Amending an Approved Application

Should you wish to make an amendment to an approved study, you will need to submit an 'amendment request' for the consideration of the Chair of the UCL Research Ethics Committee. Applications can only be amended **after** ethical approval has been granted.

You will need to apply for an amendment approval if you wish to:

1. Add a new participant group;
2. Add a new research method;
3. Ask for additional data from your existing participants;
4. Remove a group of participants or a research method from the project, and have not yet commenced that part of the project;
5. Apply for an extension to your current ethical approval.

If you need to apply for an amendment approval, please complete the Amendment Approval Request Form on the next page.

When completing the form, please ensure you do the following:

- Clearly explain what the amendment you wish to make is, and the justification for making the change.
- Insert details of any ethical issues raised by the proposed amendments.
- Include all relevant information regarding the change so that the Chair can make an informed decision, and submit a copy of the sections of your application that have changed with all changes highlighted/underlined for clarity.
- You do not need to submit your original application in full again. However, if the changes you wish to make alters several sections of your application form, you are advised to submit this.

Please email a signed electronic copy to the REC Administrator: ethics@ucl.ac.uk

Amendment requests are generally considered within 5-7 days of submission.

Amendment Approval Request Form

1	**Project ID Number:** 5060/003	**Name and Address of Principal Investigator:** Dr James Fullerton Applied Biomedical Engineering Group (ABEG), Division of Medicine, UCL Rayne Building, 5 University Street, London, WC1E 6JF
2	**Project Title:** Comparison and characterisation of two skin blister models of inflammation	
3	**Type of Amendment/s (tick as appropriate)** Research procedure/protocol (including research instruments) ☒ Participant group ☐ Sponsorship/collaborators ☒ Extension to approval needed (extensions are given for one year) ☐ Information Sheet/s ☒ Consent form/s ☐ Other recruitment documents ☒ Principal researcher/medical supervisor* ☐ Other ☐ **Additions to the research team other than the principal researcher, student supervisor and medical supervisor do not need to be submitted as amendments but a complete list should be available upon request **	
4	**Justification** (give the reasons why the amendment/s are needed) A new collaborator (Prof Adam Gibson, Dept of Medical Physics and Biomedical Engineering) was found who has expertise on multi-spectral imaging, a technique that complements our existing suite of skin assessments. His involvement means we now have access to specialist equipment in the Digitation Suite on the UCL Special Collections (Science Library). Participants will visit this facility to have pre/post blistering multi-spectral images of their forearms taken. Image acquisition is non-invasive, not anticipated to add any additional risk nor raise any new ethical concern. Due to the need to co-ordinate availability of multiple facilities and items of equipment we have made it clear that some or all the proposed skin assessments will be conducted as opposed to the full set in every participant. We realise we have under-appreciated the importance of collecting data regarding the participant experience of both blister techniques. This would clearly form a key point of reference for future researchers deciding which technique to select. As such we have designed a RedCap questionnaire to be completed after completion of all study procedures exploring this. The questionnaire will be completed online and take only 5-10mins. Due to the additional investigation and based on learning from participants completing the study to date, we have realised that we had underestimated the time needed to carry out all procedures and have increased this range from 5-10 to 5-15 hours to ensure accuracy. We do not believe additional compensation is required to compensate for this (already £200).	
5	**Details of Amendments** (provide full details of each amendment requested, state where the changes have been made and attach all amended and new documentation) Small changes to be made to the application, PIS and adverts relating to the reasons explained above. The new questionnaire is attached separately. Details of all major changes are detailed below (new text	

underlined), while typos and clarifications were corrected and documents with tracked changes are sent in attachment.

Application Section A3: Adding new collaborator details

Full Name: Adam Gibson	
Position Held: Professor of Medical Physics, with secondment as Professor of Heritage Science	
Name and Address of Department: *Medical Physics and Biomedical Engineering, London WC1 6BT*	Email: adam.gibson@ucl.ac.uk
	Telephone:
	Fax:

Application Section B2: Adding new analytical method and clarifying the self-reported information needed:

Both studies will additionally include a) laser doppler measurement of local blood flow at all time points, b) characterisation of the skin barrier function via some or all the following methods i) tape stripping (ii) transepidermal water loss measurement (TEWL) (iii) Confocal Raman Spectroscopic (CRS) measurment of skin thickness and skin hydration c) recording of anatomical changes to skin and vasculature by high definition multi-spectral photography d) self-assessment of blister healing and any clinical symptoms or concomitant medication on diary cards and (e) participant-performed photography of the site (days 1, 3, 5, 7, 14, 28, 56, 84) f) questionnaire for participant feedback for each of the methods. Laser doppler, tape stripping, TEWL and CRS measurements in healthy human subjects all represent safe, established techniques that have previously been approved by UCL REC for use in previous studies (e.g. 13271/001, 14109/001).

