MAIN PATIENT INFORMATION SHEET & CONSENT FORM (Part 1)

Investigator: Professor Paul Emery

Study Title: CCP – Next Generation: Co-ordinated Programme to Prevent Arthritis - Can We Identify Arthritis at a Pre-Clinical stage?

Protocol Number: RR17/93003

Study Sponsor: University of Leeds

Initials: _____ Subject No.: _____ Date of Birth: _____

You are being invited to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends, relatives and your GP 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.

You can find independent information on participating in clinical trials on the following web site: http://www.nhs.uk/Conditions/Clinical-trials/Pages/Introduction.aspx. If you do not have access to the internet, or prefer a hard copy of the information, please ask the research doctor or nurse, who will be happy to provide you with one.

1. What is the purpose of the study?

Rheumatoid arthritis (RA) is a common condition affecting 1-2% of the adult population in this country. We would like to find out more about the very early stages of RA. We know that early treatment of RA gives better results than if treatment is delayed. Unfortunately, it can be very difficult to catch patients in the early stage of the disease as often symptoms can be mild and can be atypical, such as initially just single joint involvement. We are interested to find out if patients may have non-specific muscular symptoms (e.g., shoulder tendonitis, carpal tunnel syndrome) in the months or years before developing RA (i.e. the “pre-clinical stage”).

A test is now available to help find out which patients are at higher risk of developing RA. This test is a blood test called “anti-CCP antibody”. The anti-CCP antibody (anti-CCP Ab) is a protein in the blood. Previous studies have shown that a large percentage of patients who are positive for anti-CCP Ab will go onto develop RA in the future i.e. Anti-CCP Ab may be a marker for RA. We would also like to invite family members of patients with RA to have the antibody test performed.

It is important to realise that

- This protein can be present in your blood for up to 10 years before development of symptoms (although it is seen more frequently in the two years prior to onset of symptoms)
- RA can still occur in patients who are negative for this marker

In simple terms, if you are positive for the anti-CCP test, you may have an increased risk of developing RA in the future (but it is not definite that you will develop RA).

We have designed a study to allow patients with newly-occurring musculoskeletal symptoms to have an anti-CCP Ab blood test performed. Patients with positive results will be invited to be followed up in specialist Rheumatology clinics where we can run further tests for RA diagnosis. We would like to offer you the chance for close monitoring and treatment at the earliest opportunity so that we can offer you the best care.

2. Why have I been chosen?

You have been invited to participate in this study because you have a new musculoskeletal complaint identified by your GP or by another health professional, or, you have a family member who has been diagnosed with RA.

3. Do I have to take part?

It is up to you to decide whether or not to take part in the study. If you decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw from the study at any time and without giving a reason. This will not affect the standard of care you receive.

4. What will happen to me if I take part?

Before the study:

You will be give you a pack which contains the study information sheets, a research blood form, and two questionnaires. If you would have any questions about the study please phone one of the research doctors at Chapel Allerton Hospital (listed on the bottom of this form). Alternatively you may be able to discuss the study with your GP or a member of staff at your GP practice involved in this research study.

Start of the Study

Part 1

If you would like to participate, please sign the consent form for PART 1 and complete the questionnaires. Only then should you arrange to get the blood test done using the research form provided. Your GP will scan the consent form and questionnaires and send it to Chapel Allerton Hospital electronically. Your research form and blood sample should be posted back to Chapel Allerton Hospital. BY HAVING THE BLOOD TEST DONE YOU ARE CONSENTING TO TAKE PART IN PART 1 OF THE TRIAL.

Your blood test may be done at your GP practice or your GP will refer you to your local blood-taking centre to have a blood test performed. Once the blood test is done, it may take several weeks for you to receive the results in the post.

- If the result is positive, you will also be contacted by a member of the research team and invited to participate in the second part (Part 2) of the study at Chapel Allerton Hospital, Leeds.
- If the result is negative then you will not be seen at Chapel Allerton Hospital, however you will receive a follow-up questionnaire at 12 months, we may approach your GP to check how you are progressing following on from the 12 month questionnaire.
- You may also be invited to take part in other aspects of the study as a control subject.

Part 2

If your test result is positive, you will be invited to participate in the second part of the study. This involves outpatient assessments at Chapel Allerton Hospital and an appointment will be made for you. The second part of the study will be discussed with you and you will have the opportunity to ask any questions. You will be provided with an information (in person or via post) to give you time to think about whether you want to participate and, if you wish, to discuss it with your friends and family. You can take as much time as you want to think about it. If you agree to participate, you will be asked to sign a consent form for this. You will be given a signed copy of the consent form and this leaflet to read and keep at home.

