Botnar Research Centre, Windmill Road, OX3 7LD
Tel: +44(0)1865613728
Chief Investigator: Dr Philip Drennan, philip.drennan@ndorms.ox.ac.uk
Co-investigator: Dr Loren Kell, loren.kell@ndorms.ox.ac.uk
Study team: translationalpharmacology@ndorms.ox.ac.uk

PARTICIPANT INFORMATION SHEET:
INVITATION TO PARTICIPATE IN ADDITIONAL STUDY PROCEDURES

Investigating the human biology of resident immunity in tissue via neoantigen challenge (INHABIT)

This information sheet is for people who have previously taken part in a KLH study. You will recall that this study involved giving doses of KLH (keyhole limpet haemocyanin) with or without other medicines called adjuvants and assessing the response in the blood and skin over a period of time (between 1 and 3 months).

We'd like to invite you to take part in additional study procedures that have been approved by the NHS Research Ethics Committee. Before you decide, it is important that you understand why the research is being done and what it would involve for you. Please take time to read this information and discuss it with others if you wish. If there is anything that is not clear, or if you would like more information, please ask us.

If you decide to participate in the additional study procedures:

1. You will attend the research facility on two occasions.
2. At the first visit we will ask you to sign a consent form related to these additional procedures. We will then ask you questions about your current health and perform a brief physical examination. If you are eligible based on the screening assessment and decide to take part, you will receive up to three injections of KLH under the skin of the forearms or back. This visit will take about 1 hour. We will take 30 mL (about 2 tablespoons) of blood.

3. At the second visit (between 1 to 28 days later) we will take a blood sample (~33 mL, about 2.5 tablespoons) and perform either up to three procedures called a skin blister, which allows us to take a small sample of fluid and cells from the sites of the KLH injection, or we will take up to three small samples of skin (punch skin biopsy) using local anaesthetic. Each skin punch biopsy will be 4-6mm in diameter, about the size of 2-3 grains of rice side by side. More information about this procedure is available later in this information sheet.
4. **Taking part in this study is entirely your choice. You will be free to withdraw from the study at any time you wish.**

Contents

1. Introduction

The immune system is the body's defence system that protects from infections and illnesses. Faulty regulation of the immune system contributes to multiple diseases including inflammatory arthritis, cardiovascular disease and cancer, and therefore represents a leading cause of disability and death worldwide. Whilst there have been revolutionary advances in our understanding of how to use drugs to treat abnormal immune responses, there remains huge unmet need for new, better medicines. Unfortunately, as many as 9 in every 10 promising drugs studied in humans ultimately do not succeed in becoming clinical treatments. A significant cause of failure is when information gained in the laboratory or in animal studies does not hold true when the drug is given to humans.

2. Why are we doing this study?

One approach to improve the efficiency of the drug development process is the use of human 'immune challenge' studies. In these studies, healthy volunteers are given small amounts of substances which are foreign to their immune system to provoke a temporary response: the 'challenge'. Depending on the nature and dose of the challenge, the body's immune system will react in a different but predictable way, elements of which mimic those seen in disease, thereby 'modelling' them. These models can help safely bridge the gap between animal experiments and people with disease, allowing us to test the effect of new drugs safely without exposing patients to risk. Sadly, whilst immune challenge models have been used in drug development for many years, this has been done in an unstructured manner, which greatly limits the usefulness of the approach.

The purpose of this research is to better understand, improve, and standardise a common method of immune challenge which uses a protein called 'Keyhole Limpet Haemocyanin' (KLH). KLH is available as a highly purified formulation, and because it is not usually encountered by the human immune system (it is derived from an inedible shellfish), it allows us to study the development of immune responses right from the time it is administered. We plan to give different groups of healthy volunteers KLH with an 'immune-boosting' agent (Montanide ISA™51, commonly referred to as an adjuvant), before measuring and comparing their response. We will then re-challenge all volunteers one month later with a specific dose of KLH or saline control in the skin on their forearms. This is similar to an allergy test, where we will take blood samples and skin biopsies to understand the nature, time course, and variability of the immune response in each individual. We will take samples from the lymph nodes in the armpits after the first KLH dose, and following re-challenge, to characterise the immune cells that are responding to KLH. In some cases, participants can undergo an optional skin rechallenge with KLH, to explore how immune memory changes over an extended period of time. The results will help us to characterise responses to repeated KLH challenge over time, which could be

used to model better different diseases and test drugs with. In turn, this will allow earlier and better evaluation of new therapeutics.

