DIRECT
DIABETES RESEARCH ON PATIENT STRATIFICATION

DIRECT: Type 2 diabetes Progression Study **Patient Information Sheet** ***<site name>***	Affix subject barcode here
Version 5.0 9th November, 2012	

Before you decide whether or not you wish to participate in this project, we need to be sure that you understand firstly why we are doing it, and secondly what it would involve if you agreed. We are therefore providing you with the following information. Please read it carefully, and feel free to ask any questions you may have and, if you want, discuss it further with your doctor, friends or family. We will do our best to provide further information and answer any questions you may ask for now or at a later date. You do not have to make an immediate decision.

What is the purpose of this Research?
The level of blood glucose control changes with time in type 2 diabetes, and this varies between patients. For example, some people remain on just diet or one type of tablets for many years and show little signs of their diabetes progressing; whereas others progress rapidly and need more and more treatment to keep their diabetes under control. It is not possible at your stage of diabetes to know how your diabetes will progress. We hope to better understand this process and find tests that we can carry out early in diabetes that predict who will progress rapidly and who will not. This will in turn help us to plan diabetes treatment on an individual basis.
We believe that changes in the way the pancreatic beta-cells release insulin is a major factor in determining the changes in blood glucose levels over time and so the focus of this project will be to assess how well your pancreas produces insulin in response to a meal. We believe that the amount of fat in the liver and pancreas might also play a role and so the study involves a magnetic resonance (MRI) scan of the liver and pancreas at the start of the study.

Who is conducting this research?
The research is being funded by the European Union, in conjunction with funding from some leading pharmaceutical companies. This group of researchers and scientists within Europe is called the DIRECT consortium and it is interested in how people with diabetes respond to treatment. The day-to-day organisation of the research in Newcastle is being co-ordinated by Professor Mark Walker. A number of centres are involved in the UK, and the Newcastle NHS Hospitals Foundation Trust is the co-ordinating centre and legal sponsor of the study (taking legal responsibility for it).

Why have you been asked?
You have been asked because you are at an early stage of the condition (having been diagnosed with diabetes within the last 2 years). This is important because we believe that we will get the clearest picture of the changes in pancreatic beta-cell function at an early stage of the condition, and this is also the time when doctors and patients try to plan longer term management of the diabetes and in particular which treatments are best for individual patients.

What does the study involve?

The study involves an initial assessment to make sure that you are suitable for the study. You will then be invited to attend the clinical research facility for the baseline assessment. This involves a meal tolerance test (a 'milk-shake' like meal with blood samples taken over 2 hours) and MRI scan and completion of a lifestyle questionnaire. We will then follow you up over a period of 18 months at which time you will be invited back for the repeat meal tolerance test. During the 18 month period you will be asked to send us every 3 months a small sample of urine through the regular post, and at the mid-point stage (9 months) we will ask you to attend the clinical research facility for a brief visit for a fasting blood test and to review your progress. We will offer reminders by text messaging if you wish.

During the 18 month period your diabetes will be managed by your usual diabetes team and they will adjust your medication according to your clinical needs. Taking part in this study will not interfere with your usual diabetes management, or any other medical treatment you may be having.

The following describes the visits in detail.

Screening Visit (Visit 1).

In this visit we will seek your consent to take part and ask you some details about your diabetes, general health and lifestyle. We will give you a container for a sample of your stool to be brought along to your next visit. We will take a small blood sample (about 1 tablespoon in volume) to do routine tests (HbA1c and U+Es) to confirm that you are eligible for the study. This will not be necessary if you have had these tests done within the previous 2 weeks as part of your diabetes care.

Baseline Visit (**Visit 2).**

This is estimated to take 4 hrs all together. You will be asked to attend the clinical research facility between 0800 and 1000am. You will be asked not to eat from midnight the night before. You will be allowed to drink water on the morning of the visit, but no other type of beverage. If you are taking diabetes tablets you will be asked to miss these for 24 hrs before the visit, but you will be asked to take your other usual morning tablets.

The following will take place in the following order:

