



INFORMATION SHEET FOR ADULTS

UK Histiocytosis Registry

You are being invited to participate in the UK Histiocytosis Registry (UKHR). This Registry has been created to collect medical information and samples from patients with histiocytosis and related disorders for research. You may be invited because you already know that you have one of these disorders or because you are about to have a biopsy to test whether you have histiocytosis or a related disorder.

Before you decide to participate, it is important to understand why the registry has been created, how it will help research and what it will involve for you. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part. Thank you for reading this.

What is the purpose of the UK Histiocytosis Registry?

Histiocytes are immune cells that are found in tissues all over the body. Histiocytosis is a rare group of diseases caused by an excess of these immune cells. Histiocytosis includes disorders such as:

- Haemophagocytic Lympho-Histiocytosis (HLH)
- Langerhans Cell Histiocytosis (LCH)
- Erdheim-Chester Disease (ECD)
- Rosai-Dorfman Disease (RDD)
- Juvenile Xanthogranuloma (JXG)
- Xanthoma Disseminatum (XD)
- Various cutaneous histiocytosis disorders
- Malignant histiocytosis
- Related disorders with histiocytes including
 - Sarcoidosis
 - Granulomatous diseases
 - Giant cell diseases
 - Vasculitis
 - IgG4-related disease

The purpose of the UK Histiocytosis Registry is to collect information and samples from patients with histiocytosis and related disorders around the UK. The Registry aims to help in a number of ways:

- understanding what causes histiocytosis;
- improving tests to diagnose histiocytosis
- finding out how many patients have had histiocytosis and what symptoms and other problems it causes them throughout life
- providing information about the healthcare resources that are required for patients with histiocytosis
- planning clinical trials to improve treatment and to test new therapies.

The Registry is collaborating with International Registries in order to collect information about everyone in the world. Joining forces will allow us to make progress more quickly, especially for the rarer forms of histiocytosis. These Registries include:

1. The International Rare Histiocytic Disorders Registry (IRHDR) based in Toronto
2. The Registry for Histiocytic Disorders (RHD) based in Vienna
3. The Erdheim-Chester Disease Global Alliance Registry (ECDGAR) based in New York.



Why have I been chosen?

You have been chosen because you have been diagnosed with histiocytosis or you are about to have a biopsy to see if you have histiocytosis or a related disorder. About 500–1,000 children and adults are living with histiocytosis in the UK, and we will be inviting as many as possible to join the registry.

Do I have to take part?

It is entirely voluntary and up to you to decide whether or not to take part. We will describe the project and go through this information sheet, which is yours to keep. If you do decide to take part, you will be asked to sign a consent form. You are free to withdraw at any time without giving a reason. If you want, all information about you will be deleted from the databases and all your stored samples will be destroyed. A decision not to take part or to withdraw at any time, will not affect the medical care that you receive. You are in control of choosing what information and samples to provide, and of what research can be performed using your samples.

What will happen to me if I take part?

You will be asked to sign a consent form that will allow us to obtain medical information about you and to use your biopsy samples for research. We may also ask for a sample of your blood at the same time as your other blood tests.

Information about you: medical information will be obtained by reading your medical notes and talking to your doctors. This will include images of your biopsy samples, medical scans and x-rays. It will include what has already happened to you and what happens in the future. You may also be offered the opportunity to take part in on-line or telephone surveys where you are asked to describe your symptoms and your experience of histiocytosis and how it has affected you. We will also ask permission to contact you in the future about histiocytosis research.

Biopsy samples: samples will be obtained from the pathology lab after a diagnosis has been made. If you are just about to have a biopsy, we will take a small part of the biopsy for research. If you are having a blood test, we may request some extra blood tubes for research (up to 60ml or 3 tablespoons).

What happens to information about me and the samples that I give?

Personal information: In order to protect your privacy, you will be given an anonymous identification code, linked to all the information about you. We will collect the minimum amount of personal information in the Registry so that you cannot be identified. This personal information will include only your year of birth, gender, ethnicity and the fact that you live in the UK. The medical team looking after you will know who you are and keep a record of your identification code, either on a secured, password-protected NHS computer in the hospital, or in paper copy stored in a locked cabinet in the hospital. When they add information to the Registry, they will use only your anonymous identification code. To add your information to the registry, each team will use a secure web-based system called REDCap which is used for many medical studies and has a very high standard of security.

Medical information: Information about your histiocytosis or related disorder will be entered onto the UK registry, under your identification code, using the REDCap software, via a secure website. It will include the date of your diagnosis, the details about your histiocytosis or other condition and the problems it causes, the genes that are affected, what treatments you have had and how you have responded. It may also contain information about any other health problems that you have. The software also permits participants to log on in a secure



way that protects your privacy and tell the registry how you feel and how histiocytosis has affected you.

Your samples: we will ask your permission to use any samples that have been taken as part of your medical care for further research tests. These samples are usually stored in your local hospital pathology department. In addition, we may request that blood samples or spare biopsy material is sent fresh to Newcastle University where the UKHR holds a 'Research Tissue Bank'. This is a collection of frozen material that can be used for different types of research.