3. Why have I been invited?

You have been invited because you have previously taken part in the main part of this study, and indicated that you would be interested in hearing about future research.

4. Are there any advantages to taking part?

You will not gain any direct benefit from the study. We hope that the information we gather from this and future studies will help us to develop new treatments for diseases caused by, or affecting the immune system.

5. Do I have to take part?

- No, taking part is entirely your choice.
- You can withdraw at any time without giving a reason, without your legal rights being affected.

6. Can I take part?

To take part in the study you had to fulfill certain eligibility criteria. Having already fulfilled these, the criteria required to participate in the additional study procedures is shorter. To be eligible, ALL of the following must apply to you:

- Be willing and able to give informed consent for participation in the study and able to comply with the study protocol.
- If female, not be of child-bearing potential or not be pregnant (negative pregnancy test on the day of both screening and vaccination) and willing to use effective methods of contraception to prevent pregnancy from the time of first dose to 60 days afterwards. This should include two methods of contraception simultaneously (e.g. condoms and the oral contraceptive pill).
- If male and with a female partner of child-bearing potential, agree to use effective methods of contraception from the time of the first dose of challenge agent to 60 days afterwards.

You CANNOT participate if any of the below exclusion criteria apply to you:

- Have had antibiotics or antiviral therapy after a serious illness within 30 days of study entry.
- Have any use of immunosuppressant or immunomodulatory agents (systemic or topical) in 3 months prior to study entry, including anti-coagulant or anti-platelet drugs.
- Have chronic medical conditions with potential effect on immune responses including diabetes, significant history of atopy, or any condition that, in the opinion of the investigator, would interfere with the study.

- Have any tattoos, moles or other skin abnormalities such as overgrown scars, called keloids, (or history of keloids) that may, in the opinion of the investigator, interfere with study assessments or increase the risk of an adverse outcome from study procedures (e.g. skin biopsy healing).
- Pregnant or breastfeeding (lactating), where pregnancy is defined as the state of a female after conception and until the termination of gestation, confirmed by a positive hCG laboratory test.
- Have an allergy to KLH, Montanide ISA-51, related vaccine adjuvants, or components of the study challenge agents.
- Have an allergy to shellfish.
- Have resided in or have significant previous travel to areas endemic for schistosomiasis (due to potential cross-reactive immune responses to KLH).
- Have a phobia of needles or minor surgical procedures.
- Are a current smoker (including vaping) or using nicotine replacement therapy.
- Have received any vaccinations within 30 days prior to screening visit, or will require vaccination prior to the end of study follow-up.
- Have any other significant disease, disorder, or finding, which, in the opinion of the investigator, may either put you at risk, affect your ability to participate in the study or impair interpretation of the study data.

7. What will happen to me if I decide to take part?

7.1. Visit 1

You should allow approximately 1 hour for this visit. This visit will take place at the Experimental Medicine Clinical Research Facility (EMCRF), based at the Churchill Hospital site, run by the University of Oxford. We will explain where you need to go before your visit.

Upon arrival you will have the opportunity to ask any further questions and, once you are happy that you fully understand what the study involves and before anything else takes place, the study doctor will ask you to sign a new consent form. You will be given a copy of the consent form to take away and keep.

The study doctor will then go through a few administrative questions as well as questions about your current health. This will be followed by a brief physical examination to see if you are suitable for the study procedures. (see more details below).

