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PARTICIPANT INFORMATION SHEET

CUREDIT Study

We'd like to invite you to take part in our research study. 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.

1. Key Facts

Who can take part?	Adults in good health, aged 18-45
Study interventions	Diphenylcyclopropenone (DPCP) applied to the skin on five occasions over 37-63 days (depending on which of the four study groups you are enrolled into).
Procedures	1. Blood samples: taken at the screening visit, and then visit 1 (day 0), visit 2 (day 28), and visit 3 (day 30) for groups 1-3. A total of 208mL of blood (about one cup) will be collected from participants in the study. 2. Taking small samples of skin using a procedure called '*punch skin biopsy*': for all study groups except the pilot group, four *biopsies* taken on the final study visit (visit 7, day 37, 49, or 63 depending on the group)
Study aims	We want to learn more about how the immune system works by studying its response to a chemical called DPCP. The immune system is the body's natural defense, protecting us against infections and diseases. When applied to the skin, DPCP causes a mild, temporary immune reaction. The medical term for this response is *contact dermatitis*. By observing this response, we can gain valuable insights into how the immune system functions.
Chief / Principal Investigator	Dr James Fullerton

Study site	NIHR Oxford Experimental Medicine Clinical Research Facility, Churchill Hospital, Headington, Oxford, OX3 7LE
What happens in the study?	• *Pre-screening*: You will complete an online questionnaire to assess suitability for the study. • *Screening:* Potentially eligible volunteers (based on the questionnaire) will attend a screening visit where we will collect information about medical history, perform a physical examination, and take blood tests, to decide their eligibility to take part and to obtain their consent. • *Visit 1:* At the next visit DPCP will be applied to the skin of the buttock using a small disc called a Finn chamber. Participants will remove the Finn chamber after 48 hours • *Visit 2:* On day 28 of the study, five different doses of DPCP will be applied to the skin of the upper arm. Participants will remove the Finn chambers after 6 hours • *Visit 3:* On day 30, 48 hours after the last visit, the skin response to DPCP will be assessed, to measure how each person responds to different DPCP doses • *Visits 4-6*: DPCP will be applied to the skin at two areas: the lower back , and upper inner arm, at each of these visits. Participants will remove the Finn chambers after 6 hours. • *Visit 7*: The skin response to DPCP will be assessed by taking measurements and images, followed by four punch skin biopsies • The screening visit, and visits 1-3 will include a blood test • For women of childbearing potential a urine pregnancy test will be performed at screening, and on all visits where DPCP is administered. • The safety of the participants will be closely monitored throughout the study
Reimbursement	Total reimbursement (screening visit and all 7 visits): £760 (groups 1-3) Further details about reimbursement are given on page 17
Risk of participation	**DPCP** is known to cause skin inflammation, similar to other contact dermatitis / eczema. Participants are likely to experience minor itch and discomfort, and occasionally blistering reactions and skin pigment changes **Punch skin biopsy** can cause some discomfort and minor bleeding. Punch skin biopsy causes a small scar which slowly becomes less visible but does persist.

	Blood donation can cause minor bruising, tenderness, and occasionally feeling faint or actually fainting. A full description of the risks of participation is given below in section 7.
Benefits of participation	By participating in this study, you will not directly receive any personal health benefit. However, you will help us develop better tools to understand the immune system, thereby potentially benefiting other people with diseases caused by, or causing, malfunction of the immune system e.g. eczema, psoriasis.

2. What is the purpose of the study?

In the CUREDIT study we are seeking to develop better ways to study the human immune system--the body's natural defence system that helps protect us from infections and diseases. The human immune system is immensely complex and we know that we can only learn a limited amount about it using standard methods such as analysing blood samples from healthy volunteers. Because of this we want to use an approach called 'immune challenge'. This involves giving participants tiny amounts of the test substance to stimulate certain immune processes, similar to the effects of a vaccine. We then observe the immune response, particularly in the skin. In simple terms, the immune response is how your body reacts to a challenge—like an alarm system activating when a potential threat is detected. By studying the way different people respond to these challenges we hope to learn more about the immune system, and in particular learn more about how new drugs can treat diseases caused by, or involving, the immune system.

In this study we will give a 'challenge' with a chemical substance called diphenylcyclopropenone ('DPCP'). DPCP is a chemical which causes an immune response in nearly 100% of people exposed to it. The medical term for this reaction is *contact dermatitis* (eczema). Because of this, DPCP has been removed from all products that people would ordinarily come into contact with, but it has been used for many years in immune challenge studies. Although not a licenced treatment for any medical condition, it is commonly used in specialty dermatology services as a treatment for a condition called alopecia. Because it has been used for such a long time, we know a lot about the safety of using DPCP for research. However, we think that there is more to learn about the immune response of healthy volunteers to DPCP, because we now have more advanced tests that we can perform on samples taken following DPCP challenge.

In the CUREDIT study we will give DPCP on multiple occasions. On the first occasion we will give DPCP to allow the immune system to develop a response to it (called 'primary sensitisation'). On the next occasion we will give a range of doses of DPCP to show how sensitive a particular participant is to DPCP. This is sometimes called a 'dose response assessment'. Next, using the lowest possible dose which has cause a detectable response, we will give DPCP on three more occasions. These occasions are referred to as 'rechallenges'. By then observing the DPCP rechallenge response at multiple time points, we can understand how the response evolves over time. The final visit of the study involves

taking a small sample of skin (*punch skin biopsy*) from each of the DPCP challenge sites, which will allow us to perform detailed analyses of the DPCP response in the skin.

3. Why have I been invited?

- You have been invited because you are aged 18-45 years, are healthy, and take no regular medications affecting the immune system. We plan to recruit a total of 21 participants, including three to a 'pilot' group, and six each to one of three different study groups (1-3). If you tell us you are healthy and have not been diagnosed with atopic dermatitis (eczema) as an adult, then it is likely you can participate.