- We will measure height, weight and waist and hip circumferences
- We will measure your Blood pressure.
- We will ask you to provide a urine sample and toe nail sample
- You will be invited to bring in a faecal sample from home. We believe this is important as it will allow us to assess the microorganisms ('bugs') in your gut and these have recently been shown to affect how the body handles sugar.
- A cannula (thin plastic tube) will be placed into one of the veins in your arm for taking blood. We will take a sample of blood for baseline samples, and then you will be given 250ml (about 1/2pint) of an energy drink which is the "liquid meal". This will be flavoured and is a commercial food supplement preparation called *Fortisip*. You'll be asked to drink this over a 5 minute period. We will then take further blood samples from the cannula at 30 min intervals over a period of 2 hours. At the end of the test, the cannula will be removed and you will be offered a drink and light snack. During the visit we will take a total of 65mls of blood (around half a cupful).
- You will then be taken for the MRI scan. This involves a scan of the tummy which takes about 30 to 40 minutes. As the MRI scanner uses a strong magnet we will check with you before this scan that you do not have any metal inside your body, such as joint replacements or surgical clips. We will ask you to lie on the scanning table for the scan and keep still during this time. The scan takes place inside an enclosed space, but you will be able to talk to the radiographers (people who do the scan) during this time and you can listen to relaxing music. The scan is completely painless and non-invasive, and does not involve radioactivity. The MRI scan can be performed on the same day as visit 2, or on a separate day provided it's within 14

days of visit 2.

- Once this is completed you will be given a light meal and asked to take your usual diabetes tablets.
- You will be fitted with an Actigraph physical activity monitor that measures daily activity over a period of 10 days. The monitor is non-invasive and is attached to the wrist. The monitor should be removed if there is a risk of contact with water (for example while taking a shower), or if it causes discomfort during sleep. Once the assessment is completed we will ask you to post the monitor back to us in a pre-paid envelope.

Mid-point Visit (Visit 3).

- This is 9 months after visit 2. Just like visit 2, you will be asked to miss your diabetes tablets for 24 hours before the visit, and to fast from midnight the night before. In the unlikely event that you have been started on insulin, we will ask you to omit the insulin dose on the morning of the visit. This time we take a sample of blood from the arm vein using a needle and syringe. The total blood volume will be 40mls (about two eggcupfuls)
- We will re-check your weight and blood pressure
- You will be given another container so a further stool sample can be brought along to your next and final visit.
- You will be given a light breakfast before leaving and asked to take your diabetes tablets. This visit will take at most 30 minutes.

Final visit (visit 4)

- This will follow exactly the same format as for visit 2, except that there will be no repeat MRI scan.
- If during the course of the study you have been started on additional tablets for the diabetes, then you be asked to omit these for 24 hrs before this visit. In the unlikely event that you have been started on insulin, we will ask you to omit the insulin dose on the morning of the visit.
- Once you have completed the meal tolerance test, you will be asked to take the omitted tablets or insulin before the light snack that will be provided.

Would there be any risks?

The insertion of the cannula into the forearm vein may cause discomfort and may result in bruising that may persist for a few days after the test.

The study does not involve a new drug. Your diabetes team may add new tablets or insulin to your treatment as part of your clinical care. Any potential side-effects with these treatments will be explained to you by the prescribing team.

The MRI scan uses a strong magnet only, and does not use x-rays or other harmful radiation. Because the MRI uses a magnet we will need to make sure you do not have any metal inside your body that is magnetic, and you will be asked about this. There are no known safety concerns with MRI scanning. No contrast injections, which are sometimes used with other types of scan, will be given during the MRI scan. There are contraindications to having an MRI scan such as a metal implant/device, but we will ask you about this before the procedure. Similarly, the procedure can cause a mild degree of claustrophobia, and if this was going to be a problem for you then you would be excused from this part of the study.

Can I drive before and after these visits?

There will be no problem driving to or from each visit. We will ensure that your blood sugar

levels are safe before you leave the research facility.

Are there any direct benefits to those taking part?

In general there is no major direct benefit to you as a participant in this study. The main benefit is that we hope to improve the care of patients with diabetes by better understanding why people get diabetes and how it can best be treated.

What will happen if the MRI scan shows up something abnormal?

The MRI scan is being carried out to look at the liver and pancreas. In so doing we obtain images of the abdomen. Occasionally abnormalities are seen. Often these have been there for years and are of no concern; rarely, a serious abnormality is seen that requires follow up by your doctor. The radiologist, involved in this study, who is an expert in MRI scans, will study any abnormality and decide on whether this needs to be followed up. In this circumstance we will tell you and your General Practitioner, and make your MRI images available to your clinical team.

What about confidentiality?

We regard the protection of your personal information (i.e., the security of any data we collect on you as part of this study) as being extremely important. We have special systems in place to make sure that once we obtain your consent and you have completed your study visits, we then separate your name, address and any NHS (health care) number from the rest of your data. This helps ensure third parties cannot link information about your health to your name, address or other information that identifies who you are.

When you have given consent to take part in the study we assign you a code known as a "study number". Your study number is then used in place of your name when keeping track of the remaining information or samples we collect from you. We will not write your name, address or health record number on any of your samples or on the forms that are used to collect information from you during the study. In this way, your study data and samples are anonymised. The only exception to this is when we send blood samples to the NHS lab, which your doctor and we will use to determine how well you have responded to treatment (for example HbA1c test which is a measure of diabetes control). When the information and samples we collect from you are exchanged amongst scientists working within our study, your samples and data will be identified using your study code only and we will never pass on your name or address to scientists or third parties who are not directly involved in your clinical care. Your name will never appear in any report or publication that arises from this study.

