Recon4IMD Project:

General Information Sheet for Patients

Dear _____,

We would like you to consider taking part in this project called Recon4IMD.

Project Overview: The Recon4IMD (Reconstruction for Inherited Metabolic Disorders) project is a research initiative aimed at advancing our understanding of inherited metabolic disorders (IMDs) and improving diagnostic and therapeutic approaches. You have been invited to participate in this project, and we appreciate your consideration in contributing to this important research.

This is a European project and the leading scientist ….

What are the project's objectives?

The Recon4IMD project aims to:

1. **Genomic, Proteomic and Metabolomic Profiling:** Analyse the genetic makeup of individuals with inherited metabolic disorders and the metabolic abnormalities produced to characterise genetic mutations.

2. **Disease Understanding:** Enhance our understanding of the underlying mechanisms of inherited metabolic disorders for the development of improved therapies.

3. **Precision Medicine:** Investigate personalised treatment approaches based on individual genetic and multi omic (genomic, proteomic and metabolomic) profiles to optimise patient care.

Why are we asking you to participate?

You have been diagnosed with an inherited metabolic disorder (IMD) or are strongly suspected to have one by the doctor who looks after you in .. Hospital. Also, you have been enrolled or registered with one of the following projects or patient registries (with ethical approval at site): U-IMD, GENOMIT or Solve-RD.

Informed Consent:

Before you can participate in the Recon4IMD project, you or your legal guardian will be required to provide an informed consent. This means that you and your guardian will be given detailed information about the project, its objectives, procedures, potential risks, and benefits.

Take the time to thoroughly review this information and address any questions or concerns you may have with the research team.

What will happen if you decide to take part in this research:

1. Blood Sampling:

• A trained phlebotomist or healthcare professional will collect a small sample of blood from you. This process typically involves inserting a thin needle into a vein (usually in the arm) to withdraw the blood. The blood sample will be sent to the laboratory for metabolomics and transcriptomic analysis to identify specific patterns with inherited metabolic disorders

2. Urine Collection:

• You will be provided with a sterile container to collect a urine sample. The collection process involves voiding urine directly into the container. It is essential to follow any specific instructions provided by the research team for the proper collection and handling of the urine sample. The urine sample will be analysed to gather additional diagnostic information.

3. Stool sample:

• You will be provided with a sterile container and/or specific wipes to collect a stool sample. This is part of a partner study called AVATAR aimed at studying the microorganism present in the gut of subjects. You can decide to take part or not by ticking the appropriate box in the informed consent form.

4. Skin Biopsy:

• If deemed necessary by the research team, a skin biopsy may be conducted to obtain a small sample of skin tissue for further analysis. If a sample is already available, we will ask you permission to use the cells collected on that occasion and won't need to do another biopsy.

The skin biopsy procedure involves the following steps:

The area for biopsy will be cleaned and numbed with a local anaesthetic to minimise discomfort.

A small piece of skin, usually 3-4 mm across, about this size  , will be carefully removed using a sterile instrument.

a) The biopsy site will be dressed in a bandage.

b) The collected skin sample will be sent to the laboratory for detailed analysis, including genetic and cellular studies.

4. Medical History and Clinical Data Collection:

• A comprehensive medical history will be obtained, including information about your symptoms, previous treatments, and any relevant medical interventions. This may involve reviewing medical records, conducting interviews, and using standardised assessment tools.

5. Follow-Up Visits:

• Taking part in the study will not lead to additional hospital admissions and visits. All the tests will be done at time of your regular follow up appointments.

Do you have to take part?

No, you can decide. If you are interested in taking part you will be given this information sheet and you will be asked to sign a consent form. You can change your mind at any time without giving a reason. This will not affect the standard of care you receive in any way

What will happen to my samples at the end of the study?

Because individual inherited metabolic diseases are rare, any samples from patients with these disorders are extremely valuable and they will be invaluable in other research projects on these disorders. If you are happy for us to do so we would like to store any left-over samples in an anonymised way for their use in subsequent projects.

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given a favourable opinion by the National Research Ethics Committee.

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

If you decide at a later stage that you do not wish to participate in this research project, that is entirely your right, and will not in any way prejudice any present or future treatment.

Information collected may still be used. Any stored blood or tissue samples that can still be identified as yours will be destroyed if you request this.