4. Do I have to take part?

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

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

5.1. Pre-screening

If you are interested in the study we will ask you to complete a pre-screening questionnaire online – we will send you the link to this, or direct you to our website where the questionnaire can be accessed. The questionnaire should take about 10 minutes to complete. Prior to completing the questionnaire, we will ask you to ensure you have carefully read this information sheet. A link to this information sheet will be available at the top of the pre-screening questionnaire. The pre-screening questionnaire covers key criteria for participation in the study, your contact details, and medical history (including medications). As part of completing this pre-screening questionnaire you will be asked to indicate your consent (via electronic signature) to allow us to collect this data.. If you are deemed ineligible based on any of the replies you give to the major inclusions and exclusions in the pre-screening questionnaire, the questionnaire will stop at this point and consent for personal identifiable data and medical history will not be collected.

If you are unable to complete the questionnaire online, you can communicate directly with the study team by phone or email and we can complete the questionnaire on your behalf.

5.2. Screening

If you appear eligible, and if you decide that you would like to proceed, a member of the study team will arrange a visit to the research facility for a physical examination, and blood tests. Face to face visits will take place at the Experimental Medicine Clinical Research Facility (EMCRF), based at the Churchill Hospital site.

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 consent form to take part in the study (this is different from the consent provided for the pre-screening information described above). You will be given a copy of the consent form to take away and keep. The exact procedures that will happen in the study, and the timelines of involvement will depend on which study group you are enrolled into—the main difference between these groups is the timing of follow-up assessments (see figures 3-6). We will make it clear what study group applies to you before you sign any consent forms.

The study doctor will then go through a few administrative questions as well as detailed questions about your health. This will be followed by a physical examination, blood tests, and (if applicable) a urine pregnancy test to see if you are suitable for this study (see more details below). You should allow approximately 1 hour for this first screening visit, and it will occur up to 90 days prior to enrolment in the study. We will ask to see some form of ID, such a driver's licence or passport.

TOPS Registration

Healthy volunteers must not take part too often in trials of new medicines and other scientific studies (such as this one), for scientific, medical and ethical reasons (i) if the gap between two studies is too short, or the studies overlap, the medicines might interact, (ii) taking too many blood samples could cause anaemia, (iii) it's unethical to expose healthy people too often to medicines they don't need

So, to help research units, the Health Research Authority keep a database of healthy volunteers and when they take part in studies--this is called TOPS. We will enter into the database your National Insurance number (if you're a UK citizen), or your passport number and country of origin (if you're not a UK citizen) and the date of your last dose of study medicine. If you withdraw from the study before you receive any study medicine, the database will show that you never received a dose..

Medical examination and clinical observations

Medical examination of your skin (including thigh / buttock, upper arms, and back), chest, and abdomen will be performed by the study doctor. A study doctor or nurse will measure your blood pressure, heart rate, temperature, height, and weight. Additionally, for women of childbearing potential a urine pregnancy test will be performed.

Blood tests

To check that you are suitable for the study and that it is safe to take part, we will take blood to test for anaemia (low red blood cells), problems with your immune system, and kidney function. These tests will be performed by Oxford University Hospitals NHS Foundation Trust, and will be linked to your NHS record (so will be visible to other healthcare professionals, such as your GP). We will take approximately 10mL (two teaspoons) of blood for these tests.

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

There is nothing else you need to do—taking part is entirely your choice and you do not need to provide any reason or explanation (see 'What will happen if I don't want to carry on with the study?' below).

5.3. Study visits

If you are eligible for the study, you will be invited to attend 7 further in-person visits – we will confirm these bookings with you well in advance and ask you to put the times and dates into your calendar so you do not forget to attend. The exact schedule of visits will depend on the study group you are recruited to—you can only participate in one of the study groups. We will make it clear which study group we are recruiting into before you agree to take part. The figures below show the study interventions and biological samples we will take for each study group.

Visit 1 (***all groups***): day 0

We will take blood samples on the visits specified in figures 3-6. If you are a woman of childbearing potential, we will perform a urine pregnancy test to confirm that you are not pregnant before proceeding further. We will also ask questions regarding your menstrual cycle because this information may help to explain differences in immune responses to DPCP. We will then take some basic observations (blood pressure, temperature and heart rate). Next, we will apply the DPCP at one location on your buttock using a device called a Finn chamber (Figure *1*), which is a special dressing which contains the DPCP. The location of the Finn Chamber will be marked with ink. You may then leave the research facility.

We will ask you to keep the Finn chamber dressing in place for exactly 48 hours before removing it yourself. You should wash your hands thoroughly after removing the Finn chamber dressing. It is important to keep the Finn chamber dressing dry during this time—a cool gentle shower or shallow bath is ok provided you can keep the area dry. You will be asked to keep an eye on the patch test site as at some point after about 14 days, it should become red, slightly raised and possibly itchy. We would like you to make a note of the date on which that occurs as it gives an indication about how quickly your immune system has developed reactivity to the DPCP.

Visit 2 (***all groups***): day 28

On day 28 you will return to the research facility. We will ask you questions about any adverse events and any other relevant medical history since your last visit. We will check your observations and if you are a woman of childbearing potential perform a urine pregnancy test. We will then apply DPCP to the upper inner arm at five sites (i.e. five Finn chambers, containing different doses of DPCP). You may then leave the research facility.

We will ask you to keep the Finn chamber dressings in place for exactly 6 hours before removing them yourself. You should wash your hands thoroughly after removing the Finn chamber dressings.

Visit 3 (***all groups***): day 30

On day 30 you will return for an assessment of the skin response to DPCP. We will ask you questions about any adverse events and any other relevant medical history since your last visit. We will then assess the skin response to the different doses of DPCP using a standard grading scale and imaging devices including ultrasound and multispectral imaging. The thickness of the skin at each challenge site will be measured with a simple instrument called a calliper. At this visit we will identify the dose of DPCP to use in the subsequent rechallenges: this is the lowest dose which produces the desired response (a clear positive '++' reaction, Figure *2*A). A visual summary of these assessment methods is shown in Figure *2*, and more details are provided in section 5.4.

