



TURTLE



<Trust/Site address 1>

<Trust/Site address 2>

<Trust/Site address 3>

<postcode>

Tel: <telephone number>

Adult Information Sheet for TURTLE

- You have been given this information sheet as you might be eligible to take part in this research study.
- Please take time to read the following information carefully and ask a member of the clinical team if there is anything that is not clear, or if you would like more information.
- **Part 1** tells you about the study and what will happen if you agree to take part. **Part 2** gives you more detailed information about the conduct of the study.
- If you wish you can discuss it with friends, relatives and/or get independent advice via your local Advice and Liaison Service (PALS) or equivalent.
- Taking part is **voluntary**. You do not need to take part and you do not need to give a reason.

How to contact the study team:

If you have any questions about this study please talk to your research team:

> <Add contact details for PI/RN, i.e. name and telephone number>

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PART 1: Purpose of the study and what will happen if you take part

Why are we doing the TURTLE study?

We want to find out if a new treatment called secukinumab can help reduce inflammation in the eyes of children with Juvenile Idiopathic Arthritis (JIA) and uveitis or chronic anterior uveitis.

JIA is the most common rheumatic disease in children. Around 1 in 1000 children in the UK develops JIA per year. Amongst these children around a quarter are at risk of inflammation of the uvea in the eye (known as uveitis). Chronic anterior uveitis is similar to JIA uveitis and is treated in the same way. The majority of children with JIA uveitis are treated with a medication called methotrexate but nearly half of children need extra medication to control their uveitis.

Adalimumab is the only licensed drug for treatment of JIA uveitis. The problem is that this drug does not reduce the inflammation in the eye for all children. We need to find other treatments that could help. In this study we will determine whether secukinumab can help children and young people with JIA uveitis and chronic anterior uveitis by comparing it against current standard treatment of adalimumab.

We will recruit 40 children and young people, aged 2-18 years, who have active uveitis that has not responded to treatment with adalimumab. Recruitment will take place across 12 hospitals in the UK.

The researchers doing this study have a lot of experience running previous studies looking at treatments for JIA uveitis. The results from this study will be used to help us improve treatments for children with JIA and Uveitis.

Why have I been chosen?

You have been chosen to participate because you have active JIA uveitis or chronic anterior uveitis.

Do I have to take part?

No, taking part is voluntary. It is up to you to decide whether to take part.

If you decide not to take part in the study then you will still receive the usual treatment your hospital offers. Your doctor can provide you with more information on this.

If you decide to take part you can also change your mind at any time without giving a reason.

What will happen to me if I take part?

If you agree to take part, you will receive secukinumab or adalimumab for 24 weeks. After 24 weeks, if there are improvements in your uveitis, then you will be able to continue with secukinumab or adalimumab for another 72 weeks after which your doctor will discuss ongoing treatment options with you. If your uveitis is not improving at 24 weeks then your doctor will discuss alternative options with you at that time.

Before you take part and receive secukinumab or adalimumab, you will be asked to sign a consent form. You will be given a copy of the consent form and the information sheet to keep.

