

HEALTH PROFESSIONAL INFORMATION SHEET

USING BLOOD SAMPLES TO DIAGNOSE DISEASE

This sheet provides technical information on a clinical research study. It is designed to inform health care professionals about the techniques used and goals of the study. It also has an overview of what will happen to participants and how data and information will be handled.

This sheet is not designed for participants. Please refer to the "Participant Information Sheet". This sheet is designed to provide additional information for GPs whose patients have decided to participate in the study.

If you require further information please use the contact details at the end of this sheet.

Part 1 covers general details and Part 2 has more specific information.

PART 1

What is the purpose of the study?

This study is a research project that is trying to find new ways to diagnose diseases from blood and urine samples. If successful, the hope is that many diseases could be diagnosed with simple tests like the ones used for diabetes and cholesterol. This would allow certain diseases to be detected earlier and more easily with less intrusion and discomfort.

The study will run for 12 months and will routinely process between 50 and 100 participants per month.

Initially these will be 'clinical laboratory tests' and not point of care kits. The approach is termed a 'multiplex assay' and consists of measuring many thousands of proteins in a sample simultaneously and using combinations of these measures to create new diagnostics and prognostics.

The initial focus of the study is on Urology and will specifically target urological cancers and the conditions usually suggested under differential diagnosis for those cancers.

How are the participants chosen?

We need participants with a variety of conditions and also people who are healthy. The 'population' the study is interested in is all patients that have been referred to a urology clinic for further investigation. Being chosen for this study does not mean a participant has a specific urological condition.

What happens to the participants that take part?

There will be no changes to treatment. We collect some additional information and samples from all participants.

Whilst at the clinic, all the people taking part in the research project will be asked to provide a small blood sample, a small urine sample (if possible) and asked some questions about any medications they are on and some medical history. Wherever possible the blood sample will be taken at the same time as any sample taken as part of the standard clinical assessment and will require no additional procedures.

When they leave the clinic they will be given a lifestyle questionnaire to fill in at home and post back in the envelope provided. This should take less than half an hour. There is also an online version that can be filled in over the internet if that is more convenient. The questionnaire has been standardised with the UK Biobank questionnaire. UK Biobank has given permission for this but this does not constitute an endorsement of this study and this study is not linked or supported in any way to UK Biobank. This is simply an effort to standardise data collection.

The medical team will continue to access participant medical records so they can look back and see if the samples can be used as an early warning for any condition participants may have or develop. All participants are free to stop this access at any point without giving a reason.

If the participants go on to have follow on treatment then the team may be interested in taking samples at follow up visits. This will be discussed on a case by case basis and again all participants are free to opt out of this. If they agree to further samples being taken as they progress through treatment then an additional 3 or 4 blood samples may be taken on different occasions.

This is an observational study. We gather information from lots of people and conditions and from this see if we can test for these in the provided samples.

What is the study trying to test?

Some conditions, for example diabetes, can already be diagnosed from blood. This study is trying to create more tests for other diseases, such as cancer.

What are the possible disadvantages and risks of taking part?

There should be no disadvantages or risks to taking part. Treatment will be unaffected by taking part or not. The blood sample is a small amount and in the worst case participants may experience some slight bruising from where the sample was taken. Wherever possible the sample will be taken at the same time as they provide samples during clinical assessment and so should involve no additional risks or discomfort.

What are the possible benefits of taking part?

The trial will not help the participants personally but the information we get from this trial could help improve the diagnosis and treatment of urological conditions in the future.

PART 2

What will happen if a participant does not want to continue with the study?

Participants can withdraw from the study at anytime and without giving a reason. If they withdraw from the study, we will destroy all identifiable samples, but we will need to use the data collected up to the withdrawal.

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:

Research Nurse: Wendy Robson, 0191 2137322

Primary Investigator: Mr Naeem Soomro, Clinical Consultant Urologist, 0191 2336161

There is a small chance that results from this study will suggest participants have a condition of which they are unaware. This will come about by a participant being associated with a group with a diagnosed condition after the analysis has been done. This will not be a diagnosis but it may suggest further standard clinical tests should be run just to be sure. In such circumstances participants will be referred to the appropriate specialist in consultation with their general practitioner, unless participants have said they do not wish to do so. Such detection has the benefit of starting treatment early but in a small number of cases may have implications for future employment and insurance.

We realise this is a difficult issue as a false diagnosis can cause a great deal of undue stress on the participant. The medical team will discuss such cases in detail and use their experience to decide the course of action that is in the best interests of the participant. If the team decides that further action is warranted the participant's GP will be consulted so a consensus decision can be made on what is in the best interests of their patient.

Will participants taking part in this study be kept confidential?