Pilot group and group 1*:* Visit 4 (day 35), 5 (day 36), 6 and 7 (day 37)

On day 35 you will return to the research facility. We will ask you questions about any adverse events and any other relevant medical history since your last visit. We will check your observations and if you are a woman of childbearing potential perform a urine pregnancy test. We will then apply DPCP to the lower back and to your upper inner arm using the dose selected at the visit 3 assessment. You may then leave the research facility. We will ask you to keep the Finn chamber dressing in place for 6 hours before removing it. You should wash your hands thoroughly after

removing the Finn chamber dressing. At this visit, and all subsequent visits, when we apply DPCP we will do so to a new patch of skin which hasn't been exposed to DPCP previously.

On day 36 and 37 you will return for further applications of DPCP to the lower back and upper inner arm using the same dose as used on visit 4. Following the application of DPCP on day 36 you may leave the research facility, and we will ask you to keep the Finn chamber dressings in place for exactly 6 hours before removing them yourself. Following the application of DPCP on the day 37 visit you may then leave the research facility, but will need to return for the final visit 6 hours later.

At the final visit (day 37, 6 hours after the last visit) you will return to the clinical research facility where the skin response to the DPCP at each of the application sites will be assessed with the same methods used in visit 3. If you are in group 1 we will then perform 4-6mm punch skin biopsies (equivalent to 2-4 grains of rice laid side by side) at the three DPCP application sites on the lower back and a control site (where no DPCP was applied). If you are in the pilot group there will be no biopsies performed.

***Group 2**:* Visits 4 (day 35), 5 (day 42), 6 (day 47) and 7 (day 49)

On day 35 you will return to the research facility. We will ask you questions about any adverse events and any other relevant medical history since your last visit. We will check your observations and if you are a woman of childbearing potential perform a urine pregnancy test. We will then apply DPCP to the upper lower back and upper inner-arm using the dose selected at the visit 3 assessment.

On days 42 and 47 you will return for further applications of DPCP to the lower back and upper inner-arm the same dose as used on visit 4. We will also assess the skin response at the sites of previous DPCP application with the same methods used in visit 3. You may then leave the research facility.

Following each of these DPCP applications we will ask you to keep the Finn chamber dressing in place for 6 hours before removing it. You should wash your hands thoroughly after removing the Finn chamber dressing.

At the final visit (day 49,) you will return to the clinical research facility where the skin response to the DPCP at each of the application sites will be assessed with the same methods used in visit 3. We will then perform punch skin biopsy at the three DPCP application sites on the upper lower back and a control site (where no DPCP was applied).

***Group 3**:* Visits 4 (day 35), 5 (day 42), 6 (day 61) and 7 (day 63)

On day 35 you will return to the research facility. We will ask you questions about any adverse events and any other relevant medical history since your last visit. We will check your observations and if you are a woman of childbearing potential perform a urine pregnancy test. We will then apply DPCP to the lower back using the dose selected at the visit 3 assessment.

On days 42 and 61 you will return for further applications of DPCP to the lower back and upper inner-arm (at a site away from the previous applications) using the same dose as used on visit 4. We will also assess the skin response at the sites of previous DPCP application with the same methods used in visit 3. You may then leave the research facility, but will need to return for the final visit 6 hours later.

Following each of these DPCP applications we will ask you to keep the Finn chamber dressing in place for 6 hours before removing it. You should wash your hands thoroughly after removing the Finn chamber dressing.

At the final visit (day 63) you will return to the clinical research facility where the skin response to the DPCP at each of the application sites will be assessed with the same methods used in visit 3. We will then perform punch skin biopsy at the three DPCP application sites on the lower back and a control site (where no DPCP was applied).

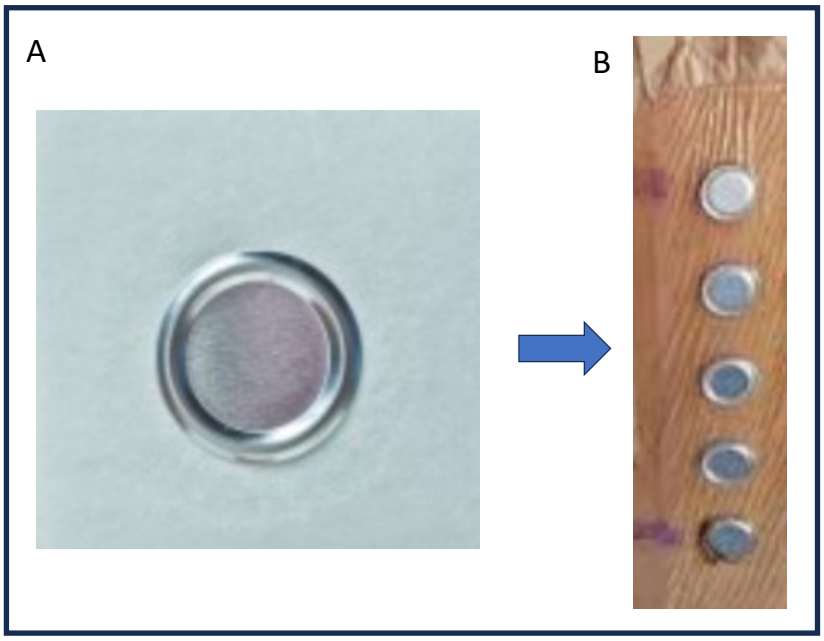

Figure 1: A) A single aluminium 'Finn Chamber', B) Finn chambers applied to the skin. The chamber applied on visit 1 is 12mm across (approximately 6 grains of rice laid side-by-side), and the chambers applied on subsequent visits are 8mm across (approx. 4 grains of rice).