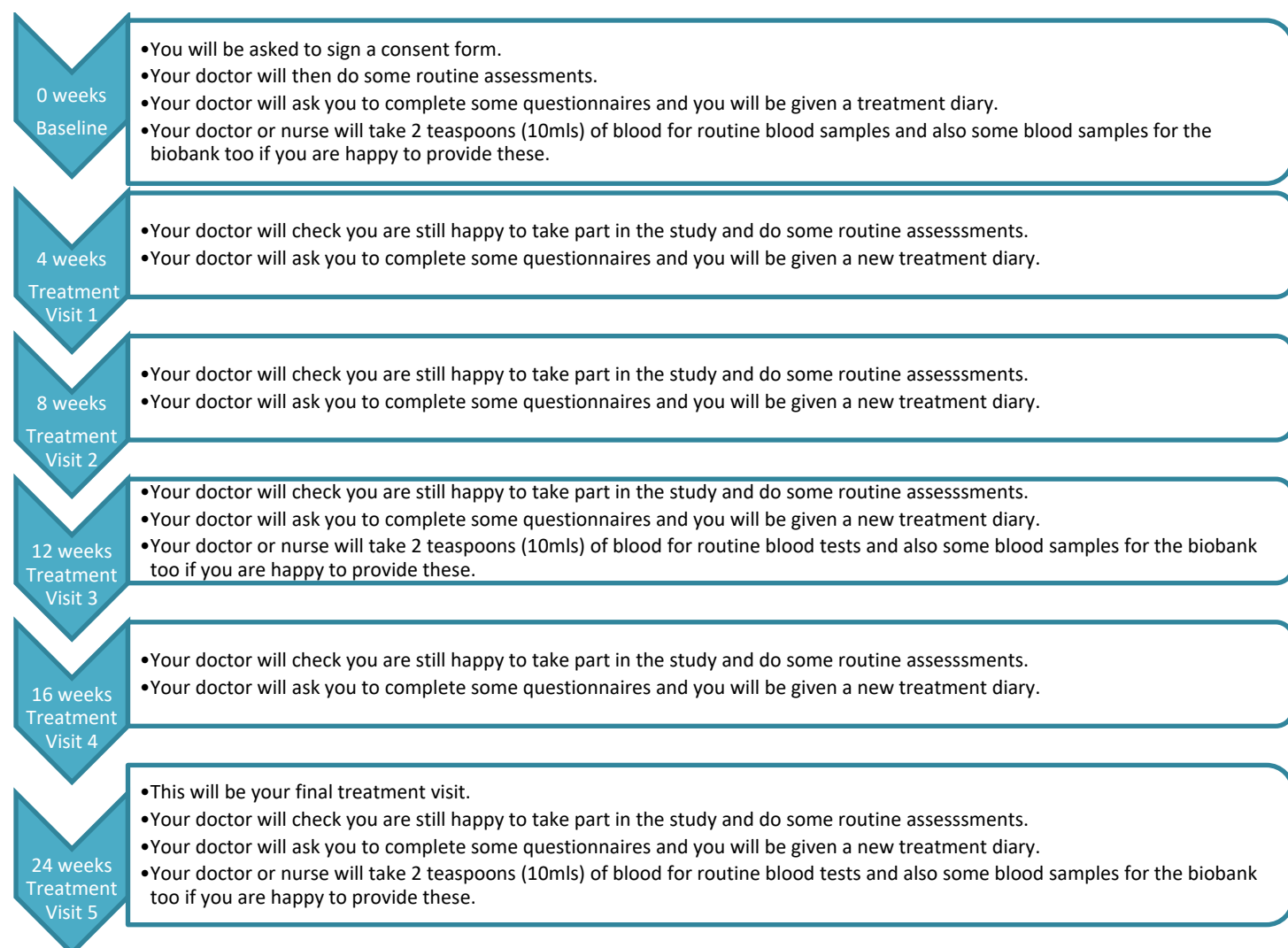
Once you have signed the consent form, we will check and confirm that this study is suitable for you and you will be asked to follow the study plan (see study timeline).

You will have to:

- Be involved in the study for up to 96 weeks
- Visit clinic at weeks 4, 8, 12, 16 and 24 during the 24-week treatment period. Clinic visits will last approximately 2 hours.
- If you are getting better with secukinumab or adalimumab after 24 weeks then we will ask you to visit clinic every 3 months for 72 weeks.
- If you are not getting better after 24 weeks then you will stop secukinumab or adalimumab treatment and we will ask you to visit the clinic 36 weeks after stopping your treatment. Your doctor will discuss ongoing treatment options with you.

- If you have a uveitis flare up an unscheduled visit may also be required.
- At each clinic visit you will:
 - Receive an ophthalmology and rheumatology review and be asked to complete some questionnaires.
 - Complete routine assessments at each clinic visit including pregnancy test (if applicable), urinalysis, physical examination, vital signs, height and weight and routine blood samples. We will take around 2 teaspoons (10mls) of blood for the routine blood samples.
- All participants will continue to take methotrexate or mycophenolate. Other biologic treatments will be stopped prior to entering the study.
- Optional exploratory work - Provide samples for biobank at the following visits: baseline, week 12 and week 24.
- Complete a treatment diary whilst taking part in the study

TREATMENT VISITS



FOLLOW UP VISITS

36 weeks
Follow Up Visit
1

- If your uveitis is better with the study treatment then you will be asked to attend a follow-up visit at 36 weeks.
- Your doctor will check you are still happy to take part in the study and do some routine assessments.
- Your doctor will ask you to complete some questionnaires and you will be given a treatment diary.