<u>Medical examination and clinical observations</u>

Medical examination of your skin, chest, abdomen, mouth and the lymph glands in your upper body may be performed. Your blood pressure, heart rate, and

temperature will be recorded. Additionally, for women of childbearing potential a urine pregnancy test will be performed.

Based on the above assessments, the study doctor will determine whether you are eligible to proceed with the additional study procedures. If you agree, these procedures will take place at this visit, but you are also welcome to return at a later date if this suits you better or if you would like more time to consider participating.

Questions on contraception use and menstrual cycle

As part of this study, we are interested in understanding whether biological sex and the use of different types of contraception influence immune responses.

If you were assigned female at birth, we will ask you some questions about your menstrual cycle and your contraceptive use. This will include the date of your most recent menstrual period and what form of contraception you are currently taking, such as the oral contraceptive pill, an intrauterine device (IUD), implant, injection, patch, or ring), and for how long you have been taking it. We will ask you to update this information at each study visit, as changes over time may be important for interpreting the study results. All information you provide will be kept confidential and handled in accordance with data protection regulations.

What happens if I decide not to take part at this stage?

There is nothing else you need to do—taking part if entirely your choice.

KLH Injections

You will receive up to three injections of KLH under the skin (‘intradermal’) of your forearm and/or back. You will need to remain at the research facility for at least 20 minutes to ensure you have no problem with the injections. We will also take 33 mL of blood (about 2.5 tablespoons).

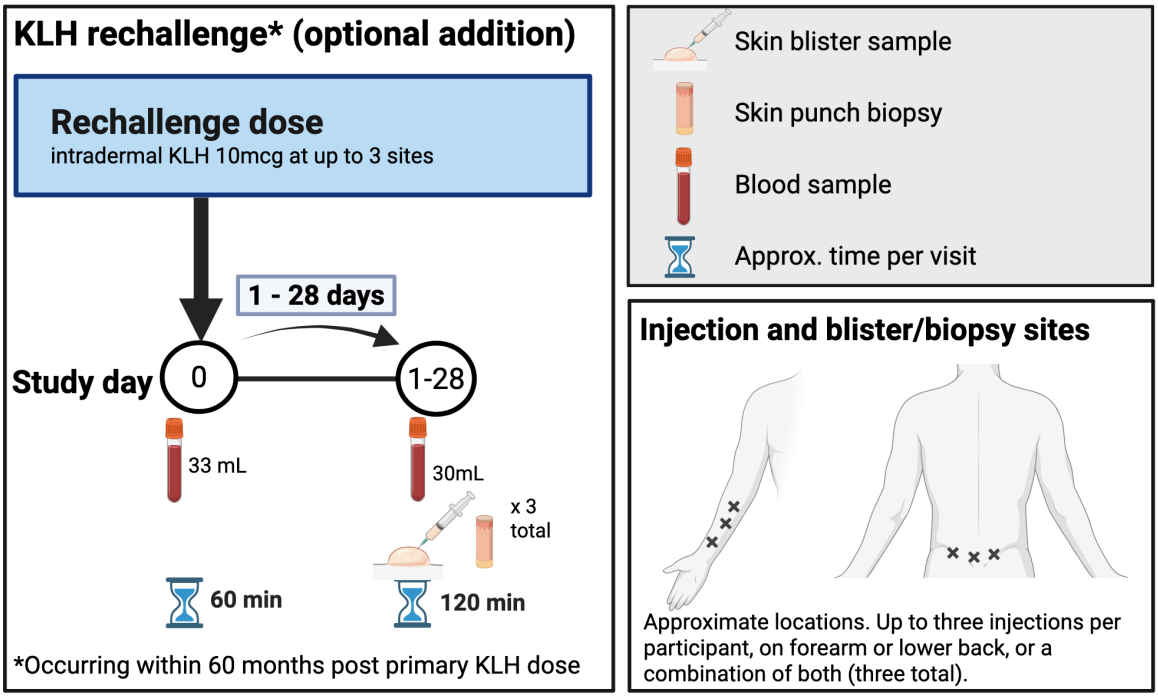

Figure 1: Outline of KLH rechallenge procedures

7.2. Visit 2

Following your first study visit, you will return 1 to 28 days later for a single follow-up visit (we will tell you when). You should allow up to 2.5 hours for this visit.

