



<Parent/Guardian's Name >
<Parent/Guardian's Address>

Parent/Guardian Information sheet (Version 2)

Research study to determine the genetic causes of Primary Sclerosing Cholangitis and Childhood Autoimmune Liver Disease

Dear parent/guardian,

Your child is being invited to take part in the **UK PSC Study** (www.uk-psc.com). This is a UK-wide project aimed at finding factors (genetic, as well as markers in the blood) involved in causing Primary Sclerosing Cholangitis (PSC) in adults and autoimmune liver disease in children. The UK PSC Study is part of the National Institute for Health Research (NIHR) research programme that provides NHS research infrastructure to support fundamental discoveries and translational research on rare diseases.

The Chief Investigator leading the study is Dr Palak Trivedi, Honorary Consultant Hepatologist at the University of Birmingham. Your child's liver doctor is a member of the broader research team.

Before you decide whether you would like your child to participate, it is important that you understand the reason for the research and what participation in the study will involve.

Please take time to read the following information carefully and spend time discussing the Participant Information Sheet that your child has received for their age group (provided to children aged 6 and over), to ensure that they have understood what is involved in the study and have asked any questions that they have. Your child will receive an Assent Form, if they are aged six or over, and they may sign this to confirm their willingness to participate in the study, if they wish to do so.

Feel free to discuss the study with your family or close friends. Please contact us if you have any questions; we would be happy to hear from you. You can find our contact details at the end of this document.

Your decision for your child to enter the study is entirely voluntary and you may choose not to participate. If you decide not to participate, this will not affect your child's future medical care.

More information, including Frequently Asked Questions, can be found on our website, **www.uk-psc.com**

Why has my child been invited? Why is it important?

In children and young people different types of autoimmune liver disease are seen including Primary Sclerosing Cholangitis, Autoimmune Sclerosing Cholangitis and Autoimmune Hepatitis. Your child has been invited because they are known to have autoimmune liver disease and are currently under the care of a liver doctor.

My child has already joined the study. Why are you contacting us again?

We are contacting you to ask you to update your consent to the study, by signing the new consent form, and for your child to provide further blood samples, for DNA extraction and/or to measure markers in the blood associated with childhood autoimmune liver disease. We would also be grateful if you could update your child's health information.

What is the purpose of the study?

We do not know what causes childhood autoimmune liver disease or PSC in adults. However, there is evidence that genetic factors are important. By studying DNA (genetic material) obtained from affected patients, we hope to achieve a better understanding of how genetic factors contribute to these diseases.

Only half of the genes for rare diseases are currently known. Discovering genes causing rare diseases is the start of a new journey. Accurate tests for rare diseases can be developed to obtain more rapid diagnosis. Once the gene causing a rare disease has been identified, the search for effective treatments can start.

Who is organising and funding this study?

This study is organised by the **UK PSC** national research collaboration (www.uk-psc.com). The investigators include doctors looking after adults with PSC and children with autoimmune liver disease across the UK.

The Chief Investigator is Dr Palak Trivedi. It is jointly sponsored by the University of Cambridge and Cambridge University Hospitals NHS Foundation Trust. It has also been reviewed and approved by the Cambridge South Research Ethics Committee (REC reference 08/H0305/45).

The infrastructure support to maintain recruitment and data analysis is from support to the Investigators by the NIHR Birmingham Biomedical Research Centre, as well as funded research collaborations with Industry.

What happens if my child participates in the study?

If you decide that your child will participate in the study, we will ask you to do the following:

- Initial, date and sign the Parent/Guardian Informed Consent Form (version 2), to show that you agree for your child to take part in the study;
- If your child is aged 16-17 years, they can initial, date and sign the adult Informed Consent Form themselves.
- Your child to sign the Child Assent Form (version 2), if they are aged 6-15 years and are able and willing to do so.
- Complete The UK PSC Paediatric Participant Questionnaire (version 1) about your child's autoimmune liver disease and their health in general. If your child is aged 11 or over, they can fill this in themselves, if they are able to do so.