48 weeks
Follow-up
Visit 2

- If your uveitis is better with the study treatment then you will be asked to attend a follow-up visit at 48 weeks.
- Your doctor will check you are still happy to take part in the study and do some routine assessments.
- Your doctor will ask you to complete some questionnaires and you will be given a treatment diary.

60 weeks
Follow-up Visit
3

- All participants will be asked to attend a follow-up visit at 60 weeks. If you did not respond to the study treatment then this will be your final study visit.
- Your doctor will check you are still happy to take part in the study and do some routine assessments.
- Your doctor will ask you to complete some questionnaires and you will be given a new treatment diary.

72 weeks
Follow-up Visit
4

- If your uveitis is better with the study treatment then you will be asked to attend a follow-up visit at 72 weeks.
- Your doctor will check you are still happy to take part in the study and do some routine assessments.
- Your doctor will ask you to complete some questionnaires and you will be given a new treatment diary.

96 weeks
Follow-up Visit
5

- If your uveitis is better with the study treatment then they will be asked to attend a follow-up visit at 96 weeks.
- Your doctor will check you are still happy to take part in the study and do some routine assessments.
- Your doctor will ask you to complete some questionnaires.

What is the drug being tested?

You will be randomised to be treated with secukinumab or adalimumab. Secukinumab will be given as a weekly injection for the first 4 weeks then 4 weekly thereafter (75mg, 150mg or 300mg based on body weight).

Secukinumab is a type of drug known as a biological therapy. In some conditions the protein IL-17A can cause inflammation to your body and joints. Secukinumab works by blocking the effects of this protein, to reduce inflammation.

Adalimumab will be given as injections every 2 weeks (dose of 20mg/0.8ml or 40mg/0.8ml based on body weight).

Adalimumab is a type of drug known as an anti-TNF (anti-tumour necrosis factor). In children and young people with inflammatory diseases a protein called TNF is overproduced in the body, causing inflammation and damage. Anti-TNF drugs block its action and so can reduce this inflammation.

You will continue to receive either Methotrexate or Mycophenolate Mofetil depending on what you are currently taking.

How will I know which treatment I am going to have?

In research studies we often split participants up into groups to look at how different treatments work. In the TURTLE study participants will be split into two treatment groups at random:

- One group will receive adalimumab together with either methotrexate or mycophenolate mofetil
- The other group will receive secukinumab together with either methotrexate or mycophenolate mofetil

It is really important that each group in the TURTLE study has a similar mix of participants in it so we know that if one group of participants does better than the other it is very likely to be because of the treatment and not because there are differences in the types of participants in each group.

We use a computer programme that will place you into one of the groups 'at random' – you might hear this described as 'randomisation' or 'random allocation', but they all mean the same thing.

In the TURTLE study you are equally as likely to be in the group receiving adalimumab as you are in the group receiving secukinumab.

The healthcare team will let you know which group you are in as soon as possible.

What are the alternatives for treatment?

Secukinumab and adalimumab are two of several treatments that may be used to try and control your symptoms of JIA- associated uveitis. Your doctor will discuss alternative treatment options with you.

If you decide that you do not want to take part in the study or if you are not eligible to take part, the treatment that you receive will depend upon the policy of your treating hospital.

What are the benefits and risks of taking part?

Like all medicines, secukinumab can cause side effects, although not everybody gets them.

Most side effects with secukinumab are mild to moderate. Very common (1 in 10 people) and common (1 in 100 people) side effects are:

- Upper respiratory tract infections with symptoms such as sore throat and stuffy nose (nasopharyngitis, rhinitis)
- Cold sores (oral herpes)
- Diarrhoea
- Runny nose (rhinorrhoea)
- Athlete's foot (tinea pedis)
- Headache
- Nausea
- Fatigue

You may also experience serious allergic reactions whilst taking secukinumab, the reactions listed below are rare:

- Difficulty breathing or swallowing
- Low blood pressure, which can cause dizziness or light-headedness
- Swelling of the face, lips, tongue or throat
- Severe itching of the skin, with a red rash or raised bumps

Secukinumab has been shown to be effective in arthritis but the effect in JIA uveitis and chronic anterior uveitis is not known.

Adalimumab has effects on the immune system (the body's own defence system) and therefore may make you more likely to develop infections. Whilst on the study you should therefore tell their doctor straight away if you develop any of the following:

- A sore throat
- A fever
- They develop chickenpox.
- Any other symptoms of infection
- If you have not had chickenpox and you come into contact with someone who has chicken pox or shingles

Chickenpox and shingles can be very severe in people who are on treatments such as adalimumab and therefore you may need antiviral treatment immediately.