We will ask you questions about your current health, and any possible reactions to the study agents. If necessary, we will do a brief physical examination or check your vital signs, e.g. if you have a skin reaction to the injection. We will then take a blood sample to measure the immune response to KLH. On this visit we will take approximately 30 mL (about 2 tablespoons) of blood.

Assessment of KLH re-challenge

Depending on the time point (between 1-28 days) at which the follow-up occurs, we will measure the skin reaction to the injections using a ruler, and a special camera called a laser Speckle imager (LSI), which measures blood flow in the skin. You will be given a special set of glasses to wear while the LSI is being used to protect your eyes. We will also take photos of the skin reaction—these will be close up photos of the skin and will not include any identifiable detail.

Skin blister procedure

We will then perform either up to three ‘skin blister’ procedure, or three skin punch biopsies (see below), or a combination of the two (up to three total), of the injected areas of skin.

The skin blister procedure should not cause significant pain. This involves applying a small suction cup to the skin of the over the site of the injections, and attaching it to gentle suction using a suction pump. A skin blister forms over about two hours, and its fluid contains immune cells that we can meaure. Once this happens, we will remove the blister fluid using a small needle, and a sample of the blister skin. We will then apply a dressing. The blister should heal without scarring over several days.

Skin punch biopsy procedure

A small piece of skin (a skin biopsy) is taken, using a special device called a punch biopsy (Figure 2), at the same sites that received the injections. This is then analysed to measure the immune cell types present there. To take the biopsy we will clean the skin with antiseptic, and then give an injection of local anaesthetic to minimise discomfort. The punch biopsy takes a tiny circular amount of skin (4-6mm in diameter, about the size of 2-3 grains of rice side by side). We will then close the skin with either an absorbable or a non-absorbable stitch. We will then put a dressing over these biopsy sites, which can be left on until it falls off, or removed carefully after 48h. After the biopsy you will be asked to keep the area dry for 48h, then you can bathe/swim normally. If a non-absorbable stitch was used, you will be asked to attend an additional 15-minute visit, 10-14 days following your biopsy, for a nurse to remove your stitch for you. If an absorbable stitch has been used, this will dissolve and fall out on its own in about 10 days. We will provide, and go through with you, a manual that will outline how to care for your biopsy.

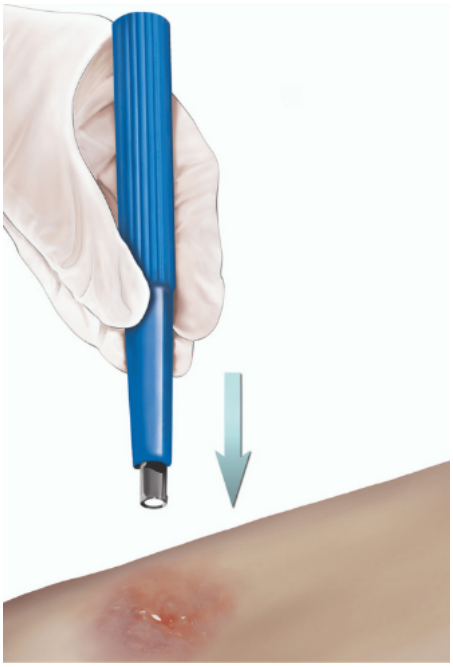

Figure 2 Punch skin biopsy procedure

From: https://www.healthdirect.gov.au/surgery/punch-biopsy-of-a-skin-lesion

End of the study

Following your final visit, we will make sure that you have contact details for the study team in case there are any problems after this, such as any concern around the healing of the skin blister sites (this is very unlikely).

8. What are my responsibilities?

It is important to consider whether you can commit to coming for all study visits, as far as possible.