For your child to donate the following samples:

- **Two blood samples**, which will be taken at their liver clinic appointment. One sample will be used to extract DNA and the other will be used to measure markers in the blood associated with these diseases.
- The blood samples requested are of a total volume of approximately 1 teaspoon, if they are aged 0-10 years, or approximately 2 teaspoons, if they are aged 11-17 years
- For your child's liver care team to return the signed Parent/Guardian or Adult Informed Consent Form, Child Assent Form (for children aged 6-15 years), completed questionnaire, and blood samples to the UK PSC research office using the freepost envelope for the questionnaires and the transport box for the samples, consent and any assent forms.
- The address to send the samples and documents to is:
The UK PSC Study
Box 238
Department of Medical Genetics
Lv 6 Addenbrooke's Treatment Centre
Hills Rd
Cambridge, CB2 0QQ
- You will find the Parent/Guardian Informed Consent Form, Child Assent Form and patient questionnaire in the recruitment pack that the research team has given to you.

What will happen next?

When we have received your signed consent form and the Child Assent Form, if your child is able to sign this, we will do the following:

- We will obtain information about your child's health from their medical records;
- We will extract a sample of your child's DNA from their blood sample (DNA is the material that contains all of your genetic information);
- We will analyse your child's DNA to obtain information about their genetic make-up;
- We will extract serum from their second blood sample, and use it to analyse markers in the blood associated with childhood autoimmune liver disease;
- We will use information about your child's health and genetic make-up in large-scale studies to look for genetic factors that contribute to PSC and childhood autoimmune liver disease.

In addition, if your child has ever had a liver biopsy, we may request a copy of the report from the pathology department from the hospital where this was done. Additionally, if available, we may request that tissue is transferred to a central laboratory for further analysis. However, your child will not be asked to have a liver biopsy for the purpose of this study, and the biopsy will not be re-reported.

What information will be collected about my child?

If your child participates in the study, we will collect his/her name and contact details so that, if we need to, we can contact him/her during the study. We will also collect information about your child's health and major life events. This information will include your child's current and past illnesses; admissions to hospital; investigations such as blood tests, scans or radiological

investigations, and any treatments he/she might have received. We will continue to collect this information into the future, so that we can see how autoimmune liver disease affects your child over time. This will include annual information from your child's liver doctors. In the event of your child's death, we will request information about when and why it happened.

With your permission, we will obtain information about your child's health and major life events from the following sources:

- Your child's medical records held by their hospital;
- Your child's medical records held by their GP surgery;
- Your child's medical records stored in NHS data centres

NHS data centres are organisations that collect and store information about how people use the NHS, such as information about outpatient clinic appointments; visits to A&E, and admissions to hospital. NHS data centres also hold information about the date and cause of death, which they obtain from the Office of National Statistics. The NHS data centres include NHS Digital in England, the Information Services Division (ISD) for NHS National Services Scotland, the NHS Wales Informatics Service, and the Health and Social Care Board Northern Ireland.

To collect health-related information about your child, we will send their name, date of birth and NHS number (or CHI number, if they live in Scotland) to the NHS data centre using a secure system. The NHS data centre will find information linked to your child's name, date of birth and NHS (or CHI) number and send it to the research team, using the same secure system. Any information obtained from your child's hospital will be collected by NHS staff or members of the UK-PSC research team or at their own hospital.

What will happen to my child's DNA sample in the future?

We will isolate, analyse and store your child's DNA and other components from the donated samples for use in studies to help us understand how genetic factors contribute to childhood autoimmune liver disease and PSC in adults. We may measure a range of chemicals in these samples and may determine the genetic code of your child.

Genes are made out of DNA. RNA is the version of the DNA code that the body uses to direct how proteins are made. We may determine the DNA/RNA code of the samples taken. This may include determining the sequence of all or part of the DNA code of your child.

If we use all of your child's DNA sample during the study, we may ask you to provide another sample of blood for extraction of DNA. It is your decision whether to provide additional samples. If you decide not to provide additional samples, your decision will not affect the healthcare your child receives in any way. At the end of the current study, some of your child's DNA sample may be frozen and stored in an approved biorepository for further analysis in future, ethically-approved studies.

With your permission, some of your child's DNA sample may be shared with other investigators who are not part of the current study including profit-making (commercial) companies and not-for-profit organisations (such as research charities), universities or hospitals, in the UK or abroad. However, it will only be shared if this has been approved by a 'Sample Access Committee', on behalf of the UK PSC study. Samples shared with other researchers will be anonymised so that your child could never be identified. Furthermore, other researchers will be made to sign a legally-binding Sample Access Agreement in which they commit to protect the confidentiality of participants and use the sample for research purposes only.

What will happen to information collected about my child?