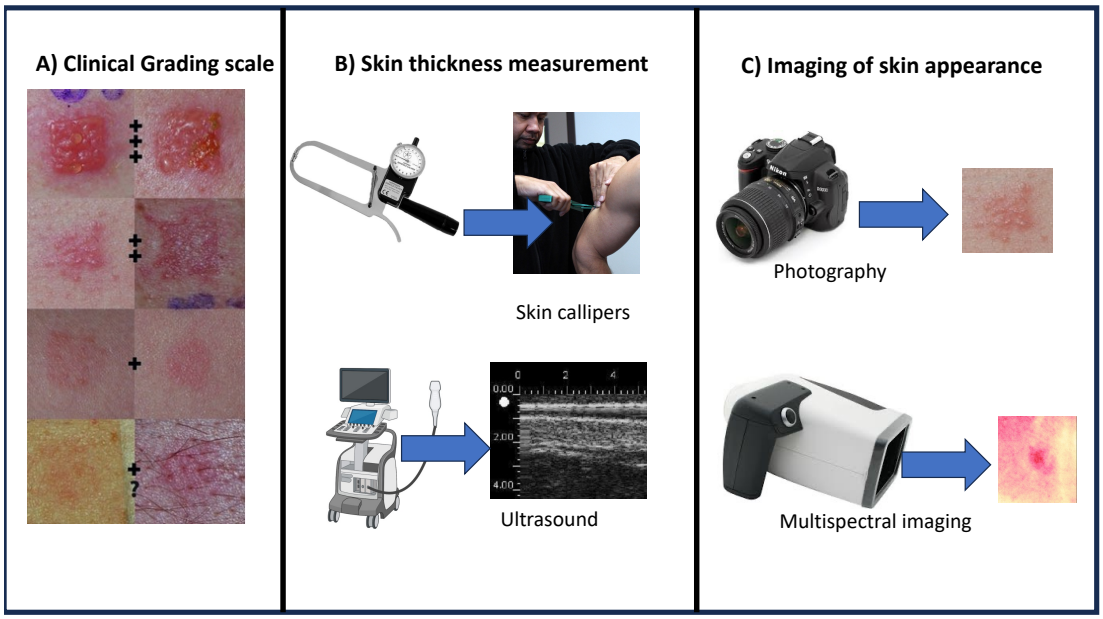

Figure 2: Assessment of the skin response: A) Clinical grading scale(From: https://www.chemotechnique.se/patch-testing/interpretation-/), B) Skin thickness measurement using skin callipers and ultrasound, C) Imaging using standard photography and multispectral imaging.

Study visits: Pilot group

The day of each visit, approximate duration, and biological samples taken for each visit is shown in Figure *3*.

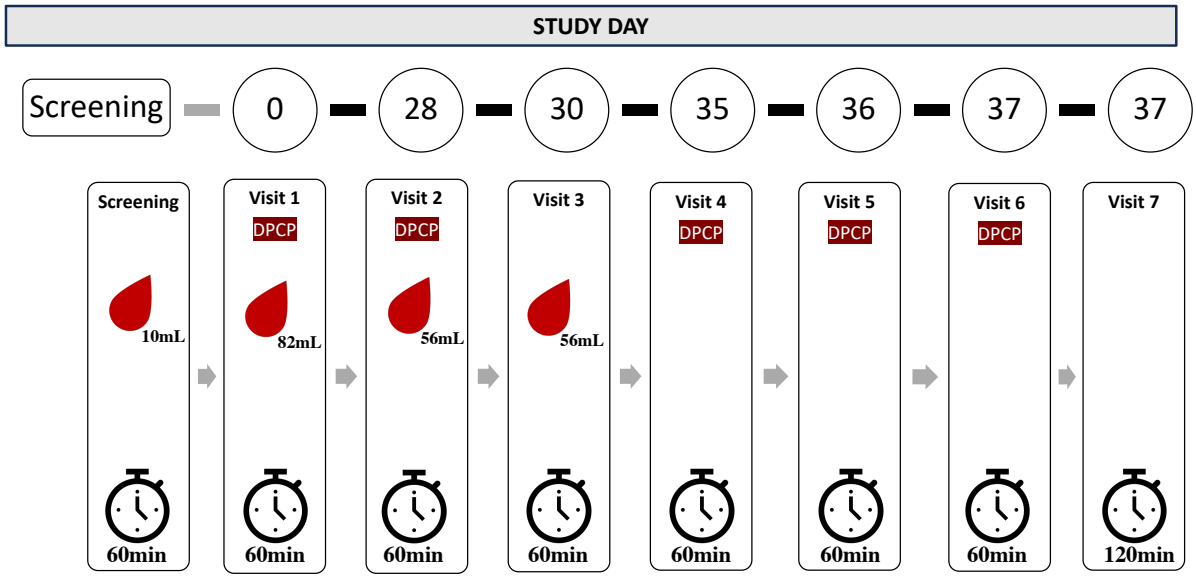

Figure 3 Pilot group visit schedule

Study visits: Group 1

The day of each visit, approximate duration, and biological samples taken for each visit is shown in Figure *4*.

