My name is Dr Timothy Barrett, and I am working with your doctor. I am based at Birmingham Children’s Hospital, UK, and I look after people with Wolfram, Alström, Bardet Biedl and other rare diseases. I am the chief investigator for EURO-WABB (www.euro-wabb.org). EURO-WABB is a research study. The study involves the development of a European registry of children and adults who have been diagnosed with rare diseases such as Wolfram, Alström and Bardet Biedl syndromes. By collecting information about these diseases, we hope to learn more about the diseases and what causes them.

An invitation to take part
We are asking if you would agree to take part in the EURO-WABB research study. Your participation in this study is entirely voluntary. Before you decide if you want to take part, it is important that you understand why the research is being done and what it will involve. Please read the following information carefully and discuss it with your family, friends, doctor or nurse if you want to. Please ask us if there is anything else you would like to know.

Part 1: Tells you what the study is about and what will happen to you if you take part.

Part 2: Gives you more detailed information about the way that the study will be run. Please take time to decide if you want to take part.

Part 1

1. Why are we doing this research?
Wolfram syndrome, Alström syndrome, Bardet Biedl syndrome and other syndromes are rare diseases with no specific treatment. The purpose of this research is to understand why people with these conditions become ill. This study aims to enroll children and adults with these rare diseases in an international registry, to obtain blood for genetic diagnosis and to understand the disease mechanisms. Given their rarity, the natural history of these diseases is still not well understood. Collecting patient data in this registry and learning about the progression of disease may speed up the development of clinical trials to test new treatments when they become available. Knowing more about these syndromes at the molecular level may also help to develop specific treatments for this disease.
2. **Why have I been chosen?**
You have been approached because your doctor thinks you may have a rare disease. This study is planned to start in July 2011 and will include up to 600 children and adults with rare diseases. You are being asked to take part in this study to understand your condition better. We will do this by studying the genetic cause in a blood sample from you, and by following your progress over time. This will help us to understand what happens to people with rare diseases, and to offer future studies for new treatments to either halt or delay its progression.

3. **Do I have to take part?**
No. It is up to you to decide whether or not you take part. It is important to understand that taking part in this study is voluntary and you are free to withdraw at any time without a reason. This will not affect your care in any way.

Before any tests are carried out, your doctor or nurse will explain the tests that will be done in this study and you are asked to read this information sheet thoroughly. If you are happy to take part and are satisfied with the explanations from your doctor or nurse, you will be asked to sign and date the consent form. A copy of the signed and dated information sheet and consent form will be given to you to keep.

4. **What will happen to me if I agree to take part?**
If you agree to take part, your doctor will ask you questions about your illness. Your doctor may also add anything from your NHS medical notes that he or she thinks may help understand your illness. Your doctor will then put this information on an anonymous database with the information from many other people with the same condition. You can have a copy of the information held about you on the database if you like. The anonymised data will be held on the registry for a minimum of five years, and may be stored for longer.

You may be asked to donate an extra blood sample. The amount of blood will be 10ml or 2 teaspoonfuls. You will not come to any harm as the body makes blood all the time. This blood sample will be sent to a laboratory to do or repeat the genetic test. Any sample left over may be stored.

We may also ask you to provide a small skin biopsy from your outer arm under local anaesthetic. The amount of skin taken is about the same size as a match head. The skin grows back again very fast. The skin biopsy is to make permanent cell lines from the skin cells. Cell lines are cells grown in a laboratory and have the same characteristics as the original sample cell. The cells are able to multiply almost indefinitely, which means that they can be used for different research studies without running out. Although not part of this project, it is possible that these cell lines may be used in future to make stem cells. Stored blood samples and cell lines will be used to study your disease and its complications over many years.

Both procedures will take place at the hospital. If the hospital already has these samples stored, we may ask your permission to use these samples for research.

It is important to understand that you can take part in the registry without taking part in the skin biopsy or blood sample parts of the study.
5. What are the side effects of the study and will I be at risk?
There are no bad side effects to this study; the good effects are that this study will give us more information about your illness and help to offer the most effective treatment.

6. What are the other possible disadvantages and risks of taking part?
Blood testing is part of normal assessment of your illness. The total amount of blood to be taken during the study is 10mls, which is 2 teaspoonfuls. Every effort will be made to help you if you feel worried or anxious during the blood test. A special cream (a local anaesthetic) can be used to help numb the skin.

Skin biopsies may be taken from your outer arm. A local anaesthetic (injection) will be used so that the procedure shouldn’t cause discomfort. After the procedure you will be given advice about how to look after the skin break. Very rarely this skin break may become infected. If this happens, you should see your GP who will decide if any treatment is required for the infection.

7. What are the potential benefits of taking part?
If you have not yet had a genetic test for your condition, then this will be done as part of the study and you will receive the results. There are no direct benefits to you in taking part. However, if we can put together the clinical features from a large number of patients, we may be able to identify times when interventions may help you. We will also keep you regularly informed of new discoveries in the causes and treatment of the syndrome.

8. What happens when the research stops?
When the doctor has the genetic results from your blood test, he or she will tell them to you at your next outpatient visit; and discuss with you whether your treatment is affected by the result. When the research stops, your medical care will continue just as before; but hopefully with new information to help your doctor look after you better.