Very rarely, people taking adalimumab may develop a condition called 'drug- induced lupus', which is usually mild. If this is the case then you would discontinue from the study and the condition would usually disappear once the treatment has been stopped.

It is possible that there may be a slightly increased risk of certain types of cancer in patients using anti-TNF drugs. Such a link has not been proven but is the subject of current research. Please discuss this with your research doctor if you are concerned.

Some children have allergic reactions to drugs. Most allergic reactions to drugs occur within two hours after the drug is given.

Adalimumab may cause a reaction at the injection site. You may experience redness, swelling or pain etc. These reactions are usually not serious.

All people taking part in the study will need to have a recent test for tuberculosis (TB) as part of screening. Anyone who tests positive for TB will need to have a chest X-ray. This X-ray should be considered extra to any that you would have if you did not take part. X-rays use ionising radiation to form images of your body and provide your doctor with other clinical information. Ionising radiation may cause cancer many years or decades after the exposure.

We are all at risk of developing cancer during our lifetime. 50% of the population is likely to develop one

of the many forms of cancer at some stage during our lifetime. Taking part in this study will add only a very small chance of this happening to you. The risk in this study is believed to be very small and estimated as 2 in a million or 0.0002%.

We will take a scan of your eye using an Optical coherence tomography (OCT) scan. This scan uses light waves to get a detailed image of your eye. The OCT scan is quick and safe and is not invasive.

Your participation in this study may help other young adults and children in the future by providing important information about secukinumab and about JIA-associated uveitis and chronic anterior uveitis. It may help to provide a better understanding of the disease and better treatment in the future. The information that comes from the study may improve the scientific and medical knowledge surrounding the basis of these medical conditions.

Reasonable travel expenses can be reimbursed for any visits to the Hospital for this study that are not already part of standard care.

What will happen to me if I also provide samples for the optional exploratory work?

We would like to invite you to donate blood samples to the Biobank at the University of Bristol. These blood samples are optional and will be collected at baseline, week 12 and week 24. If you decide not to donate samples you can still take part in the study.

These blood samples will be used to see whether there may be a link between genes and the way that they respond to treatment with adalimumab or secukinumab and for other related research. Through this work, scientists hope to learn more about JIA- uveitis and chronic anterior uveitis and develop more effective treatments in the future.

The blood samples will be taken at the same time as any other routine clinical bloods are taken. The amount of extra blood taken will depend on your weight, for people that weigh less than 25kg we will take around 1 teaspoon of blood (5mls), for people that weigh more than 25kg we will take around 4 teaspoons of blood (20mls).

Your samples will be considered as a gift to the University of Bristol and will be kept for a minimum of ten years.

What happens if I change my mind?

If at any point you decide to stop taking part in the study, you will still receive treatment and the follow up usually offered by your hospital.

Information on how we will handle your information and samples in the event of you withdrawing is detailed in Part 2 of this Information Sheet.

What if new information becomes available?

Sometimes during the course of a research study, important new information becomes available about the treatment/drug that is being studied. If this happens, the doctor will tell you about it and discuss with you whether you want to continue in the study. If you decide to withdraw your doctor will plan for your care to continue. If you decide you should continue in the study you will be asked to sign an updated consent form.

On receiving new information, the doctor might consider it to be in your best interests to withdraw from the study. He/she will explain the reasons and arrange for your care to continue.

If the study is stopped for any other reason you will be told why and your continuing care will be arranged.

What happens when the study stops?

It is intended that the results of the study will be presented at conferences and published in medical journals so that we can explain to the medical community what our research results have shown. They may also be used to apply to the regulatory authorities to make the drug widely available and/or for related research. Confidentiality will be ensured at all times and you will not be identified in any publication. Summary results from this study will be presented on the study website and can also be provided to you by post if you would like.

Any information derived directly or indirectly from this research, as well as any patents, diagnostic tests, drugs, or biological products developed directly or indirectly as a result of this research may be used for commercial

purposes. You do not have any right to this property or to any share of the profits that may be earned directly or indirectly as a result of this research. However, in signing this form and donating blood samples for this research, you not give up any rights that you would otherwise have as a participant in research.

What if there is a problem?

Detailed information is given in Part 2 of this information sheet about what to do if you have a complaint about how you have been dealt with during the study and what redress is available to you in the event that you are harmed by taking part in the study.