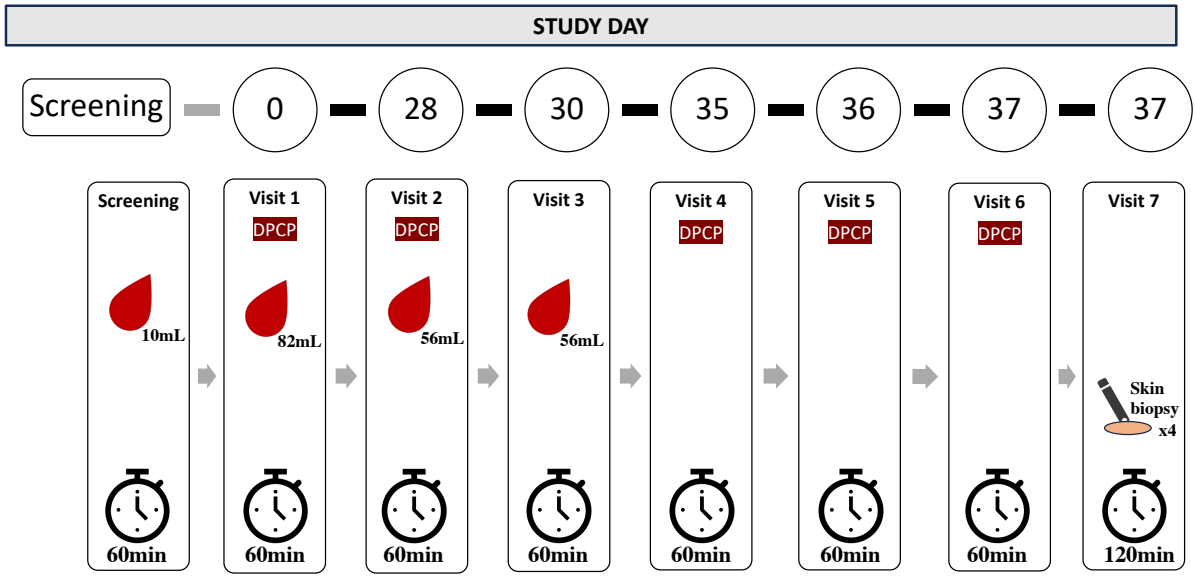

Figure 4 Group 1 visit schedule

Study visits: Group 2

The day of each visit, approximate duration, and biological samples taken for each visit is shown in Figure *5*

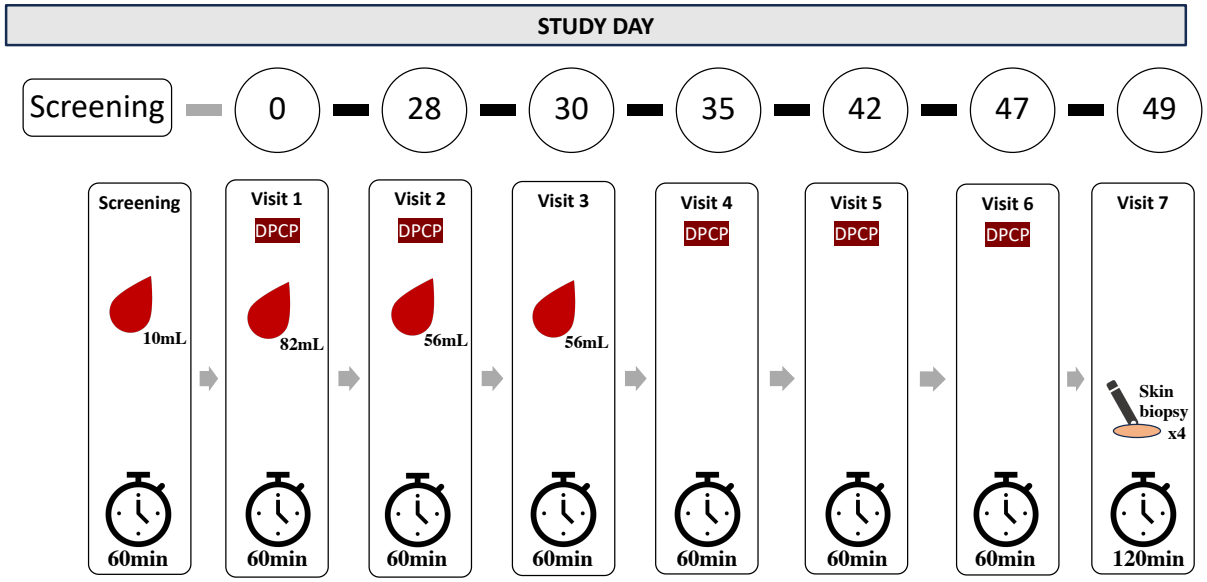

Figure 5 Group 2 visit schedule

Study visits: Group 3

The day of each visit, approximate duration, and biological samples taken for each visit is shown in Figure *6*

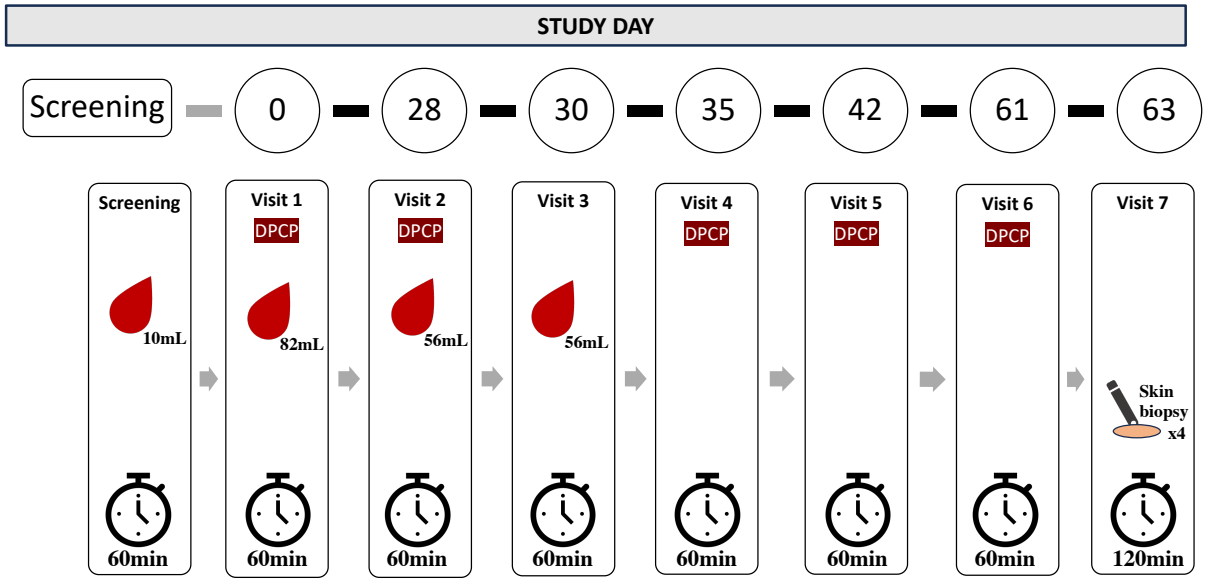

Figure 6 Group 3 visit schedule

5.4. Study procedures

When you arrive at the study site, we will ask questions to confirm you are still healthy and suitable for the study. Your blood pressure, heart rate, and temperature will be recorded. For women of childbearing potential, a urine pregnancy test will be performed.