Who will use your information and samples?

Access to information and samples stored in the registry is supervised by an Access Committee who are a group of doctors, scientists and patient representatives. They will meet regularly to decide on the most important research questions and how the information and samples will be used to answer these research questions. We expect that most of the research will be done by doctors and scientists in the UK who see patients with histiocytosis, but the Access Committee will also consider applications from research teams outside the Registry and outside the UK.

Information provided to International Registries: The information that we will send to International Registries will only include your identification number, year of birth, gender, ethnicity, the fact that you live in the UK and details about your histiocytosis. Access to and use of the information contained in an international Registry is controlled by a Chief Investigator. They are bound by similar obligations as we are in the UK, in order to maintain data security and to use the information for the purposes it was intended for. The International Registries are interested in different types of histiocytosis and need different information:

1. The International Rare Histiocytic Disorders Registry (IRHDR) is for patients with 'non-Langerhans Cell Histiocytosis' and has been set up under the supervision of the Histiocyte Society in Toronto, Canada. We will submit your information to the IRHDR using a secure online website (using REDCap software). If you have been diagnosed with a rare histiocytosis that is not Langerhans Cell Histiocytosis then your biopsy samples will be sent for review to make sure that the diagnosis is consistent. This will be performed in a centre in Germany. We will send your anonymized biopsy samples and disease details; this may include electronic copies of any x-rays or scans that have been done, and clinical photographs. The samples will only be labelled with your identification code and none of your personal details. If the diagnosis changes in a way that would influence your treatment then your doctor will be informed. Further information on the IRHDR is available on request.
2. The Registry for Histiocytic Disorders (RHD) is for adults with any type of histiocytosis and has been set up under the supervision of the Histiocyte Society in Vienna in Austria. The RHD is very similar to the UK Histiocytosis Registry. There is no need to send biopsy samples or x-rays and scans. We will submit the same information that we have collected for the UK Histiocytosis Registry on adult patients using a secure online website. More information is available on request.
3. The Erdheim-Chester Disease Global Alliance Registry (ECDGAR) is for patients with Erdheim-Chester Disease and is being set up by the Memorial Sloan Kettering Cancer Center in New York, USA. We will submit your information to the registry using a secure online website (using REDCap software). For this registry, we will also ask permission to make electronic copies of any x-rays or scans that have been done, to be stored in a research database in an anonymous form (we call this digitisation and electronic image capture of radiology images). You may also be asked to complete a patient questionnaire as

part of the information for this registry, using a website hosting the REDCap software. More information is available on request.

How long will my information and samples be stored for?

We will keep your information and samples for as long as the UKHR exists. The aim is to maintain the UKHR for at least 10 years. If the UKHR closes, the information and samples will either be archived for future ethically approved research or destroyed. Information sent to International Registries will also be archived or destroyed if the UKHR ceases to exist.

What are the possible disadvantages and risks of taking part?

There are none that we can identify except the time it takes to read this information and to give your consent to join. Some patients may be asked to fill out online questionnaires but this is also voluntary. Your information and samples will be stored in secure locations, and you have control over which information and samples you provide.

What are the possible benefits of taking part?

There may be no benefit to you if you take part. If you have a rare form of histiocytosis, your diagnosis will be checked by an expert for the IRHDR. If you become eligible for new trials or treatments for histiocytosis then we will inform your doctors. However, most of the time, studies using the registry information and samples will help us improve treatments for future patients rather than the participants themselves. Your information and samples are considered to be a 'gift' from Newcastle University where the UKHR is held. This means that you will not be paid or receive any financial reward.

Will my taking part in this project be kept confidential?

Yes. Your personal details and participation will be kept confidential at all times. We will handle all information about you in line with rules of conduct known as 'Good Clinical Practice'. If we need to communicate with the medical team caring for you, we will use your registry identification code. The medical team will know who the code belongs to but the registry or anyone else will not know your personal details. Sometimes the Registry will need to contact your medical team for the following reasons

- to double check the information against your medical record if we think that there may have been an error in transferring information
- to invite you to take part in suitable future research or clinical trials
- to contact you if the research discovers anything that may help your medical team to look after you
- in case you decide not to carry on with the study, so that we can withdraw your information and samples.

Information collected by the registry may be sent to researchers in countries where the laws are different to the General Data Protection Regulations in the UK. This should not affect your privacy because we are not collecting personal information other than the year of your birth, gender, ethnicity and residence in the UK. As an additional assurance, any researchers receiving information or samples from the UKHR will sign a confidentiality agreement and confirm that a satisfactory security arrangement is in place to hold the information and samples during the duration of the research study. Finally, all researchers will return the information and unused samples to the UKHR at the end of the research project.

What type of research will be carried out using my information and samples?