9. What if there is a problem?
If there is anything you are worried about, talk to your doctor or nurse. There is more information about what to do if there is a problem in part 2.

10. Will my personal data collected during the study be kept confidential?
Yes. All information about taking part in this study will be kept confidential. More information regarding confidentiality may be found in part 2.

11. Contact for further information
If you require further information, please feel free to ask any questions you wish.
Researcher Name(s): Prof Timothy Barrett
Address: Diabetes Unit
Birmingham Children’s Hospital
Steelhouse Lane
Birmingham, B4 6 NH
Telephone: 0121 333 9267
Part 2

12. What happens if new information about my condition comes along?
Sometimes new information comes along about the illness that is being studied whilst a study is still happening. You may feel differently about this study, and your doctor will discuss whether or not you still want to take part. If you decide to withdraw from the study, that is no problem, and your doctor will continue to provide care. If you continue, you may be asked to sign an updated consent form containing any new information.

Also, on receiving new information the study doctor might consider it to be in your best interests to take you out of the study. He or she will explain the reasons but continue looking after you. If the study is stopped for any other reason, we will tell you why, but your medical care will continue.

13. What will happen if I don’t want to carry on with the study?
It is important for you to understand that taking part in this study is voluntary and you are free to withdraw at any time without a reason. You do not have to take part in this study to be treated for your condition.

If you decide to stop taking part in the study, you will only need to inform your doctor and he or she will withdraw you from the study. This will not affect your standard of care or the benefits to which you are entitled. Should you wish to stop after you have given a blood sample, you can choose either to have all your tissue samples and data permanently destroyed; or anonymised so that no-one will ever be able to link your name to the tissue and/or data. Any research results already generated from your tissue and/or clinical data cannot be destroyed or recalled.

What if there is a problem?
Complaints:
If you have a concern about any aspect of this study, please speak to your doctor or one of the study doctors. We will do our best to answer these questions (see contact details in Part 1). If you are still unhappy and wish to complain formally, you can do this using the NHS complaints procedure. You can ask how to do this at your hospital.

Harm:
If you have an accident while having the blood sample taken on NHS premises, the NHS has the indemnity for this study. We will make sure you are closely supervised while having the blood test in the hospital.

14. Will anyone else know I am taking part in this study?
Yes. If you have given your consent to take part in this study, any of your medical records may be looked at by your doctor to collect health information for the study. Also, people from the regulatory authorities (such as the Department of Health) may look at your medical notes to check that the study is being carried out properly.
None of your personal data, such as name and contact details, will be uploaded onto the registry. Only non personal data will be put onto the registry. Your blood data will be assigned a code number. A master list linking the code number and your identity will be kept separate from the research data. The master list will be kept in a locked file and your data will only then be identified by a subject number (this is a number you get you join the study). Any laboratory samples (e.g. blood samples) will be identified in the same way. None of your personal details will be used in any presentations and publications as required by local/regional/national regulations. The information about you and your blood and tissue samples are confidential and will not have your name and address on them. The information is also anonymous but has a unique identifier (the subject number referred to above). In this way the researchers analysing your data and blood or tissue sample will not know who they are from; but if they find something that may affect the way we need to treat you, they can pass the information to me with your unique identifier. I can then identify you to pass the information back to your local doctor and make sure you are offered the best available treatment.

16. Involvement of your General Practitioner/Family Doctor (GP)
We will tell your GP (and other specialist doctors who are involved in your healthcare) about you taking part in the study. We might also need to ask for more information from your GP about your medical history/medications you have taken and the GP may be told about your progress during the study.

17. What will happen to any samples I give?
With your consent, any samples will be anonymised so that they are only known by your registry unique identifier. All UK samples will be stored in Birmingham in a licensed bio-repository. Samples will be stored for as long as they have research value and may be shared with other approved research workers in the UK or abroad. This means that, with your agreement, the samples will be stored for a minimum of three years, and may be stored for longer.

Blood samples will be used for genetic analysis of genes associated with your disease.

It is possible that the samples you donate may be used in future, as yet unidentified studies that relate to your disease or its complications.

Tissue samples, e.g. from a skin biopsy, can be used to generate adult stem cells which carry one of the genes associated with your disease. These stem cells may then be used to produce cells representative of specific organs (such as heart kidney etc).

18. Will any genetic tests be done?
Yes. Your DNA will only be used to look at mistakes (mutations) in the genes related to your condition. It will only be made available to scientists studying these conditions. In a few cases, the genetic tests may find a result that will affect the way you are treated. If this happens, the results will be passed back to your Consultant to put you on the best possible treatment.

19. What will happen to the results of the research study?
Once the study is complete, the results will be published and a final report written. You should contact the study doctor if you would like to get copies of any information that is published. You
20. **Who is organizing and funding the research?**
The study is organized by The University of Birmingham, UK, and funded by the European Union Directorate General for Health and Consumers.

21. **Who has reviewed this study?**
This study has been reviewed by independent expert peer reviewers for The European Union Directorate General for Health and Consumers.

The study will be run in accordance with all suitable guidelines aimed at ensuring proper conduct and safety of anyone taking part, including the Guidelines on Good Clinical Practice and the Declaration of Helsinki.

If you wish to take part in the study you will be asked to sign the consent (agreement) form. A copy of your signed consent form and this information sheet will be given to you to keep.

*Thank you for taking the time to read this information sheet.*