

INFORMATION SHEET FOR RELATIVE OF DECEASED PATIENT

UK Histiocytosis Registry

Please accept our deepest condolences for the loss of your loved one. We are contacting you because your relative was diagnosed with histiocytosis or a related disorder and we would like to include some of their medical information and tissue samples, if available, in the UK Histiocytosis registry (UKHR). The Registry has been created to collect medical information and samples from patients with histiocytosis and related disorders in order to help future generations of patients. In for your relative to be included, we need your permission, on behalf of them. Before you decide, it is important for you to understand why the registry is being created, how it will help research and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish before you make a decision. Ask us if there is anything that is not clear or if you would like more information.

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 has your relative been chosen?

Your relative has been chosen because they were diagnosed with histiocytosis or a related disorder. About 500–1,000 children and adults are currently living with histiocytosis in the UK, and we will be inviting as many as possible to join the registry.

Do I have to consent on my relative's behalf?

No, it is entirely voluntary and up to you to decide whether or not to give your permission. We will describe the study and go through this information sheet, which is yours to keep. If you do decide to go ahead, you are still free to withdraw your permission at any time without giving a reason. If you want, all information about your relative will be deleted from the databases and all stored samples will be destroyed. A decision not to take part, or to withdraw at any time, will not affect the care that you or your family receive. You are in control of choosing which of your relative's information and samples to provide.

What will happen if I consent?

You will be asked to sign a consent form that will allow us to obtain medical information about your relative and to use their blood and biopsy samples for research.

Information about your relative: medical information will be obtained by reading your relative's medical notes and talking to their doctors. This will include images of their biopsy samples, medical scans and x-rays.

Biopsy and blood samples: tissue samples will be obtained from the pathology lab. If any of your relative's blood was stored, we will request some blood tubes for research.

What happens to information about my relative and the samples that we give?

Personal information: In order to protect your relative's privacy, they will be given an anonymous identification code, linked to all the information about them. We will collect the minimum amount of personal information in the Registry so that they cannot be identified. This personal information will include their year of birth and death, gender, ethnicity and the fact that they live in the UK. The medical team who looked after your relative will know who they are and keep a record of their 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 relative's identification code. To add your relative's 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 relative's histiocytosis will be entered onto the UK registry, under their identification code, using the REDCap software, via a secure website. It will include the date of their diagnosis, the details about their histiocytosis or other condition and the problems it caused, the genes that were affected, what treatments they had and how they responded. It may also contain information about any other health problems that they had.

Your relative's samples: we will ask permission to use any samples that have been taken as part of your relative's medical care for further research tests. These samples are usually stored in the local hospital pathology department.

Who will use your relative's 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 relative's identification number, year of birth and death, gender, ethnicity, the fact that they lived in the UK and details about their histiocytosis or related condition. 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 relative's information to the IRHDR using a secure online website (using REDCap software). If your relative was diagnosed with a rare histiocytosis that is not Langerhans Cell Histiocytosis, then their 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 relative's 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 relative's identification code and none of their personal details. 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 has been set up by the Memorial Sloan Kettering Cancer Center in New York, USA. We will submit your relative's 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). More information is available on request.

How long will my relative's information and samples be stored for?

We will keep your relative's 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 consent for your relative to join. Your relative's information and samples will be stored in secure locations, and you have control over which information and samples are provided.

What are the possible benefits of taking part?

There may be no benefit to you or your family for taking part. If your relative had a rare form of histiocytosis, their diagnosis will be checked by an expert for the IRHDR and you will be informed if new information is found. Your relative's information and samples are considered to be a 'gift' from you to Newcastle University where the UKHR is held. This means that you will not be paid nor receive any financial reward.

Will my relative's taking part in this study be kept confidential?

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

- to double check the information against their medical record if we think that there may have been an error in transferring information
- in case you decide not to carry on with the study, so that we can withdraw their information and samples.

Information collected by the registry may be sent to researchers in countries where the laws are different to the Data Protection Act in the UK. This should not affect your relative's privacy because we are not collecting personal information other than the year of birth, 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 study.

What type of research will be carried out?

Your relative's 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 studies will include a wide range of lab 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. In the consent form that follows we will ask for specific permission about the following research method:

- Sequencing their 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 their DNA from any donated blood and from biopsies. We will determine their genetic makeup and any genes that have gone wrong to cause their histiocytosis. This may involve sequencing part of or even all of their DNA code.

Will I find out if my relative had 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 relative's information and samples?

Your relative's 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. A

special committee consisting of experts of histiocytosis will review these applications to make sure that your relative's information and samples are used only for high quality and relevant research studies.

Will my relative's 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. However, we will not release any personal information to researchers outside the UK. 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 your relative 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 the UKHR, you will have no claim to earnings made from commercial products that are developed.

Who is organising and funding the creation of the registry?

The study is co-ordinated by doctors from Newcastle University and the Freeman Hospital, Newcastle upon Tyne. 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 the UKHR to contribute to these running costs. Your relative's doctor will not be paid for including your relative in this study.

Who has reviewed this study?

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

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

If you don't want to carry on with the study, you can contact us or your relative's medical team. You do not need to give any reason and it will not affect how you are treated. 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 will be addressed. If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions (see contact details below).

If you prefer to raise your concerns with someone independent of the study, 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: Histio 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.