Blood tests

We will take blood samples to measure the status of your immune system, as a baseline prior to the first application of DPCP, and following the first application (visits 1-3). We will perform assessments to understand which parts of the immune system are turned on in responses to the DPCP such as cells and genes. We will also do tests for evidence of previous infections with viruses which very commonly infect people as children or in early adulthood (cytomegalovirus), as these viruses may affect the immune response to DPCP, or provide additional insight into the way your immune system reacts to infection/inflammation. We may also perform assessments of your DNA (the body's 'instruction manual') to see if this can explain any differences in the immune response we observe. The total volume of blood taken on occasion will be approximately up to 82mL (about 4 tablespoons), and the total amount of blood taken over the course of the study will be approximately 208mL (about one cup).

DPCP application.

DPCP will be applied on five occasions. The timing of these applications will vary according to study group and is shown in figures 1-4. The approximate sites of these applications is shown in Figure *7*

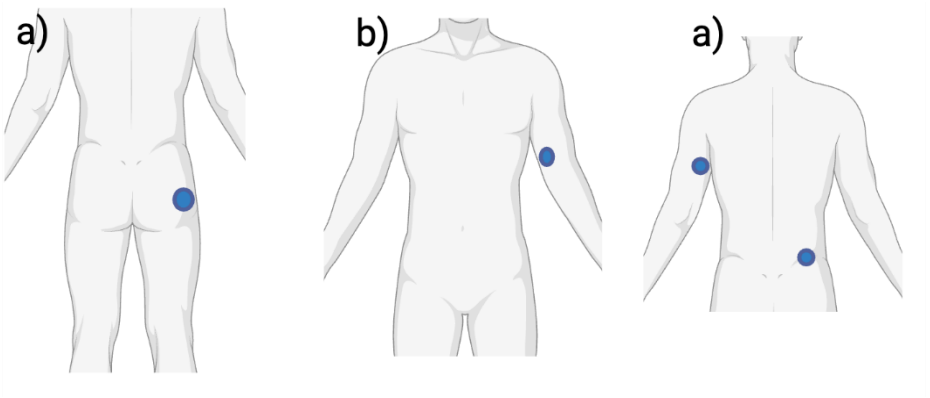

Figure 7 : Approximate sites of DPCP application: a) Primary, b) dose-response assessment, c) rechallenges

Skin assessment:

Clinical assessment: We will assess the skin response using a validated scoring system which assess the strength of the skin response to DPCP (Figure *2*A) – this is based on the amount of redness and minor swelling which can be detected by a trained observer.

Calliper measurement: The thickness of the skin at each of the challenge sites will be measured with a simple instrument called a calliper – to take the measurement we gently 'pinch' the skin between the ends of the calliper and the calliper measures the thickness of this skin. This is a fast and painless technique (Figure *2*B).

Ultrasound: We will use an ultrasound machine to look at the thickness of the skin at the site of DPCP application (Figure *2*B). We use gel to help improve the ultrasound pictures. The ultrasound procedure is painless and harmless, and should take less than 5 minutes to complete.

Photography: We will take close up images of the skin responses to track the changes in the skin (Figure *2*BC. The pictures will include just the site of DPCP application and surrounding skin and will not contain any identifying information.

Multispectral imaging: We will use a special camera called a multispectral imaging camera to take a close-up picture of the skin response (Figure *2*C). The multispectral imaging procedure is painless and harmless and it takes just a few seconds to take each picture. The pictures will include just the site of DPCP application and surrounding skin and will not contain any identifying information.

Punch skin biopsy:

We will take up to four biopsy samples of skin at the final visit, using a special device called a biopsy punch. The skin will be taken from either areas where you were given the DPCP applications or from a 'control' site where no DPCP was administered. In all cases the biopsies will be taken from upper lower back. 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 small circular piece 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 special plasters (steristrips), and a single dissolvable stitch, if necessary. We will then put a dressing over these biopsy sites, which can be left on until it falls off, or removed carefully after 48h.

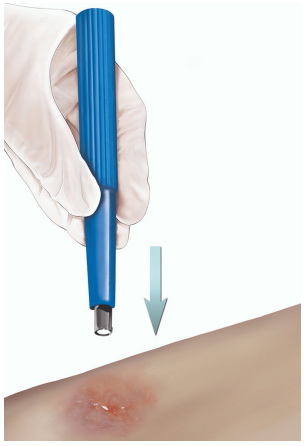

Figure 8 Punch skin biopsy procedure. From https://www.healthdirect.gov.au/surgery/punch-biopsy-of-a-skin-lesion

After the biopsy you will be asked to keep the area dry for 48h, then you can bathe/swim normally. If a stitch has been used this will dissolve and fall out on its own in about in about 10 days. or it can be removed by soaking and gently removing at 10 days.

Participant experience questionnaire

On your final visit will ask you to complete a paper based questionnaire about your experience in the study to date, e.g. how you found the study procedures, and whether you would volunteer for similar studies in the future, based on your experience in this study.

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 punch biopsy sites (this is very unlikely).

6. What should I consider?

It is important to consider whether you can commit to coming for all study visits.

If you take part in the study we will ask you to adhere to the following restrictions on your activity:

- During the study
    - To avoid excessive sun exposure from the time of screening through to the final visit, including recreational sunbathing
- Within 12 hours of the start of each visit:
    - To abstain from ingesting (eating or drinking) tea, coffee, cola drinks and other caffeine containing substances, and chocolate.
- Within 24 hours of the start of each visit:
    - To abstain from ingesting any alcohol
    - To abstain from strenuous exercise. You may participate in light recreational activities during this time (e.g. mild intensity exercise for 30 minutes or less).
    - To abstain from consuming non-steroidal anti-inflammatory drugs and antihistamines
- Within 30 days of the study and while participating in the study:
    - To abstain from any nicotine containing products (including cigarettes and vapes).
    - To abstain from recreational sun-bathing.
    - To abstain from use of topical creams, ointments, or gels containing corticosteroids or non-steroidal anti-inflammatory drugs.
- Within 60 days of the study and while participating in the study
    - To abstain from use of sun-beds

<u>Looking after the sites of DPCP application (Finn Chambers)</u>

It is important that you take care to ensure the Finn Chambers remain in place for the required amount of time.