Will taking part in the study be kept confidential?

Yes. All the confidential information about your participation in this study will be kept confidential. Detailed information on this is given in Part 2.

PART 2: Detailed Information about the conduct of the study

Who is running the study?

University Hospitals Bristol and Weston NHS Foundation Trust (UHBW) is the Sponsor of this study and is responsible for managing it. It is based in the United Kingdom. UHBW has asked the Liverpool Clinical Trials Centre (LCTC, part of the University of Liverpool) to carry out the day to day running of the study. Optional blood samples collected during the study together with some data will be sent by Hospitals to the Bristol Biobank.

The study has been reviewed by the Health Research Authority (HRA), National Research Ethics Service Committee (REC) and Medicines and Healthcare products Research Agency (MHRA) to make sure that the study is scientifically and ethically acceptable.

This study is funded by Novartis. Your doctor will not receive any personal payments for recruiting participants into this study. The hospital may receive additional funding to help with any extra costs that supporting this study might incur.

How will my information be collected and handled?

The collection and handling of their personal data will be managed in accordance with GDPR and the Data Protection Act. University Hospitals Bristol and Weston NHS Foundation Trust (UHBW) and Liverpool Clinical Trials Centre (LCTC) are the Data Controllers for this study and will need to use information from your medical records for this research project.

Your hospital will collect information from your medical records and transfer this securely to LCTC. This information will include your name, your initials, date of birth and contact details. People will only use this information to do the research or to ensure that the research is being done properly and the accuracy of the data collected. Data collected by your hospital may be shared with individuals from UHBW, the LCTC, the Bristol Biobank and regulatory organisations and include a review of your medical and research records, and the consent form you signed.

People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead.

Data will be sent from your hospital to the LCTC.

Safety and pregnancy information will be provided confidentially and securely to the company who supply secukinumab (Novartis).

We will notify your GP and local clinician that you will be taking part in the study for their information.

We will keep all information about you safe and secure.

Once we have finished the study, we will keep the data for 25 years so that the results, if needed, can be inspected or audited. We will write our reports in a way that no-one can work out that you took part in the study.

What are my choices about how my information is used?

You can choose to stop being part of the study at any time, without giving a reason, but we will keep information about you that we have already collected.

If you choose to stop taking part in the study, we would like to continue collecting information about your health from your hospital. If you do not want this to happen, tell us and we will stop.

In some cases, however we may need to continue to collect limited information about any side-effects of the study treatment you experienced or pregnancies. We will only do this where we are required to do so by law.

If you choose to withdraw from the study, we won't collect any more samples from you, but we will continue to store the samples we have already collected and these will be made available to future researchers. If you do not want us to do this, please let us know and we will and destroy samples where possible. It may however not be possible to stop this where the samples have already been provided to researchers.

We need to manage your records, and the consent form you sign in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.

Information sharing for other research

When you agree to take part in a research study, the information about your health and care may be beneficial to researchers running other research studies in this organisation and in other organisations.

These organisations may be universities, NHS organisations or companies involved in health and care research in the UK or abroad. Your information will only be used by organisations and researchers to conduct research which is in accordance with the UK Policy Framework for Health and Social Care Research in the UK, or equivalent standards elsewhere.

If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study. To maximise benefits of future research it may be important to link the data and samples collected within this study with other data sources. This may require sharing your personal identifiers with Universities, Hospitals, pharmaceutical companies and other organisations to enable data to be linked together. This will only happen when participants have donated blood samples for future research and is essential for the purposes of the research and confidential and secure transfer methods will be used.

Where can I find out more about how my information is used?

You can find out more about how we use your information:

- at the study website www.turtle-trial.org.uk
- at www.hra.nhs.uk/information-about-patients
- by asking one of the research team
- by sending an email to turtle.trial@liverpool.ac.uk
- in the Health Research Authority leaflet available from www.hra.nhs.uk/childdataandresearch

- by contacting the University of Liverpool Data Protection Officer at LegalServices@liverpool.ac.uk
- In the LCTC's "Privacy Notice" available from: <https://www.lctc.org.uk/privacy>
- by contacting UHBW's Data Protection Officer at InformationGovernance@uhbw.nhs.uk

If you are not happy with the way your information is being handled, or with the response received from us, you have the right to lodge a complaint with the Information Commissioner's Office at Wycliffe House, Water Lane, Wilmslow, SK9 5AF (www.ico.org.uk).