If you feel that you may only able to come to the clinic for a single visit, we would invite you to do so and discuss the option of follow up via telephone to see how you are managing with your symptoms. We can reimburse you at the University of Leeds standard rate, or a standard railway ticket bought in advance as early as possible, after confirming your

appointment. Travel and hotel arrangements (where needed) will be arranged before attendance.

However if you feel this is too far to travel, you can continue under the care of your GP who will have a copy of your anti-CCP antibody test result, and we will advise your GP to refer you to your local rheumatologist if necessary. We will also ask that you complete a follow-up questionnaire after 12 months.

If you come to the clinic at Chapel Allerton Hospital, the research doctor will carry out a 'baseline visit', which includes the following:

- Questions about your medical history and medications you have been taking.
- , height and weight.
- Blood samples for laboratory tests. Up to 90 ml of blood (up to 6 tablespoons) will be taken for all required tests. We will also store some blood at each visit which will allow us to test for other new antibody tests that become available in the future.
- X-rays of your hands/feet and other involved joints (if clinically indicated) at baseline, 48 weeks and annually thereafter as clinically indicated.
- X ray of your chest at baseline. Although this is not always performed in routine clinical practice in those with joint symptoms, it is a commonly used and safe test to assess the lungs; it may be useful to assess the lungs as part of this study as there is a link between anti-CCP antibodies and lung inflammation.
- Assessments will be completed regarding your current symptoms, general well-being and ability to carry out everyday tasks.
- Ultrasound (US) of your hands, feet and other joints as clinically indicated. Ultrasound is done frequently on patients in our CCP – Next Generation clinic and is standard practice in our clinic.
- Magnetic Resonance Imaging (MRI) of your joints and muscles may be performed in a subgroup of patients at baseline and again at 48 weeks.

You will be asked to return for outpatient visits 4 more times (at 12 weeks, 24 weeks, 36 weeks, 48 weeks). The clinical assessments will be the same as that in the first visit. If you have developed new symptoms then you would be managed according to routine practice at the CCP – Next Generation Clinic.

You will be invited to continue to attend the clinic if you do not develop inflammatory arthritis within the initial 48-week period. Patients who are unable to make it to their face-to-face visits for their 12 week, 36 week and annual visits may be offered a telephone visit instead if clinically indicated.

For each clinic visit, you will be asked to fill in a study questionnaire form. Your initials are also collected as part of the code for the study.

5. What do I have to do?

There should be no reason to change your current way of life if you participate in this study. You are also able to take part in other clinical trials.

6. What will happen to my samples?

After filling in the consent form for the study, you will be asked to provide some blood samples for the study. These samples will be posted to Chapel Allerton Hospital by the site of your recruitment, i.e. by your GP or hospital. Consent forms and questionnaires are also returned to Chapel Allerton Hospital. Once the completed, signed consent forms are received in Chapel Allerton Hospital and checked, your blood samples will be anonymised using the trial number and sent for processing. Only the trial number and codes generated by the lab technicians will be used to distinguish between samples. None of your personal identifiable information will be used during sample processing.

We will remove your personal details from all research samples after separation into their constituent parts. However, it will be possible to link the clinical and laboratory databases through a unique laboratory code to enable use to study long-term disease outcomes and response to future therapies you may receive.

If you decided not to consent to the biological sub-study (please see biological sub study information sheet), your blood samples will be destroyed after your anti-CCP antibody test is done.

7. What if I do not wish to take part?

All studies are always completely voluntary. If you do not wish to take part this will not affect the treatment you receive. You may also withdraw from the study at any point after taking part if you wish to do so. If you withdraw, unless you object, we will still keep the data we have already collected from you, as this is valuable to the study. A decision not to take part or to withdraw at a later stage will not affect your legal rights or any standard treatment you receive.

8. What are the possible disadvantages and risks of taking part?

Collection of blood may cause symptoms such as local pain, bleeding, bruising, fainting, and rarely infection.

9. What are the possible benefits of taking part?

There is good evidence that treating patients with RA is much better if it is done as early as possible. As we are seeing you regularly in clinic then we will be able to commence treatment at an early stage if this is needed.

It cannot be guaranteed that you will gain personal benefit from this study: however, beneficial information may be acquired for patients who develop RA and may help us to treat these future patients better.

10. What if new information becomes available?

Sometimes during the course of a research project, new information becomes available. If this happens, the research doctor will tell you about it and discuss with you whether you want to continue in the study. If you decide to continue in the study, you will be asked to sign an updated consent form after reading a new information sheet.

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

11. What happens when the research study stops?

Once the study is over, your research doctor will decide whether you need to be continued to be monitored in the Rheumatology Unit or whether you can be followed by your GP.

