DIRECT: Variation in response to GLP-1 Receptor Agonists **Patient Information Sheet for Group C** ***<site name>***	
Version 1 May 19, 2014	

You have previously started a new injection treatment (GLP-1 Receptor Agonists (GLP-1RA)) for your diabetes, and we would like to invite you to participate in a research project relating to this treatment. However, before you decide whether or not you wish to participate, 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.

Please note that we may have contacted you previously about a study we are conducting on GLP-1RA treatment. If you were not eligible to take part in the previous study you may still be eligible to take part in this shorter 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 present or respond to treatment. The day-to-day organisation of the research in <*region*> is being co-ordinated by <*local PI*>. A number of centres are involved in the UK, and the University of Dundee with NHS Tayside is the co-ordinating centre and legal sponsor of the study (taking legal responsibility for it).

What is the purpose of this Research?
You have previously started on an injection to help treat your diabetes. These injections are a type of drug called a GLP-1 Receptor Agonist (GLP-1RA), and currently there are several available types of this drug called Exenatide (Byetta/Bydureon), Liraglutide (Victoza) or Lixisenatide (Lyxumia). This type of treatment has been used around the world for the last few years and can have some dramatic results both in terms of stabilising blood sugar levels and helping with weight loss. This is why this treatment is becoming increasingly popular with patients and their doctors. However, some patients' blood sugar levels do not improve very much with these injections.

The purpose of this study is to try to find out why people respond differently to treatment with GLP-1RA. This raises a number of potential issues. If, as a result of this research, we could predict in advance that someone is not likely to respond to treatment it would save them the inconvenience of having to inject the treatment for at least 6 months and put up with potential unnecessary side effects. Conversely, if we understand why some people respond very well to this sort of drug, we may be able to develop better drugs that work in more people.

Why have you been asked?

You have been asked as you have started one of the GLP-1RA injections (Exenatide, Liraglutide or Lixisenatide) in the past and you used this treatment for at least 4 months.

What does the study involve?
As you are in the group of people who have used GLP-1RA treatment, we would like you to take part in some tests. This is a very simple study consisting of one visit only (lasting about 1 hour) where we take a few tubes of blood, take some basic body measurements and ask a few questions about your diabetes. You do not have to change your medication at all. The visit can be arranged to be somewhere local to you. The study visit can take place at any time.

Visit 1

Firstly, we will seek your consent to take part.

- *You do not need to change anything that you are normally doing.*
- You will remain on all your usual medications.
- You will take your usual diabetes medications, including your GLP-1RA (exenatide/liraglutide/lixisenatide) injection, if you still use this treatment.
- Firstly, we will take some blood samples which will be analysed for your DNA and RNA (this is what holds your genetic code). We will also take a sample of your blood fluid or plasma. The volume of blood we will take for this is approximately 20ml (less than an eggcup in volume).
- We will ask you some details about your diabetes and treatment.
- We will ask you about any other health problems you may have.
- We will ask you some questions about your family history to find out if your parents or siblings (if you have them), are affected by diabetes.
- We will ask you some questions about whether or not you smoke and also some questions about your intake of alcohol in an average week.
- We will measure your height and weight.

The study is now complete.

Would there be any risks?
The insertion of a needle into the forearm may cause discomfort and may result in bruising that may persist for a few days after the test.

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.

Will my GP be told of my participation in this study if I agree to take part?
Yes, with your permission we will write to your GP to let him/her know that you have agreed to take part. We will also let your GP know of any clinically important findings about your health.

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 that we then separate your name, address and any CHI (health care) number from the rest of your data, which 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. In general, we will not write your name, address or health record number on any of your samples or on the forms that are used to collected information from you during the study. In this way, your study data and samples are anonymised. 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 and we will never pass on your name or address to scientists or third parties who are not directly involved in your clinical care, such as your GP. 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 Dundee. 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. >delete if not appropriate for site

What will be done with the information collected about me and my 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 blood samples. These data and samples will be stored indefinitely and used as part of this study to investigate different types of diabetes, why people get diabetes, why some people progress rapidly to insulin and why some people respond well or poorly to the diabetes drugs GLP-1RA (such as liraglutide, exenatide and lixisenatide). 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.

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. 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. This data 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 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 additional use will require appropriate ethics committee approval.

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 potential 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 East of Scotland Research Ethics Committee REC1, which has responsibility for scrutinising all proposals for medical research on humans in Tayside, has examined the proposal and has raised no objections from the point of view of medical ethics. It is a requirement that your records in this research, together with any relevant records, be made available for scrutiny by monitors from University of Dundee and NHS Tayside, whose role is to check that research is properly conducted and the interests of those taking part are adequately protected.

Could you 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 you 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). 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 insurance companies?
Sometimes insurance companies ask people if they've ever had any genetic tests. However participation in this study does NOT constitute a "genetic test" as defined by insurance companies. The fact that you are taking part in this study will not affect your ability to get insurance. Data will never be released by us to a third party unless we are legally required to do so.

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.

Complaints?
If you believe that you have been harmed in any way by taking part in this study, you have the right to pursue a complaint and to seek compensation through the University of Dundee who are acting as the research sponsor. Details about this are available from the study manager at the coordinating centre at University of Dundee Tel: (01382) <*xxxxxx*> or you can contact your local research team on the contact number at the foot of this document.

Also, as a patient of the NHS, you have the right to pursue a complaint through the usual NHS process. To do so, you can submit a written complaint to the Patient Liaison Manager, Complaints Office, at your participating site. Note that the NHS has no legal liability for non-negligent harm. However, if you are harmed and this is due to someone's negligence, you may have grounds for a legal action against NHS Tayside but you may have to pay your legal costs.

<Patient Liaison Manager address at participating site>

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.

<Contact details of study team>

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.

Thank you for considering our request to take part in this study. Your involvement may help the current generation of those who suffer from diabetes, and might help to offer new treatments for our children's generation and beyond.