If you take part in the study we will ask you to avoid the following activities surrounding the re-challenge KLH dose and follow-up visit:

8.1. Caffeine, Alcohol, and Tobacco

- Participants will abstain from ingesting caffeine- or xanthine-containing products (e.g. tea, coffee, cola drinks, and chocolate) for 12 hours prior to each scheduled study visit, until the final immunological study assessment for that visit (i.e. tea / coffee etc. is permitted during a study visit once immunological assessments have taken place)
- Participants will abstain from alcohol for 24 hours before each study visit until discharge from the study facility for that visit.
- Participants will not be permitted to use nicotine containing products from 30 days prior to first visit until the final follow-up visit.

8.2. Activity

- Participants will not be permitted to use sun-beds from 60 days prior to the first dose until the final follow-up visit.
- Participants will be advised to avoid excessive sun exposure from screening through to final study visit, including recreational sunbathing.
- Participants will abstain from strenuous exercise (e.g., contact sports, weightlifting, or any other moderate/high intensity exercise) for 24h prior to and after each study visit. Participants may participate in light recreational activities during this time (e.g. mild intensity exercise for 30 minutes or less).

Following the skin blistering procedures you will need to take care to not disturb the skin too much until the skin is healed.

Women of childbearing potential

For female participants, we consider you to be of childbearing potential unless you have had previous surgical sterilisation (e.g. hysterectomy, bilateral salpingectomy,

bilateral oophorectomy). Female participants of childbearing potential are required to use a **two** effective forms of contraception from the day of first administration of KLH until 60 days after the last administration of KLH. Acceptable forms of contraception for participants of childbearing potential include:

- Established use of oral, injected or implanted hormonal methods of contraception
- Placement of an intrauterine device (IUD) or intrauterine system (IUS)
- Barrier methods of contraception (condom or occlusive cap with spermicide).
- Male sterilisation, if the vasectomised partner is the sole partner of for the subject.
- True abstinence (defined as refraining from heterosexual intercourse) when this is in line with the preferred and usual lifestyle of the subject. Periodic abstinence and withdrawal are not acceptable methods of contraception.

We would not anticipate any adverse effects from KLH exposure during pregnancy. However, if you do become pregnant before the KLH rechallenge, you will be withdrawn from the study.

9. Are there any possible disadvantages or risks from taking part?

The disadvantages of taking part relate to the inconvenience of attending for study visits, and the small risk of adverse effects of the study procedures. You should consider the following risks before agreeing to take part:

9.1. Potential risks of the challenge agents

Keyhole Limpet Haemocyanin (Immucothel)

KLH is a highly purified protein obtained from the blood of an inedible shellfish. It has been used for over 50 years for challenge studies similar to ours, at doses up to 5 times greater than those used in our study. The specific product we are using (Immucothel) is a registered medicine in some countries.

Expected common (more than 1 in 10 risk) adverse effects are limited to mild responses at the injection site e.g. pain, redness, warmth, swelling, tenderness or itching. Other potential foreseeable risks (less than 1 in 10 risk) would be similar to those seen with standard vaccinations, including mild systemic reactions e.g. flu-like illness with feverishness, fatigue, malaise, arthralgia, sore muscles and headache. In almost all cases we would expect these to last no more than a few days. In very rare cases (less than 10,000 risk), local reactions could be more severe. If this were to occur we would not give any further injections and would withdraw you from the study, while also providing any appropriate medical care that you might need, or referring you to your GP or other NHS service as required.

There are some very rare but serious adverse effects that can occur with commonly used vaccinations. Although KLH is not a vaccine, it is similar to a vaccine in that it is foreign to the body and provokes an immune response, and it is therefore reasonable to expect a similar potential for these adverse effects. These include

severe allergy (anaphylaxis) and problems with nerves such as Guillain-Barre Syndrome. The risk of these is extremely low (1 to 2 in a million risk).