Application Section B3: Adding location for image collection (UCL Digitisation Suite)

Division of Medicine, UCL; School of Pharmacy, UCL and the UCL Digitation Suite (UCL Special Collections, Science Library)

Application Section B6: Increasing the time commitments requested from subjects

Payment has been set at £200/subject to offer adequate compensation for time (estimated to total ~5-15 hours inc. travel), inconvenience and the interventional nature of the study.

Application Section C4: Increasing the time commitments requested from subjects

We estimate that the first visit to obtain consent will take approximately 1 hour, a visit to generate blisters should take approximately 4 hours and a visit to harvest the blisters and collect blood to take another hour. In total the subjects will be present in the unit for approximately 15 hours in Study A (~17 hours with travel and follow-up) and 5-6 hours in Study B.

Both advert and email advert: Increasing the time commitments requested from subjects

The study will require between 5-15 hours of your time and take place at UCL.

PIS section 'Name and Contact Details of the Researcher(s)' : Adding new collaborator

Professor Adam Gibson, Medical Physics and Biomedical Engineering, London WC1 6BT

PIS section 'What will happen to me if I take part?': Adding skin imaging to the list of tests, changing estimated time for blister formation and adding questionnaire to the follow-up assessments.

iv) Multispectral imaging to photograph the forearm under different illumination wavelengths and determine whether this can provide a means of non-invasively monitoring the formation of blisters in human volunteers.

	The negative pressure will gradually be increased then decreased (according to a protocol, but modified on an individual basis) to gradually form a blister over approximately 2 hours. In addition, you will be sent an online questionnaire on completion of the procedures to obtain your feedback on both methods used to raise the blisters. **New document – Participant questionnaire:** Document attached for review
6	**Ethical Considerations** (insert details of any ethical issues raised by the proposed amendment/s) The extra analysis proposed is hi resolution imaging of subjects forearms. 'Standard' photographs were already included in the original application so do not amount to a new intervention, nor raise new ethical considerations. The revised time requests from the participants does not seem sufficiently different to impact the original proposed compensation.
7	**Other Information** (provide any other information which you believe should be taken into account during ethical review of the proposed changes) None

Declaration (to be signed by the Principal Researcher)

- I confirm that the information in this form is accurate to the best of my knowledge and I take full responsibility for it.
- I consider that it would be reasonable for the proposed amendments to be implemented.
- For student projects, I confirm that my supervisor has approved my proposed modifications.

Signature 

Date: 14/2/20

NOTE TO APPLICANTS: IT IS IMPORTANT FOR YOU TO INCLUDE ALL RELEVANT INFORMATION ABOUT YOUR RESEARCH IN THIS APPLICATION FORM AS YOUR ETHICAL APPROVAL WILL BE BASED ON THIS FORM. THEREFORE ANYTHING NOT INCLUDED WILL NOT BE PART OF ANY ETHICAL APPROVAL.

YOU SHOULD READ THE ETHICS APPLICATION GUIDELINES AND HAVE THEM AVAILABLE AS YOU COMPLETE THIS FORM.

APPLICATION FORM

SECTION A APPLICATION FOR ETHICAL REVIEW: HIGH RISK

A1

Project Title: Comparison and characterisation of two skin blister models of inflammation

Date of Submission: 27June2019	Proposed Data Collection Start Date: 01Aug2019
UCL Ethics Project ID Number: 5060/003	Proposed Data Collection End Date: 31Aug2020

Is this application for continuation of a research project that already has ethical approval? ***For example, a preliminary/pilot study has been completed and this is an application for a follow-up project? If yes, please provide the information requested below.***

Project ID for the previous study: N/A

A2

Principal Researcher

Please note that a student – undergraduate, postgraduate or research postgraduate cannot be the Principal Researcher for Ethics purposes.