If your child participates in the study, information collected about him/her will be used to help us understand how genetic factors contribute to childhood autoimmune liver disease. It will be used to improve understanding of rare diseases, in general. This information will be stored in a secure computer database, called the UK PSC database, and your child's identity will be protected. The database will have the same level of protection as confidential information stored by your child's own hospital. Access to the UK-PSC Database is tightly restricted.

Only the following individuals are allowed to see all of the information stored in the database:

- Authorised members of the UK-PSC and registered biorepository research teams;
- Regulatory authorities, such as the Research and Development (R&D) Department at Cambridge University Hospitals NHS Foundation Trust or your local hospital.

Identifiable information (such as your child's name, address and NHS or CHI number) will be destroyed ten years after the study has ended. Non-identifiable information about your child (such as the results of medical investigations) will be retained indefinitely for further analysis in future, ethically-approved studies, undertaken by UK-PSC.

With your permission, information about your child may be shared with other investigators who are not part of the current study, including profit-making (commercial) companies and not-for-profit organisations (such as research charities), universities or hospitals, in the UK or abroad. However, information about him/her will only be shared if this has been approved by a 'Data Access Committee' on behalf of the UK PSC Study. Information shared with other researchers will be anonymised so that your child could never be identified. Furthermore, other researchers will be made to sign a legally-binding Data Access Agreement in which they commit to protect the confidentiality of participants and use the information for research purposes only.

What will happen to my child's genetic information?

Genetic information obtained from your child's DNA sample will be stored indefinitely in the UK-PSC Database, as described above. With your permission, your child's genetic information will also be stored indefinitely in a secure electronic archive called the European Genome-phenome Archive (EGA), maintained by the European Bioinformatics Institute (EBI) in Hinxton, Cambridge, UK.

Genetic information stored in the EGA will be anonymised, so that your child could never be identified. Anonymised genetic information stored in the EGA may be shared with other researchers who are not part of the current study. Other researchers might be from profit-making (commercial) companies and not-for-profit organisations, such as research charities, or universities or hospitals, in the UK or abroad. However, these researchers will be made to sign a legally-binding Data Access Agreement in which they commit to protect the confidentiality of participants and use the information for research purposes only.

Does my child have to take part?

Participation in this study is entirely voluntary. If you decide not to participate, this will not affect your child's future medical care. Even if you agree to participate, you may still withdraw your child from the study in the future, without having to give a reason.

What are the advantages of taking part?

There are no immediate advantages in terms of the care your child currently receives in the clinic and on the ward. However, you will be making a contribution to science and future

improvements in NHS care. The results from this study may help us to achieve a better understanding of the genes that cause PSC in adults and autoimmune liver disease in children. This may result in improved treatment and management of these conditions for all patients in the future.

What are the risks and disadvantages of taking part?

The only disadvantage of taking part in the study is having blood taken. There may be some discomfort from having blood taken and there is a small risk of bruising, inflammation or fainting. To minimise risk, we will aim for blood samples to be taken by experienced staff at the same time as the blood tests requested by your child's doctor in the clinic. Also, if your child wishes, we can apply cream or spray before the blood draw to minimise any pain or discomfort.

Will my child's participation in this study be kept confidential?

Yes, the UK PSC Study conforms to strict data handling and access procedures and uses secure data systems developed to NHS standards. All aspects of this study comply with the Data Protection Act (1998).

As described above, information collected as part of the study will be stored in a secure computer database, called the UK-PSC Database, which has the same level of protection as confidential information stored by your own hospital. Access to the UK-PSC Database will be restricted to authorised members of the UK-PSC and regulatory authorities from Cambridge University Hospitals NHS Foundation Trust or your child's own hospital. Identifiable information (i.e. your child's name, address and NHS or CHI number) will be used only to access your child's medical records or contact you in the course of the study. Identifiable information will be destroyed ten years after the end of the study. Non-identifiable information (such as the results of medical investigations) will be stored indefinitely.

If your child joins the study, he/she will be assigned a unique study number. Your child's DNA sample will be labelled with this number, not their identifiable information. Information shared with other researchers or the EGA will also be labelled with this number, not your child's identifiable information. In this way, samples and information shared with other researchers or the EGA will be anonymised, so that your child could never be identified. During the study and for ten years after the study has ended, samples and shared information will be 'linked-anonymized' because the study number will be linked to identifiable information kept secret in the UK-PSC Database. Dr Palak Trivedi (Chief Investigator), of the University of Birmingham, will act as the main custodian of the data.