9.2. Potential risks of tests performed as part of the study

To minimize the risk of problems all study procedures will be performed by experienced professionals using appropriate precautions and equipment.

Blood donation

If you take part in the additional study procedures and follow-up visit the total amount of blood taken will be about 63mL, which is about 15% of a standard blood donation. As such it would not be expected to cause problems for an otherwise healthy volunteer. The blood donation itself requires the use of a needle into a vein of the arm, and this can cause minor bruising and tenderness in around 1 in 10 people, and occasionally feeling faint or actually fainting (in around 1 in 20 to 1 in 100 people). We will provide food and water following blood donation. Very rarely, in less than 1 in 10,000 people, sites of blood tests can become infected and require antibiotic treatment (we will provide these, unless you require treatment outside of normal working hours, at which point we would direct you to normal NHS services). The blood tests will be taken by experienced members of the study team which should minimize the risks of side effects.

Intradermal injection

The risks of intradermal injection are similar to those of intramuscular injection. Intradermal injections can cause stinging at the time of injection. There can also be discomfort, redness, and itching for a few days afterwards. Very rarely (in less than 1 in 10,000 people) a small sore can form at the time of injection which can longer to heal or cause scarring.

Skin blister

Skin blister is safe procedure and should not cause significant pain or discomfort, although there can be some minor discomfort when the blister fluid is removed from the blister (with a needle) and the skin sample is taken. Infection is very unlikely (occurs in less than 1 in 10,000 people). Scarring following these procedures is also very unlikely (less than 1 in 10,000 risk).

Skin punch biopsy

Skin punch biopsy is a commonly performed diagnostic procedure. The potential risks (1 in 10 people) include minor bruising, bleeding, and skin discomfort. A 4-6mm punch biopsy will be performed using local anaesthetic to reduce discomfort. The injection of anaesthetic can cause stinging during injection which fades quickly

as the anaesthetic takes effect. It is common (in at least 1 in 10 people) for a small scar or persistent skin discoloration to be visible once the skin has healed—this usually fades over time but may be permanent. In rare cases (less than 1 in 1000), certain individuals can develop more prominent scars (called keloids). We will exclude people from the study who are known to have developed keloids previously, or have a family history of this, because we know this increases the risk of keloids. There is a very small risk (1 in 50) of infection following skin biopsy—this is minimized by use of skin antiseptic at the time of biopsy, and careful technique of the doctor performing the biopsy. We will provide, and go through with you, a manual that will outline how to care for your biopsy.

10. Will my General Practitioner (GP) be informed of my participation?

If we incidentally find an issue during the study that may be important for your health (e.g. high blood pressure, blood test abnormalities), we will inform your GP, or ask you to contact them, to ensure appropriate follow-up can be arranged.

11. Will my taking part in the study be kept confidential?

Information about participants will be kept confidential and managed in accordance with applicable policies and regulations. Confidentiality will be maintained as far as it is possible unless you tell us something which implies that you or someone you mention might be in significant danger of harm. In this case, we would have to inform the relevant agencies but we would discuss it with you first.

Further information about how your personal data is used is provided in the section “What will happen to my data”.

12. Will I be reimbursed for taking part?

You will be compensated by bank transfer for your travel costs, time and inconvenience related to taking part in this study. If you agree to return for further intradermal KLH injections (with subsequent visit and skin blister/biopsy procedure), you will be compensated £100 total for attending these two visits.

To claim this reimbursement, at the completion of your involvement in the study we will send you an electronic claim form via email – once you complete this we will submit the information to the University finance team and the payment will be made directly into your bank account. This process can take up to 1-2 months.

Your bank details will be stored securely for 7 years in accordance with University of Oxford Financial policy.

We will not pay tax or National Insurance from the money due to you. It is your responsibility to pay these and to check how any compensation received from taking part in the study affects any state benefits to which you are entitled. Contact HM Revenue & Customs for information (http://www.hmrc.gov.uk/ or telephone 0300 200 3300).