Participant Comfort and Safety:

• The research team will prioritise your comfort and safety throughout all procedures. If you experience any discomfort or if you have concerns at any point, please communicate with the

research team immediately. Adequate measures will be taken to address any issues and ensure a positive and safe research experience.

Additional Information:

- Different analyses will be conducted at different European Centres by experts in the field. This collaboration allows for a comprehensive and specialised approach to understanding inherited metabolic disorders.

The research team will provide specific instructions and guidelines for each procedure, including any necessary preparations or restrictions before the scheduled appointments.

- It is essential to notify the research team of any allergies, medical conditions, or medications you are currently taking to ensure their safety during the procedures.

By participating in these procedures, your contribution will play a crucial role in advancing our understanding of inherited metabolic disorders and may lead to advances in diagnosis and treatment options for these conditions. Your cooperation and open communication with the research team are highly valued and appreciated.

Confidentiality: All information collected during the Recon4IMD project will be treated with the utmost confidentiality.

Each individual participating in the study will be allocated a unique identifier. Only designated individuals of the research team and your clinical care team will be able to link this identifier to an individual. The unique identifier generated, will be entered on your hospital record at the hospital where the consent has been taken. This is so that clinical staff can be aware of what studies you have been recruited to. The doctors looking after you will have access to their case notes. Researchers, sponsors, regulatory authorities & R&D will have access to the laboratory results generated by this study.

The use of some types of personal information is safeguarded by the Data Protection Act 2018 (DPA). The DPA places an obligation on those who record or use personal information, but also gives rights to people whose information is held.

We will ask for your permission to put information about you onto a computer database to store the information. We will remove all personal details, such as names and addresses, so that you cannot be recognized from it. Anonymised data generated from the samples may be stored in a managed access data archive such as the European Genome-Phenome Archive EGA (regulated by a data access committee) and shared with other researchers around the world without divulging identifiable details.

There is a very small risk that an individual could be identified from their DNA or RNA sequence data if this can be matched to other data which is linked to identifiable information. The chance of this happening is very small. The recipient of any cell line/samples/data must agree not to make any attempt to identify the original donors. The recipient must also agree that any genetic or genomic data generated from the use of the cell lines/samples/data will be held securely and only used in biomedical research, and will only be made available to third party researchers under a Data Access Agreement.

If results of this research study will be published in scientific journals or presented at conferences for the purpose of advancing medical knowledge and benefiting future patients, all the data presented will be anonymised and any possible identifier removed.

Personal data will be stored and accessible for 6-12 months after the end of the study. Research data generated from the Recon4IMD study will be stored for 25 years.

Potential Risks: While every effort will be made to ensure your safety, it is important to acknowledge potential risks associated with participation, such as discomfort during sample collection or rare complications. If a skin biopsy is performed a procedure-specific informed consent will be discussed by the clinical team. The skin biopsy will leave a tiny scar, which should disappear with time. Bruising may occur after a blood test.

The results of the tests may reveal unexpected results that are not related to why you are having this test. These may be found by chance and you may need further tests or investigations to understand their significance. You can decide you do not want to know these results by ticking the box in the Informed Consent Form.

Benefits: Your participation may contribute to the advancement of medical knowledge and the development of more effective treatments for inherited metabolic disorders.

We do not anticipate any direct benefit to you. Anyhow, if you do not have a definite diagnosis and relevant information for your care result from these tests, we will let your lead clinician know so they can discuss with you and decide whether further tests are required, if you are happy for us to do so.

Who is funding the project?

Recon4IMD is co-funded by the European Union's Horizon Europe Framework Programme (101080997), the Swiss State Secretariat for Education, Research and Innovation (23.00232), and by United Kingdom Research and Innovation (10083717 & 10080153).

Who is the sponsor of the project?

The sponsor for this project is the National University of Ireland Galway, University Road, Galway, Ireland H91 TK33.

What if you have any questions or are unhappy?

An independent research ethics committee has approved this project and believe that it is of minimal risk to you. If you have any queries or complaints you are free to report these to your clinician or if you wish to complain formally this can be done by contacting the ….

Contact Information: If you have any questions or concerns at any stage of the Recon4IMD project, please feel free to contact:

Thank you for considering participation in the Recon4IMD project. Your involvement is crucial in advancing our understanding of inherited metabolic disorders and improving the lives of those affected.

Sincerely,