another healthcare professional or anyone else about the study if you wish.

This study is being performed to try to improve antenatal care, and in an attempt to identify Down’s syndrome by a safer test than is currently available. The tests currently used (amniocentesis/ chorion villus sampling) carry a 0.5-2% miscarriage risk.

Part 1

1.1 What is the purpose of the study?

This study aims to develop the Iona test, a scientific technique to allow early and safer (‘non-invasive’) diagnosis of unborn babies with Down’s Syndrome (and other chromosomal abnormalities) from a simple maternal blood test. Currently, the only method to make an absolute diagnosis of Down’s Syndrome involves either taking a biopsy from the placenta (chorion villus sampling) or obtaining a sample of amniotic fluid from around the baby (amniocentesis). Both of these tests carry the potential risk of miscarriage (1-2% for chorion villus sampling, 0.5-1% for amniocentesis). Developing a test like the Iona test, that identifies Down’s Syndrome/chromosomal abnormality from maternal blood, would avoid having to perform as many amniocentesis/chorionic villus sampling tests in the future.

1.2 Why have I been invited?

You have been invited because you are at a stage of pregnancy in which pre-natal
diagnostic testing (amniocentesis/chorion villus sampling) is usually performed. You are attending for consideration of these tests because your screening test (combined or quadruple test or ultrasound scan) has been reported as ‘high-risk’ for a chromosomal problem such as Down’s Syndrome. You are being invited to join the study along with all of the other eligible women in similar position attending the unit. Over the full course of the study, over 1000 women will be participating.

1.3 Do I have to take part

No. It is entirely up to you to decide whether or not you would like to take part. We will describe the study and go through this information sheet, which we will then give to you. If you are interested, we will then ask you to sign a consent form to show you have agreed to take part. You are free to withdraw at any time, without giving a reason. This would not affect the standard of care you receive.

1.4 What will happen to me if I take part?

If you are happy to take part in this study, the step-by-step procedure will be as follows. One of the healthcare professionals looking after you today will take you through a consent form for you to sign, confirming that you agree to take part.

Then a blood test sample (two standard-sized tubes, maximum 20mls/four teaspoons equivalent) will be taken from a vein in your arm, in the normal way (that is, the same as for blood samples you may have had taken previously in your pregnancy). This would be the only procedure that would be over and above your standard care. Otherwise, the care you receive will be identical to that if you were not participating in the study, and no normal treatments will be withheld.

Your blood sample will then be taken to the laboratory, and fetal DNA levels will be measured in the sample with a view to developing a future clinically useful Iona blood test.

Your direct involvement in the research would only be in providing the blood sample today. After this time there would be no commitment for you to do anything further, or have any more interaction with the research team.

No confidential information that could personally identify you will be removed from the hospital site looking after you, or be available to any research team members not employed by either Premaitha Health, or the Central Manchester University Hospitals NHS Foundation Trust.

1.5 What will I have to do?

If you agree to take part you would be asked to donate a blood sample, and answer some brief questions (for example, your age, when your last period was i.e. how many weeks have you been pregnant, and whether you have any significant illnesses), when your baby is due and what you consider your ethnic origin to be. This is all that is asked of you – we would however ask your permission to look at your pregnancy notes, to look at the results of your screening tests and to follow the outcome of your pregnancy.

1.6 What is the procedure that is being tested?

The procedure being tested is a potential method to achieve more accurate pre-natal test for chromosomal abnormalities (such as Down’s Syndrome) safely, by a maternal blood test. This aims to avoid the need for women to have to undergo more invasive diagnostic
procedures (such as amniocentesis) in the future. At present, the laboratory method being used has demonstrated feasibility and the technique is being further refined so that it can be developed into a reliable and widely available test in the future.

1.7 What are the alternatives for diagnosis or treatment?

The blood test involved in the study is an additional procedure, rather than an alternative. The care and pathways all pregnant women will receive does not change whether you agree to take part in this study or not.

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

The important thing is that you are receiving the 'gold standard' currently available prenatal care. Participation will not affect this high standard of existing care.

The specific risks involved in this study are simply those of having a standard blood test taken. Blood tests are generally relatively safe procedures; however there is some risks of giving a blood sample such as bruising and pain at the site. Other possible, but less common risks include: nerve damage, re-bleed, allergy (e.g. to the nurses gloves), inflammation of the vein, blood pressure change and arterial puncture.

Since participating in the study will not otherwise change the course of standard pre-natal care, there should not be any other disadvantages involved in taking part. The volume taken in the blood test involved is small (i.e. 20ml), and is not thought to represent any health risk.

1.9 What are the possible benefits of taking part?

There are no direct benefits to you from taking part. It is hoped that the methods under study could make prenatal diagnosis safer and less stressful for pregnant women in the future.

1.10 What happens when the research study stops?

Most of the DNA we extract from your blood sample will be used up in developing the Iona test. We would like your permission to keep any of the remaining genetic material isolated from your sample to be used to validate future, hopefully cheaper and better technologies for the same purpose (detection of chromosomal abnormalities/reassurance and confirmation of health). If you prefer this did not happen, we will destroy any material isolated from your blood sample.