13. What will happen to the samples I give?

Blood, skin, and blister fluid samples that you give will be primarily stored and analysed in facilities based at NDORMS, University of Oxford. Your samples will be used in a form that does not identify you, mainly by the Translational Pharmacology research team, but also ethically approved research projects which may take place in hospitals, universities, non-profit institutions or commercial laboratories worldwide.

We will ask for your consent for the use of your samples to be stored indefinitely, and used in future ethically approved studies. If you agree to this, your samples will be used mainly by local researchers (if applicable), but ethically approved research projects may take place in hospitals, universities, non-profit institutions or commercial laboratories worldwide. If you agree to your samples being used in future research, your consent form will be held until the samples have been depleted or destroyed. To help keep your information confidential, your sample and any information recorded about you in this study will be assigned a study code that is used instead of your name and other identifiers. However, your DNA is unique to you so it can never be completely anonymous. Raw and summary data generated from this study, that does not contain any participant identifying information, will also be shared with the study funder, UCB Pharma.

14. What will happen to my data?

Data protection legislation requires that we, the University of Oxford (whose legal name is The Chancellor Masters and Scholars of the University of Oxford), state the legal basis for processing information about you. In the case of research, this is a 'task in the public interest'. The University of Oxford is the sponsor for this study and is responsible for looking after your information and using it properly.

We will need to use information from you for this research project. We will share your information related to this research project with the following types of organisations: the local NHS Trust, a national volunteering database (see above) and, only where necessary for context, research partners (both academic and commercial organisations).

We may use third party service providers or subcontractors to help with some of the research activities we carry out (e.g. IT provision, survey provision, transcription services etc.). We may therefore share your personal data with these providers when it is necessary to do so to allow them to carry out the services we require them to provide. However, we require all our third-party providers to have appropriate security measures in place to protect your data and we only allow them to process your data for the specific purposes we have stated in our instructions.

This information will include your:

- NHS number
- Name
- Contact details
- Demographic data (e.g. age and sex)

People will use this information to do the research or to check your records to make sure that the research is being done properly. Responsible members of the University of Oxford, regulatory authorities, and the relevant NHS Trust may be given access to data for monitoring and/or audit of the study to ensure that the research is complying with applicable regulations.

We will keep all information about you safe and secure by:

- limiting access to data to only those people who need it for the research
- using the minimum personally-identifiable information possible
- storing it as securely as possible, for instance in locked cabinets on University premises for written documents, or on password-protected University-controlled computers for electronic information

International Transfers

We may share data about you outside the UK for research related purposes to:

- Permit additional analysis
- Contextualise data arising from the study
- Gain the insight of academic partners

If this happens, we will only share the data that is needed. We will also make sure you can't be identified from the data that is shared where possible. This may not be possible under certain circumstances – for instance, if you have a rare illness, it may still be possible to identify you. If your data is shared outside the UK, it will be with the following sorts of organisations:

- Higher education institutions (i.e. Universities)
- Commercial organisations

We will make sure your data is protected. Anyone who accesses your data outside the UK must do what we tell them so that your data has a similar level of protection as it does under UK law. We will make sure your data is safe outside the UK by doing the following:

- (some of) the countries your data will be shared with have an adequacy decision in place. This means that we know their laws offer a similar level of protection to data protection laws in the UK

- we use specific contracts approved for use in the UK which give personal data the same level of protection it has in the UK. For further details https://ico.org.uk/for-organisations/uk-gdpr-guidance-and resources/international-transfers/

- we do not allow those who access your data outside the UK to use it for anything other than what our written contract with them says

- we need other organisations to have appropriate security measures to protect your data which are consistent with the data security and confidentiality obligations we have. This includes having appropriate measures to protect your data against accidental loss and unauthorised access, use, changes or sharing

- we have procedures in place to deal with any suspected personal data breach. We will tell you and applicable regulators when there has been a breach of your personal data when we legally have to. For further details about UK breach reporting rules https://ico.org.uk/for-organisations/report-a-breach

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

After the study ends, the retention period (this means the length of time we keep your data for) will begin and we will keep your data for a minimum of 3 years in line with the University Policy on Management of Data. Once the retention period has finished, the study data will be kept in a way that does not identify you.