Will I be told the results of tests performed on my child's samples?

We will not routinely tell you the results of tests performed on your child's samples. However, if we inadvertently discover that he/she has a genetic abnormality which is known to cause a particular disease, we will inform his/her liver doctor. The liver doctor will meet with you to discuss the finding. Your child will then be referred to a genetics doctor to confirm the finding and plan further management. This policy is based on the Genomics England project. For a list of the particular genetic abnormalities that would prompt us to contact your child's liver doctor, please see the Genomics England website (<http://www.genomicsengland.co.uk/>).

Please be aware that the government has extended the genetic test insurance moratorium until 2019. This means there are restrictions that prevent providers from using genetic test results to deny people insurance cover until that set date. **Even so, if you do not want us to inform your child and their doctor of any genetic abnormality that we may find, please leave Box 12 on the consent form empty.**

What will happen to the study results?

The results of the study will be published in scientific journals and presented at medical meetings both locally and nationally. Your child will not be identified in any reports or publications.

Results that have been published in the scientific literature will also be reported on the UK-PSC website (<http://www.uk-psc.com/>). Furthermore, important results will be reported in the newsletters or on the websites of UK-based patient support groups, such as PSC Support and the PSC Trust and these can also be made available to you at your request.

Will I receive any money for my child taking part?

You will not receive any funding for your child taking part in this study and no travelling expenses will be reimbursed, as the study visit(s) will be timed to coincide with a routine visit to the hospital.

What happens if a scientific discovery is made using my child's donated samples?

If your child participates in the study, any sample he/she donates to the study will be given as an absolute and non-returnable gift, meaning it is given without conditions and without receiving payment. For example, if research using the donated samples leads to new and better tests or treatments for PSC in adults or autoimmune liver disease in children, your child will not receive any form of compensation or payment. The study team will work with others in the public and private sector (e.g. the pharmaceutical industry) to successfully develop scientific discoveries for the benefit of all patients.

Participation in future studies

In the future, there will be other studies carried out by researchers who are not part of the current study. By looking at information stored in the research database, we may identify your child as suitable to participate in one of these other studies. If so, we may contact you to ask whether they would like to take part. You would be provided with full information about this other study, with age-appropriate information for your child, and it would be your decision whether to participate in it. Your child would also have the opportunity to sign an Assent Form, if they wished to and were able to do so.

If you decided not to participate in this other study, your decision would not affect your child's ongoing medical care. **If you do not want to hear about other studies taking place in the UK, please leave Box 16 on the consent form empty.**

What happens if I decide to withdraw my child from the study?

You are free to withdraw your child from the UK PSC Study at any time without giving a reason. If you choose to withdraw your child from the study, you will not be contacted by the study again. Please note this will not affect the care your child receives from the NHS in any way.

You can withdraw your child from the study at one of two levels:

- **Withdrawal and data deletion** - this means that we will delete all of the data we hold about your child, apart from their name, address, date of birth and NHS/CHI number. Your child's samples will also be destroyed. This approach prevents your child's information from contributing to future research. However it would not be possible to

remove your child's data from research that had already taken place. We will make no further contact with your child relating to UK PSC.

- **No further participation, but retain data** – this means that you consent for UK PSC to retain and use any data and samples already collected for your child. This will enable us to study PSC and childhood autoimmune liver disease with the maximum number of study participants. We will make no further contact with your child relating to UK PSC.

If you wish to withdraw your child from the study, please contact the study team (Tel: 0121 371 8101; email ukpsc@uhb.nhs.uk).

What if something goes wrong?

We think it is unlikely that your child will be harmed in this study. However, if they are harmed by taking part in this study, owing to someone's negligence and provided the study protocol has been followed, then you may have grounds for legal action under the NHS Indemnity Scheme. If they suffer harm which is not the result of someone's negligence, there are no special compensation arrangements. Regardless of this, if you wish to complain, or have any concerns about the way you have been approached or treated during the course of this study, you should contact the study organizers. You can also contact the Patient Advice and Liaison Service (PALS) at the hospital your child attends for their PSC.

Further information

If you would like further information, please visit the study website www.uk-psc.com. If you have any questions you can also contact the study Project Manager, <insert name> , (0121 371 8101 or email: ukpsc@uhb.nhs.uk).

Thank you for taking the time to read about the study. We realise that participation is voluntary and are very grateful to those who consider entering the study.

Yours faithfully,



Dr Palak Trivedi
Chief Investigator