12. Other information

All your written and computer records will be kept strictly confidential at all times. Data Protection Act regulations have been complied with to ensure confidentiality. Data could be stored either at the University of Leeds or at the NHS.

13. What will happen to the results of the research study?

The results from the study will be compiled on a database. Once every patient involved in the study has completed the study, the results will be analysed by Statisticians.

14. Who has reviewed the study?

The Leeds (East) Research Ethics Committee has reviewed this study.

15. What will happen to my data?

The University of Leeds is the sponsor for this study based in the United Kingdom. We will be using information from you and/or your medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. The University of Leeds will keep identifiable information about you for 15 years after the study has finished.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained.

Your information could be used for research in any aspect of health or care, and could be combined with information about you from other sources held by researchers, the NHS or government.

You can find out more about how we use your information [at URL and/or by contacting https://dataprotection.leeds.ac.uk/wp-content/uploads/sites/48/2019/02/Research-Privacy-Notice.pdf

16. Will my taking part in this research trial be kept confidential?

Yes. If you consent to take part in this study, the records obtained while you are in this study as well as related health records will remain strictly confidential at all times. The information will be held securely on paper and electronically at Chapel Allerton hospital under the provisions of the Data Protection Act 2018. You will be allocated a trial number, which will be used as a code to identify you on all trial documents.

Where this information could identify you, the information will be held securely with strict arrangements about who can access the information. The information will only be used for the purpose of health and care research, or to contact you about future opportunities to participate in research. It will not be used to make decisions about future services available to you, such as insurance.

Where there is a risk that you can be identified your data will only be used in research that has been independently reviewed by an ethics committee.

The NHS (GP Surgery and Leeds Teaching Hospitals Trust) will use your name, NHS number and contact details to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Individuals from University of Leeds and regulatory organisations may look at your medical and research records to check the accuracy of the research study. The NHS will pass these details to the University of Leeds along with the information collected from you and your medical records. The only people in the University of Leeds who will have access to information that identifies you will be people who need to contact you to regarding the study, to offer you future opportunities to participate in research, for your medical care or audit the data collection process. The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS number or contact details.

Your records will be available to people authorised to work on the trial but may also need to be made available to people authorised by the Research Sponsor (the University of Leeds), which is the organisation responsible for ensuring that the study is carried out correctly. Coded health information may be sent to other countries, some of which may not have the same level of personal data protection as within the United Kingdom. However, your name will not be passed to anyone else outside the research team or the sponsor.

17. Contact for further information

In the event of study related questions or problems, your research doctor can be contacted at the following telephone number.

Chapel Allerton Hospital
Drs Jackie Nam, Kulveer Mankia, Laurence Duquenne and Leticia Garcia

Monday to Friday 9am to 5pm:

- Research admin office Tel: (0113) 39 24734
- Research Nurse Office Tel: (0113) 39 24729

If calling after hours or in an emergency, please call:

- Ward C2 Tel: (0113) 39 24202

Finally, thank you for taking the time to read the information and considering whether to take part in the study

The Leeds Teaching Hospitals NHS
NHS Trust

MAIN CONSENT FORM - PART 1

(To consent to have the anti-CCP blood test)

If you are happy to participate in the first part of the trial, sign this consent form, put the signed consent form in the envelope provided and then get your blood test done using the form provided.

Title of Project: CCP – Next Generation: A Co-ordinated Programme to Prevent Arthritis - Can We Identify Arthritis at a Pre-Clinical stage?

SUBJECT INITIALS ☐☐☐ SUBJECT NO. ☐ SUBJECT DOB ☐☐☐

Name of Researcher: Professor Paul Emery

Please write your initials in the boxes below

1. I confirm that I have read and understand the information sheet v3.0, dated 01.07. 2021 for the above study, that I have had the opportunity to ask questions and that I have received satisfactory answers to the questions that I have asked. ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐

3. I understand that my medical records may be looked at by authorised individuals from the Sponsor for the study, the UK Regulatory Authority or the Independent Ethics Committee in order to check that the study is being carried out correctly. I give permission, provided that strict confidentiality is maintained, for these bodies to have access to my medical records for the above study and any further research that may be conducted in relation to it. I also give permission for a copy of my consent form to be sent to the Sponsor for the study ☐

4. I agree to take part in the above study ☐
   - If the blood test is positive, I will be invited to participate in the second part of the study.
   - If the test is negative, then I will be managed by my GP and I will not be followed in the Rheumatology Clinic at Chapel Allerton Hospital in Leeds.
   - If I do not attend the Rheumatology Clinic Chapel Allerton Hospital in Leeds, I will be sent a questionnaire at 12 months regarding my symptoms.

Name of Patient **(Please print your name)**	Date	Signature
Name of Person taking consent (Investigator/delegated individual)	Date	Signature