Towards the end of the study we store the file and consent form containing your name, address, health record number and study number in a special locked database held separately from the rest of the information. This is never shared with anyone outside of the research team in Newcastle. The only reason for safely storing this information is to allow information from your past and future clinical/ NHS record to be extracted and linked anonymously to the study data for the next 10 years.

What will be done with the information collected about me and blood and urine samples?

The anonymised data we collect from you directly and, with your permission, indirectly from your medical records relating to your diabetes will be linked to your anonymised MRI images and blood and urine samples. These results and samples will be stored for the duration of the Direct project and used as part of this study to investigate different types of diabetes, why people get diabetes and why some people respond well or poorly to the diabetes drugs. The studies to be carried out will include genetic tests on your DNA and other genetic material as well as measuring other substances in the blood and urine. On completion of the

DIRECT project all anonymised biochemical and genomic data generated during the study will be transfered to a managed access secure data repository such as the European Genome-Phenome Archive (EGA). This is a secure database established by the European Bioinformatics Institute (EBI) for the sharing of data with the research community.

Who will have access to my anonymised data and samples and how will this be controlled?

This study is being conducted by a large group of European doctors and scientists at Universities and Hospitals as part of a consortium that includes a number of companies from the pharmaceutical industry who are collaborating on this project. None of these groups will ever have access to your name, date of birth or address. Your anonymised data will be held on highly secure computers internationally, including Denmark. These results will be accessible by members of the consortium and by approved members of the scientific research community, but access to the data and your blood and urine samples will require approval by a data access committee who ensure that all use of the data and samples is for scientific research and who ensure that appropriate data security and confidentiality is safeguarded. When the DIRECT study has completed all analyses, the samples will continue to be stored securely at the Peninsula NIHR Clinical Research Facility at the Royal Devon & Exeter Foundation Trust.

Where commercial companies conduct research or provide financial assistance to non-commercial researchers to do the research, they could require the commercial rights to benefits arising from the discoveries. To allow research collaborators to proceed you are asked to waive any future claim to financial benefit through participation in the study. So for example, if a company discovered the basis of a new diabetes drug by using your blood sample (as one of thousands of blood samples), and went on to profit from this discovery, you would have no future claim on this profit.

Who has reviewed this study?

The National Research Ethics Service, which has responsibility for scrutinising all proposals for medical research, has reviewed the proposal via their Newcastle Committee. It is a requirement that the research records are made available to monitors from Newcastle Hospital NHS Foundation Trust whose role is to check that research is properly conducted and the interests of those taking part are adequately protected.

Could I choose not to take part?

Yes, of course. Participation in this study is entirely voluntary. If you chose not to participate, you wouldn't have to give a reason why and it would not affect any future medical care you may receive. It is in your and our best interests that you only participate in this study if this is something you freely decide to do.

Could I withdraw from the study?

Yes. You would be free to withdraw from the study at any time by contacting your local diabetes study team (contact details are at the end of this document). You would then carry on with your diabetes treatment as planned by your health care team. We would still store and utilise your samples and data collected up until that point unless you specifically ask us not to by formally withdrawing your consent. If you decided to withdraw your consent, we would destroy any of your samples held by us and from then on any anonymised data collected from you would not be included in the analyses we perform as part of this study. Blood results that had been placed on the NHS clinical system would not be destroyed. Importantly, if your anonymised data had already been included by researchers in an analysis from which results had been derived and reported, this could not be changed.

What about travel expenses?

Your travel expenses will be reimbursed in full.

Will there be any further contact?

At time of participation we will ask you to indicate if you are willing to be re-contacted by the study team in the future to be invited to participate in any ethically approved research related to this project.

Will my GP be informed that I am taking part in the study?
Yes if you agree, your GP will receive a copy of the results that we provide for you.

What if I have a complaint?
If you are harmed as a result of taking part in this study, then compensation can be sought from the study sponsor under the NHS Indemnity arrangements. A copy of the guidelines is available on request. However, the sponsor will not compensate you where harm results from any procedure that is not in accordance with the study protocol. Under these circumstances, your right at law to claim compensation for harm where you can prove negligence is not affected.

Who should I talk to if I have any further questions or concerns?

If you have any questions regarding this study you can phone the study team.

Professor Mark Walker Tel: 0191 2464661

Or if you wish to seek independent advice then please contact <details of local contact> who is a clinician with an interest in diabetes who is independent of the research team.