1.11 What if there is a problem?

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. The detailed information on this is given in Part 2.

1.12 Will my taking part in the study be kept confidential?

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. The details are included in Part 2. The health professionals running the study are Premaitha Health, and Central Manchester Foundation Trust employees and they will be the only people with access to your personal data. Your anonymised data (which has all identifying features removed i.e. name, date of birth and hospital number removed) will only be shared with the Central Manchester University Hospitals NHS Foundation Trust and
Premaitha Health for the purposes of future scientific publication on the technology being developed and features that are academically noteworthy.

This completes Part 1.

If the information in Part 1 has interested you and you are considering participation, please read the additional information in Part 2 before making any decisions.
Part 2

2.1 What will happen if I don't want to carry on with the study?

You may withdraw from the study at any time. If you choose to withdraw from the study, we will destroy all your identifiable samples, but we would ordinarily need to use the data collected up to the time you withdrew.

2.2 What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions (contact the study Research Midwife, Linda Peacock on 0161 701 6961 or Dr Edward Johnstone, the Research Doctor, on 0161 701 6976).

If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Details can be obtained from the Patient Advice and Liaison Service (PALS), Central Manchester University Hospitals NHS Foundation Trust: Telephone number: 0161 276 4971 or email pals@cmft.nhs.uk.

2.3 Will my taking part in this study be kept confidential?

The research team has a duty of confidentiality. All information which is collected about you during the course of the research will be kept strictly confidential, and any information about you that leaves the hospital will have your name and address/any other identifying features removed so that you cannot be recognised. Participants have the right to check the accuracy of data held about them and correct any errors.

2.4 Involvement of the General Practitioner/Family Doctor (GP)?

Your GP would not ordinarily need to be specifically informed of your participation in this study; however the hospital consultant in charge of your care will be aware of your inclusion.

2.5 What will happen to the samples I give?

The samples taken will be new blood samples taken solely for the study. The samples, and any data generated from them, will not be identifiable as yours outside the hospital. The only link to your identity will be by way of a unique, anonymous number. All identifiable data will be retained securely in the hospital site. No researchers other than health professionals working at Central Manchester University Hospitals NHS Foundation Trust, or Premaitha Health will have access to your personal data. The research health professional acting as your liaison with the study will enter the information into a folder held for the purposes of the study. This folder will be kept in a locked room in the hospital. Data may also be entered into a file on a secure computer. Samples will not be transported outside the UK. The samples themselves will be kept until the end of the study. If you have given us permission to keep any of the remaining genetic material isolated from your blood sample, this will be stored in our laboratory for potential use in future studies, subject to appropriate ethical approvals. Otherwise, we will destroy any material isolated from your blood sample.

2.6 Will any genetic tests be done?

This study aims to try to determine if it might be possible to make accurate pre-natal testing for Down’s Syndrome safer, by using measurements of the fetal DNA obtainable from maternal blood samples. As such, all of the samples provided will be subject to tests
involving fetal DNA assessments. These will not take the form of what is usually considered ‘genetic’ testing, and will not be aimed at identifying participants themselves, or genetic disease predisposition in participants themselves.

2.7 What will happen to the results of the study?

The study aims to test early-stage/cutting-edge technology for detection of chromosomal abnormality. The laboratory method is still experimental and will need to be further examined in larger studies later. The results of the tests will not be ‘validated’ or considered clinically reliable until a great many participants have been tested over a course of several years. Therefore, individual results of the study will not be communicated back to research participants.

When complete, the data from the study may be used in research papers to be published in scientific/medical journals. Participants’ identity will always be kept confidential and data used in the any form of publication would be entirely anonymous. No participant in this research will ever be identified, or identifiable, in any publication or other report arising from the study.

2.8 Who is organising and funding the research?

This study is being organised as a collaboration between Premaitha Health Ltd and Central Manchester University Hospitals NHS Foundation Trust. Premaitha Health Ltd is the “sponsoring” organisation that is funding and insuring the research. The research midwife helping to conduct the research is being paid for the time she devotes to the study.

2.9 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. The study has been reviewed and given favourable opinion by Mid- and South Buckinghamshire Research Ethics Committee (now known as the South Central Berkshire Ethics Committee).

2.10 Further information and contact details

If you would like further information about the study, please consult the following:

1. General information about research and antenatal testing

   a. NPSA (National Patient Safety Agency) site offering advice on clinical research [http://www.npsa.nhs.uk](http://www.npsa.nhs.uk)


   c. NHS information resource detailing Down’s Syndrome prenatal screening procedures [http://www.screening.nhs.uk/downs/procedures.htm](http://www.screening.nhs.uk/downs/procedures.htm)

2. Specific information about this research project

The health professional administering this information sheet and undertaking your informed consent should be able to answer most of your questions:
Alternatively, the Study Co-ordinator:

Rosalyn Mazey - rosalyn.mazey@premaitha.com (0161 667 6867)

Or the Principal Investigator:

Dr Edward Johnstone - edward.johnstone@manchester.ac.uk
mailto:Brenda.kelly@obs-gyn.ox.ac.uk (0161 701 6976)