Do not:

- Do not any apply ointment/cream to your body on the morning of your study visits.
- Do not get the Finn chamber dressing wet while it is in place. You may have a cool gentle shower or a cool shallow bath provided the dressing does not get wet. On the first day of the study (where the Finn chamber is applied for 48h) it is best to avoid any bathing/showering until the following day, to reduce the risk of disturbing the chamber.
- Do not wear your best clothes or pale-coloured clothing as the marker ink may permanently stain clothing.
- Do not participate in sports or any heavy physical work while the Finn chamber dressing is in place, as sweating may cause the patches to fall off.

Do:

- Do wear old, loose fitting closing during the daytime and overnight to protect the Finn Chamber dressings while they are in place.
- If the Finn Chamber dressing starts to peel off, tape the edges down using the tape you have been given. If the whole dressing comes loose, remove it and contact the study team for further advice.

Skin biopsies

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

Blood donation for other reasons

- You should not donate blood within 3 months of the study, as the total amount of blood donated during this study is about half a standard blood donation.

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 an effective form of contraception from the day of first administration of DPCP until 6 months (180 days) days after the last administration of DPCP. 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)
- Male sterilisation, if the vasectomised partner is the sole partner 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.

Note that following methods ARE NOT considered acceptable method of contraception

- Barrier methods of contraception (condom or occlusive cap with spermicide).
- Periodic abstinence and withdrawal.

We ask that participants contact the study team (with the contact details provided above), if they become pregnant (or suspect they are pregnant) within 180 days of exposure to DPCP. In this event, with your consent, we will request that you have a pregnancy test within 7 days. If pregnancy is confirmed, the study team will advise on the need for any additional investigation or follow-up related to the potential exposure of the pregnancy to DPCP, and provide information regarding your participation in the study to the obstetric team at the hospital you register (book) with. We will also seek your consent to collect additional information about the outcome of the pregnancy. The occurrence of pregnancy and the pregnancy outcome will be reported anonymously (de-identified) to the study funder (J&J Innovative medicine).

Male participants with partners who are women of childbearing potential

There are no specific contraceptive requirements for male participants in this study.

Information collected in the event of pregnancy of the participant

If you become pregnant within 180 days of exposure to DPCP, we will request additional information from you, related to your pregnancy. This may be throughout your pregnancy, once your baby is born and for some time (up to 12 weeks) after the birth. The type of information requested may include the following:

- How and when the pregnancy was confirmed and conceived
- Expected delivery date
- Your medical history (if relevant to your health during pregnancy/your baby's health)
- A history of previous pregnancies
- Any medications you may have taken since you became pregnant
- Any procedures you have received (for example X-rays or surgery) since becoming pregnant
- Information on the progress and outcome of the pregnancy, including the diagnosis of any congenital abnormality or birth defect.

To collect this information, members of the study team will contact you around the following time-points:

- Week 12 of pregnancy
- 12 weeks after delivery

7. 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:

7.1. Potential risks of the challenge agents

Diphenylcyclopropenone (DPCP)

Expected common adverse effects are limited to mild responses at the application site e.g. stinging pain, redness, warmth, swelling, tenderness or itching; stronger reactions can produce small blisters. In very rare cases, more severe local and widespread skin reactions could occur. If this were to occur we would not give any further DPCP 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.

Frequency	***Side effect***
Very common (in more than 1 in 10 participants)	Local contact dermatitis (expected effect in 100% of participants) associated with redness and skin itching
Common (more than 1 in 100 but fewer than 1 in 10)	*Moderate itching or burning sensation, blistering*
Rare (fewer than1 in 1000)	Severe itching or burning sensation, blistering, swelling. Transient lymphadenopathy

	Contact urticaria or dermographism (wealing of skin when scratched) Widespread autoeczematisation Erythema multiforme-like reaction Hyperpigmentation, hypopigmentation, vitiligo

7.2. 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 study and complete all follow-up the total amount of blood taken will be about one cup (208mL). 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, tenderness, and occasionally feeling faint or actually fainting. Very rarely sites of blood tests can become infected and require antibiotic treatment. The blood tests will be taken by experienced members of the study team which should minimize the risks of side effects.

Skin punch biopsy

Skin punch biopsy is a commonly performed medical procedure. The potential risks include minor bruising, bleeding, and skin discomfort. A 4-6mm punch biopsy (equivalent to 2-3 grains of rice laid side-by-side) will be performed using local anaesthetic to reduce discomfort. The injection of anaesthetic can cause stinging during injection which fades very quickly as the anaesthetic takes effect. It is normal 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, 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. The risk of keloid scars is greater in individuals with darker skin tones. There is a very small risk 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.

8. What are the possible benefits of taking part?

By participating in this study, you will not directly receive any personal health benefit.

However, you will help us develop better tools to understand the immune system, thereby potentially benefiting other people with diseases caused by, or causing, malfunction of the immune system, e.g. eczema / atopic dermatitis.

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

We will not routinely send a letter to your GP informing them of your participation in the study. 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.

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

All information that is collected about you during the course of the study will be kept strictly confidential. It is available only to the study team. Responsible members of the University of Oxford may be given access to data for monitoring and/or audit of the study to ensure that the research is complying with applicable regulations.

To help keep your information confidential, your sample and any information recorded about you in this study will be protected by assigning you a study code, which will be used on all study documents and any electronic database(s). All documents will be stored securely and only accessible by study staff and authorised personnel. We will only use your NHS number where this is necessary to link to your NHS records. The study staff will safeguard the privacy of participants' personal data.