What will happen to the blood samples I give as part of the optional exploratory work?

We are required by law to ensure that any samples are sent with a copy of the consent form you complete. This ensures that the samples are collected and processed with your permission. The samples themselves will not be labelled with any personal identifiers but will be linked to the consent form by a unique number. The consent form will contain personal identifiers (your name, your date of birth and your contact details (if provided)). A copy of the consent form and the blood samples will be sent to the Bristol Biobank who will also be provided with some of the data (demographic, clinical and laboratory) we collect about you in this study.

These samples will not be analysed as part of this study but will be used for future research, including genetic studies. The samples and associated clinical data may be shared with researchers in the UK and abroad. We will not be able to share with you the results from these samples including any results related to genetics.

The samples, consent forms and clinical data will be kept in a secure place in the Biobank until we need them for future research.

What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak with one of the local research team who will do their best to answer your questions.

If you remain unhappy and wish to complain formally, you can do this by contacting your local NHS Advice and Liaison Service (PALS) or equivalent. Members of the local hospital team should be able to provide this information to you.

Every care will be taken in the course of this clinical study. However, in the unlikely event that you are harmed by taking part in this research project, compensation may be available to you under the NHS Indemnity scheme. The hospital where you receive treatment has a duty of care to you whether or not you agree to participate in the study and the study Sponsor

accepts no liability for negligence on the part of the hospital's employees. However, if you are harmed and this is due to someone's negligence at the hospital, then you may have grounds for a legal action for compensation against the NHS Trust where you are being treated but you may have to pay for your legal costs. The normal National Health Service complaints procedures should be available to you.

Thank you for taking the time to read and consider this information sheet. Should you decide you can take part in the study, you will be given a copy of the information sheet and a signed consent/ form to keep.

<Trust/Site address 1>
 <Trust/Site address 2>
 <Trust/Site address 3>
 <postcode>

Tel: <telephone number>

FOR SITE USE ONLY:

Site Name:												
Participant Study Number												
Participant Initials:				Participant DOB:								

Adult Consent Form

To be completed by the Participant

Once you have read and understood each statement please enter your initials in each box. Initial

1. I have read and understood the information sheet for this study. I have had the opportunity to ask questions and have had these answered satisfactorily.
2. I understand that participation is voluntary and that I am free to withdraw from the study at any time, without giving a reason, and without my care or legal rights being affected. However, I understand that the study team may need to continue to collect some limited information for safety reasons.
3. I agree to participate in the above study.
4. I give permission for a copy of this fully completed consent form to be sent to the LCTC (where it will be kept in a secure location) to allow confirmation that my consent was given.
5. I understand that relevant sections of my medical notes and any data collected during the study may be looked at by authorised individuals from the central study team (LCTC) and representatives of the Sponsor, regulatory authorities and the local NHS Trust. I give permission for these individuals to have access to my records and data.
6. I agree to my GP and local clinician being informed of my participation in the study.
7. I understand that a copy of this consent form which includes my name, and my data will be held by the LCTC and at my hospital
8. I understand that my child's personal data will be archived in a confidential manner for 25 years from the end of the study.
9. I agree to allow information and data or results arising from this study to be used in future healthcare and/or medical research in the UK and abroad, providing my confidentiality is maintained.

The statements below are optional (you can still take part in the study even if you do not wish to agree to these):

10. I consent for my blood samples to be collected for future research to be transferred along with a copy of this Consent Form and data relevant to my samples to the Bristol biobank. I understand that my samples and data may be shared with researchers in the UK and abroad.
11. I agree to allow my personal identifiers to be used to link my blood samples and associated clinical data with data from other sources, for future research.
12. I agree that I may be contacted in the future in relation to this or other related studies.

(if you agree to this statement provide your details below):

13. Telephone number:																				
Email address:																				

<Trust/Site address 1>

<Trust/Site address 2>

<Trust/Site address 3>

<postcode>

Tel: <telephone number>

FOR SITE USE ONLY:

Site Name:

Participant Study Number

Participant Initials:

Participant DOB:

/

/

To be completed by the Participant:

Your full name
(please print):

Your signature:

Date:

To be completed by the Researcher (after participant has completed the form):

Researcher full name (please print):

Researcher signature:

Please file the original wet-ink copy in the TURTLE Investigator Site File, and make three copies: one for the participant, one for the medical notes and one to be sent to the LCTC.