There are very strict rules about collecting medical research information under the 1998 Data Protection Act. We must comply with this act and keep

participant information safe. Any Information that leaves the hospital will have names and addresses removed.

The information accessed for the research will be about diagnosis and long term state of health.

Participant GPs will not normally be notified that participants are taking part in this study, but a member of the medical team will do so if requested by the participant.

All information which is collected during the course of the research will be kept strictly confidential, and any information which leaves the hospital will have names and addresses removed so that participants cannot be identified.

What will happen to the samples?

The blood and urine samples will be sent anonymously to a laboratory and processed. The result of the processing is to measure relative quantities of many thousands of constituents of blood (or urine). Reports have suggested that in excess of 10,000 distinct proteins can be measured in plasma. Many of these proteins have been predicted from the genome but have yet to be assigned a function. There are many measurement techniques but at present it is possible to measure a few thousand proteins simultaneously from a single sample and single processing technique. Many of the proteins (e.g. PSA) are already clinically useful. The following link gives an example of such a multiple measurement array with clinically relevant analytes <http://www.whatman.com/SerumBiomarkerChip.aspx> .

Further research has shown that some of the markers (e.g. PSA) can be made more reliable by not just taking a single measure and comparing it to an absolute concentration. This study will be extending this by taking the thousands of relative measures from a single sample and combining them in a way that is diagnostic or prognostic of the target conditions.

These measurements will be combined with information from the questionnaire and medical records and analysed to see if any of the measures can be used to diagnose specific diseases. Only the direct medical team have access to these records.

Currently this form of analysis is specialised, complex and relatively expensive. Processing a single sample costs hundreds of pounds. The hope is that such processing will provide far more sensitive and specific tests and that multiple conditions can be tested for at one time bringing down the 'per condition' price.

The research will take a set of samples for the week and after processing try and predict what condition each participant had. This blind prediction will be given to the clinical team who will confirm the results and also explore any miss-predictions for a clinical basis. This information will be fed back to improve the prediction system. This will repeat each week with new blind samples. Over time we would expect to improve our prediction accuracy. The

system will be able to handle patients having multiple conditions and can also predict multiple diseases at once.

Initially we will be taking around 10 mL of blood (a single vacutainer) which produces about 8.5 mL of plasma to analyse.

We would like to consider the 'samples as a gift to science'. By this we mean that, if participants are happy for us to do so, remaining sample not used in this study could be used in ethically approved follow on research. The same strict controls on confidentiality will be in place. An example of this may be trying to find new treatments for cancer. Participants can opt out of this and have their samples only used in this study. If they consent to this further use, the remaining samples will be transferred to a government licensed tissue bank where they can only be used in research that has been reviewed and received a favourable ethical opinion.

No genetic tests will be done as part of this study.

What will happen to the results of the research study?

- The results will be published in scientific journal.
- If diagnostic signatures of disease are validated they will be commercialised and put into practice as soon as is practical
- At no time will participants be identified in person.

An overview of results of the research will also be presented on the sponsor's website <http://www.biosignatures.com/FreemanUrology/> to allow participants to follow overall progress.

Who is organizing and funding the research?

The driving force behind this research study is a local company:

Biosignatures Ltd. -- Biosignatures, is a small team based in Newcastle and is passionate about the region and what its people can do. If successful this study would be recognised internationally and showcase the scientific abilities of the region.

This study has been designed and conceived by Biosignatures who are also providing the funding. Although it is hoped that the research will go on to benefit patients within the NHS the clinical staff have been contracted to participate in this study and did not instigate it.

The sponsor is paying the hospital to employ a full time research nurse and to have some time from the experts in the clinic. The contract is for a fixed time and there is no per patient payment or incentives for any of the clinical staff. No Biosignatures staff work in the clinic and everyone you meet will be employed, trained and managed by the hospital.

Who has reviewed this study?

All research in the NHS is looked at by an 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 opinion by Newcastle and North Tyneside Research Ethics Committee.

This study has also been reviewed and approved by the Newcastle Upon Tyne Hospitals NHS Foundation.

Thank you for reading this information leaflet. If you have problems or questions please do not hesitate to get in touch.

Please use one of the following contact numbers:

Freeman Urology clinical team:

Research Nurse: Wendy Robson, **tel:** 0191 2137322

Principal Investigator: Mr Naeem Soomro,

email: naeem.soomro@nuth.nhs.uk **tel:** 01912336161

Address: Urology Renal Medicine, Freeman Hospital, NE7 7DN

Biosignatures Ltd.,

Chief Investigator: Dr David Bramwell

email: info@biosignatures.com

web: <http://www.biosignatures.com> ,

tel: 0191 6453645,

Address: Keel House, Garth Heads, Newcastle Upon Tyne, NE1 2JE

Additional and updated information is available here:

<http://www.biosignatures.com/FreemanUrology/>