What are your choices about how your information is used?

You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have. You have the right to ask us to remove, change or delete data we hold about you for the purposes of the study. We might not always be able to do this if it means we cannot use your data to do the research. If so, we will tell you why we cannot do this.

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. This will be stored locally by the Translational Pharmacology group.

You can find out more about how we use your information, including the specific mechanism used by us when transferring your personal data out of the UK, by:

- asking one of the research team: philip.drennan@ndorms.ox.ac.uk
- sending an email to translationalpharmacology@ndorms.ox.ac.uk
- calling us on 01865 613728
- contacting the University's Data Protection Officer data.protection@admin.ox.ac.uk
- looking at the University's privacy notice available at: https://compliance.admin.ox.ac.uk/research-data.

If you would like to find out more about the use of confidential data in research, the HRA has developed a general information leaflet which is available at: https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/data-protection-and-information-governance/gdpr-guidance/templates/template-wording-for-generic-information-document/.

15. What will happen if I don't want to carry on with the study?

Participation is entirely voluntary. If you change your mind you can withdraw at any time without giving a reason and without penalty. If you withdraw from the study, any samples and data collected before your withdrawal will be used for research as detailed in this participant information sheet, unless you specifically request otherwise. However, if any of your anonymised data has been incorporated into the study, it will not be withdrawn or erased in order to maintain the scientific integrity of the study.

16. What happens at the end of the study?

The results of this project will be disseminated via standard scientific channels: publication in scientific journals, poster and oral presentations at scientific conferences. The data will contribute to the fulfilment of doctoral research project and presented in the thesis. You will not be able to be identified in any of these.

17. What if we find something unexpected?

If we incidentally find an issue during the study that may be important (e.g. high blood pressure, blood test abnormalities), we will inform your GP, or ask you to contact them, to ensure appropriate follow-up can be arranged.

18. What if there is a problem?

If you wish to complain about any aspect of the way in which you have been approached or treated, or how your information is handled during the course of this study, you should contact the Chief Investigator, Dr Philip Drennan (contact details

at the top of this form) or you may contact the University of Oxford Research Governance, Ethics & Assurance (RGEA) office at rgea.complaints@admin.ox.ac.uk.

The investigators recognise the important contribution that volunteers make to medical research, and will make every effort to ensure your safety and wellbeing. The University of Oxford, as the research sponsor, has appropriate insurance in place in the unlikely event that you suffer any harm as a direct consequence of your taking part in this study. If something does go wrong, you are harmed during the research, and this is due to someone's negligence, then you may have grounds for a legal action for compensation. While the Sponsor will cooperate with any claim, you may wish to seek independent legal advice to ensure that you are properly represented in pursuing any complaint. The study doctor can advise you of further clinical action and refer you to a doctor within the NHS for treatment, if necessary. NHS indemnity operates in respect of the clinical treatment provided.

19. Who is organising and funding the study?

- This study is sponsored Union Chimique Belge (UCB Pharma).
- The funding agreement between the University of Oxford and UCB provides that the University of Oxford will give UCB a royalty-free licence to commercially exploit the results of the study.
- All researchers involved in this study are employees of the University of Oxford. No members of the study team will receive additional payments for enrolling you in this study.

20. Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect participants' interests. This study has been reviewed and given favourable opinion by the **East of England – Cambridgeshire and Hertfordshire Research Ethics Committee**.

21. Further information and contact details:

Please contact Dr Philip Drennan (Chief Investigator, Clinical Pharmacologist, and Clinical Research Fellow, NDORMS) or Dr Loren Kell (Co-Investigator, Postdoctoral researcher) using the details at the top of this form if you would like further information or to ask any questions.

Thank you for reading this information sheet and for considering taking part in this research study.