Your information and samples will only be used for ethically approved research directly on histiocytosis and related conditions, using research methods that you agree to. The research projects will include a wide range of laboratory and hospital-based research. For example: to find out what causes histiocytosis, to develop better tests to diagnose and predict the severity of histiocytosis, and to develop better treatment. We will also use



information to identify suitable individuals with histiocytosis for future research and clinical trials. In the consent form that follows we will ask for specific permission about the following research methods:

- Sequencing your DNA to understand what genes have caused histiocytosis. DNA is the genetic code that genes are made from. We will isolate, analyse and store a sample of your DNA from your donated blood and from your biopsy. We will determine your genetic makeup and any genes that have gone wrong to cause your histiocytosis. This may involve sequencing part of or even all of your DNA code.
- making cell lines that can grow for a long time by themselves in the laboratory, including 'stem cells', in order to preserve a supply of material.
- growing histiocytosis in mice to study the effect of histiocytosis on different organs

Will I find out if I have genes that are associated with other diseases?

The research will only study genes that are likely to be associated with histiocytosis. The research will not look for genes that are associated with other diseases and you will not receive information about the genetic risk of diseases that are not related to histiocytosis. It is possible that genes that cause histiocytosis might also be associated with other illnesses. This type of knowledge is advancing all the time and we cannot predict the chance that a histiocytosis gene will be linked to another illness.

Who will be using my information and samples?

Your information and samples will be used by scientists and doctors from universities, hospitals, and other research institutions as well as their collaborating industrial partners to carry out research in histiocytosis. Any researchers proposing to use the information or samples of the UKHR will have to make a formal application to the UKHR. The UKHR Access Committee will review these applications to make sure that your information and samples are used only for high quality and relevant research projects.

Will my information and samples be used by researchers outside the UK?

Yes, the UKHR may be used by researchers outside the UK. This is because more accurate information can be obtained by including as many participants as possible. In order to ensure that UKHR resources are handled appropriately, written agreements (called a Data Transfer Agreement and a Material Transfer Agreement) will be arranged between the UKHR and the researchers. This ensures that researchers outside the UK follow high standards and will protect the contribution that you and other participants have made to the Registry.

What will happen to the results of research studies using the UKHR?

All researchers using the information or samples from the UKHR will send us a copy of their research findings at the end of their studies. The results may be published in a scientific journal or may be presented at a scientific meeting. All research activity will be published on the UKHR website. (www.UKHR.org.uk) and will be reported to the Research Ethics Committee annually. Copies can also be requested through your medical team or from UKHR.

What happens if a commercial company wants to use the UKHR?

Sometimes research can be helped by commercial companies. You will be asked if this is OK. If a commercial company is permitted to use the resources of UKHR, you will have no claim to earnings made from commercial products that are developed.

Will I be contacted to give more information or samples in the future?

Yes, we may contact you for other research studies in the future, and it is possible that some of these research studies may require more information or samples. However, you do not have to take part in any of these future studies unless you want to.



Who is organising and funding the creation of the UKHR?

The project is co-ordinated by doctors from Newcastle University and Newcastle Hospitals NHS Foundation Trust. The research is funded by Histiocytosis UK, project number HistoUK/2016/08/01. The UKHR requires funding for running costs to keep it going. We will ask if it is OK for us to ask researchers obtaining samples and information from UKHR to contribute to these running costs. Your doctor will not be paid for including you in this project.

Who has reviewed this project?

This project has been reviewed by international and national experts commissioned by Histiocytosis UK before we were awarded the funding. In addition, this project has been reviewed and given favourable opinion by the North East - Newcastle & North Tyneside 2 Research Ethics Committee, to protect your safety, rights, wellbeing and dignity.

What will happen if I don't want to carry on with this project?

If you do not want to carry on with the project, you can contact us or your medical team. You do not need to give any reason and it will not affect your treatment. We will ask you if the UKHR may keep the information and samples that have been collected already. You may ask for everything to be discarded or destroyed if you wish.

What if there is a problem?

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. If you have a concern about any aspect of this study, you should ask to speak to your medical team or the UKHR team who will do their best to answer your questions (see contact details below).

If you prefer to raise your concerns with someone not involved in your care, you can contact the Patient Advice and Liaison Service (PALS). This service is confidential and can be contacted on Freephone: 0800 032 0202

Alternatively, if you wish to make a formal complaint you can contact the Patient Relations Department through any of the details below:

Telephone: 0191 223 1382 or 0191 223 1454

Email nuth.patient.relations@nhs.net

Address: Patient Relations Department
The Newcastle upon Tyne Hospitals NHS Foundation Trust
The Freeman Hospital
Newcastle upon Tyne
NE7 7DN

UKHR contact for further information

If you have questions regarding the UKHR, you can contact Dr Matthew Collin, Professor of Haematology, Institute of Cellular Medicine, Newcastle University; Tel (0191) 2139382; email matthewcollin@nhs.net. Further information about the UKHR can be found on our website: www.UKHR.org.uk

If you would like to find out more about histiocytosis, the following websites may be useful for you. However, we are not responsible for the contents of these websites: Histo UK (www.histiouk.org).

Thank you for reading this leaflet, it is yours to keep; you will also be given a copy of the signed consent form that you may wish to keep.