11. Will I be reimbursed for taking part?

You will be compensated for your travel costs, time and inconvenience related to taking part in this study. The total amount of compensation you receive will depend on your degree of involvement:

- £30 if you attend the screening visit, but do not enter the main study (either due to your choice or decision of the study team).
- £100 if you attend the screening visit, and take part in the visit 1 study procedures, but do not complete all study procedures and follow-up (e.g. If you withdraw from the study, either due to your choice or the decision of the study team).
- Pilot group: £440 for completing the screening and all study procedures and follow-up.
- Groups 1-3: £760 for completing the screening and all study procedures and follow-up.

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.

Note that the study payment includes compensation for travel expenses. We will not provide further reimbursement for travel expenses in addition this payment.

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).

12. What will happen to the samples I give?

Your samples will be used in a form that does not identify you, mainly by researchers based at NDORMS, University of Oxford but analyses for this study may take place in hospitals, universities, non-profit institutions, or commercial laboratories worldwide. Because they will be shared in a form that does not link back to you, it will not be possible to withdraw them after they are shared.

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 anonymised 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 do not agree to this, then any samples remaining at the end of this study will be destroyed—we will do this within 18 months of completion of the study.

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 or other identifiers. However, your DNA is unique to you so it can never be completely anonymous.

13. What will happen to my data?

Data protection regulation requires that we 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. It is the data controller, and is responsible for looking after your information and using it properly.

We will be using information provided by you in order to undertake this study and will use the minimum personally-identifiable information possible. We will keep your contact details for 12 months after the study has finished. Your consent form will be stored for 3 years after the study has finished, unless you agree to for your samples to be used in future research or for us to contact you about future research (see below). Your bank details will be stored for 7 years in accordance with University of Oxford financial policy.

If you agree to your samples being used in future research, your consent form will be held securely until the samples have been used up.

If you agree to your details being held to be contacted regarding future research, we will retain a copy of your consent form securely until such time as your details are removed from our database. We will keep the consent form and your details separate from one another and any research data.

Blood tests sent to local NHS Trust laboratories (including screening and visit 1 blood tests) will be registered using your NHS number, and will thus be visible to other healthcare professionals and retained indefinitely, but only members of the study team will be able to link these results to the other results related to your involvement in this study (via your unique study identification number).

Data stored in the TOPS database: Only staff at the NIHR Oxford Clinical Research Facility and other medicines research units can use the database. We may call other units, or they may call us, to check your details. Data entered in TOPS is retained for the minimum period required and this is determined based on whether you receive a dose of the study medicine or not. If you receive a dose of the study medicine, this data will be retained indefinitely in TOPS. If you do not receive a dose, your data will be retained in TOPS for two years. If we need to contact you about the study after you've finished it, but we can't because you've moved or lost contact with your GP, we might be able to trace you through the information in the database

Data protection regulation provides you with control over your personal data and how it is used. When you agree to your information being used in research, however, some of those rights may be limited in order for the research to be reliable and accurate. Further information about your rights with respect to your personal data is available at https://compliance.web.ox.ac.uk/individual-rights

You can find out more about how we use your information by contacting by contacting the Chief Investigator, Dr James Fullerton, or translational.pharmacology@ndorms.ox.ac.uk. The University's data protection officer can also be contacted at data.protection@admin.ox.ac.uk.

14. 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, simply by telling a member of the study team that you wish to do so (either verbally or in writing). There will be no penalty for withdrawing and this will not affect your legal rights. 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 or uploaded to open access research repositories, it will not be withdrawn or erased in order to maintain the scientific integrity of the study. Any data entered into TOPS will be retained if you withdraw from the study.

15. What will happen to the results of this study?

The results of this project will be disseminated via standard scientific channels: publication in scientific journals, poster and oral presentations at scientific conferences. Anonymised data may be uploaded to open access research repositories. 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. When you enter the study we will ask if you would like to be informed of the results when they become available, and how you would like to receive them (e.g. email, post, and/or link to a website).

16. What if we find something unexpected?

If we incidentally find an issue during the screening or during study that may be important (e.g. high blood pressure, blood test abnormalities) we will inform you of this. Depending on the results, you may not be eligible for the study, and you may be advised to contact your GP for further tests or review. We will also provide copies of these results to your GP. In some cases, the study doctor may simply recommend that the blood tests be rechecked on a later date, before deciding on eligibility. You will be compensated for this additional blood test on a pro-rata basis.

17. 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 James Fullerton (contact details at the top of this form) or you may contact the University of Oxford Research Governance, Ethics & Assurance (RGEA) office on 01865 616480, or the director of RGEA, email 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.

18. How have patients and the public been involved in this study?

Our research group works closely with our patient engagement network ('OPEN ARMS') to ensure that our research can truly benefit people living with inflammatory and immune system conditions. We will work with OPEN ARMS to communicate the results of this study (e.g. via newsletters and public 'meet the researcher' events) with the aim of highlighting how research involving healthy volunteers can contribute to our understanding of different immune system diseases and the development of new treatments. More information about OPEN ARMS can be found at https://www.ndorms.ox.ac.uk/get-involved/open-arms-1/open-arms

19. Who is organising and funding the study?

- This study is sponsored by the University of Oxford.
- It is being funded by J&J Innovative Medicine.
- 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 a favourable opinion by London – Hampstead Research Ethics Committee (25/LO/0288).

21. Participation in future research:

We will ask you if you are willing to be approached to be involved in future studies. Your contact details will be held separately on password protected computer servers maintained by NDORMS, University of Oxford. Agreeing to be contacted does not oblige you to take part in future research, and you can be removed from this register at any time you wish.

22. Further information and contact details:

Please contact us at translationalpharmacology@ndorms.ox.ac.uk if you would like further information or to ask any questions. Alternative you can contact directly Dr James Fullerton (Chief Investigator and Clinical Pharmacologist, james.fullerton@ndorms.ox.ac.uk) or Dr Philip Drennan (Co-Investigator, Clinical Pharmacologist, and Clinical Research Fellow, NDORMS, philip.drennan@ndorms.ox.ac.uk).

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