Full Name: Dr James Fullerton	Position Held: NIHR Clinical Lecturer
Name and Address of Department: Applied Biomedical Engineering Group (ABEG), Division of Medicine, UCL Rayne Building, 5 University Street, London, WC1E 6JF	Email: j.fullerton@ucl.ac.uk
	Telephone: 07803 729439
	Fax:

Declaration To be Signed by the Principal Researcher

- I have met with and advised the student on the ethical aspects of this project design *(applicable only if the Principal Researcher is not also the Applicant).*
- I understand that it is a UCL requirement for both students & staff researchers to undergo Disclosure and Barring Service (DBS) Checks when working in controlled or regulated activity with children, young people or vulnerable adults. The required DBS Check Disclosure Number(s) is: N/A
- I have obtained approval from the UCL Data Protection Officer stating that the research project is compliant with the General Data Protection Regulation 2018. My Data Protection Registration Number is:
- I am satisfied that the research complies with current professional, departmental and university guidelines including UCL's Risk Assessment Procedures and insurance arrangements.
- I undertake to complete and submit the 'Continuing Review Approval Form' on an annual basis to the UCL Research Ethics Committee.
- I will ensure that changes in approved research protocols are reported promptly and are not initiated without approval by the UCL Research Ethics Committee, except when necessary to eliminate apparent immediate hazards to the participant.
- I will ensure that all adverse or unforeseen problems arising from the research project are reported in a timely fashion to the UCL Research Ethics Committee.
- I will undertake to provide notification when the study is complete and if it fails to start or is abandoned.

SIGNATUR [redacted] **DATE:** 13Feb2019

A3 **Applicant(s) Details** *(if Applicant is not the Principal Researcher e.g. student details):*

Full Name: João Joaquim Dias de Matos Oliveira		
Position Held: PhD student		
Name and Address of Department: *Applied Biomedical Engineering Group (ABEG), Division of Medicine, UCL Rayne Building, 5 University Street, London, WC1E 6JF*	Email: joao.oliveira.18@ucl.ac.uk	
	Telephone: 07952 089135	
	Fax:	
Full Name: Richard Day		
Position Held: Professor of Regenerative Medicine		
Name and Address of Department: *Applied Biomedical Engineering Group (ABEG), Division of Medicine, UCL Rayne Building, 5 University Street, London, WC1E 6JF*	Email: r.m.day@ucl.ac.uk	
	Telephone: 020 3108 2183	
	Fax:	
Full Name: Majella Lane		
Position Held: Senior Lecturer in Pharmaceutics		
Name and Address of Department: *UCL School of Pharmacy, 29-39 Brunswick Square, London, WC1N 1AX*	Email: m.lane@ucl.ac.uk	
	Telephone: 0207 7535821	
	Fax:	
Full Name: Adam Gibson		
Position Held: Professor of Medical Physics, with secondment as Professor of Heritage Science		
Name and Address of Department: *Medical Physics and Biomedical Engineering, London WC1 6BT*	Email: adam.gibson@ucl.ac.uk	
	Telephone:	
	Fax:	

A4 **Sponsor/ Other Organisations Involved and Funding**

a) Sponsor: ☒ **UCL** ☐ **Other institution**
If your project is sponsored by an institution other than UCL please provide details:

b) Other Organisations: If your study involves another organisation, please provide details. *Evidence that the relevant authority has given permission should be attached or confirmation provided that this will be available upon request.*

c) Funding: What are the sources of funding for this study and will the study result in financial payment or payment in kind to the department or College? *If study is funded solely by UCL this should be stated, the section should not be left blank.* NIHR Surgical MedTech Cooperative Proof of Concept Award

A5

Signature of Head of Department [or Chair of your Departmental Research Ethics Committee/Departmental Ethics Lead]
(This must not be the same signature as the Principal Researcher)

A. I have discussed this project with the principal researcher who is suitably qualified to carry out this research and I approve it.

I am satisfied that *[please highlight as appropriate]*:

(1) Data Protection registration:

- **has been satisfactorily completed**
- **has been initiated**
- **is not required**

(2) a risk assessment:

- **has been satisfactorily completed**
- **has been initiated**

(3) appropriate insurance arrangements are in place and appropriate sponsorship [funding] has been approved and is in place to complete the study. ☒ **Yes** ☐ **No**

(4) a Disclosure and Barring Service check(s):

- **has been satisfactorily completed**
- **has been initiated**
- **is not required**

Links to details of UCL's policies on the above can be found at: http://ethics.grad.ucl.ac.uk/procedures.php

****If any of the above checks are not required please clarify why below.**

DBS not required as neither underage nor vulnerable individuals will be recruited. All participants will provide full informed consent.

PRINT NAME: Prof Derek Gilroy

SIGNATURE: [redacted] **DATE:** 13Feb2019

SECTION B DETAILS OF THE PROJECT

****It is essential that Sections B1 and B2 are completed in simple understandable lay language that a non-expert could understand or you risk your project being rejected**

B1 **Please provide a brief summary of the project in simple lay person's prose outlining the intended value of the project, giving necessary scientific background.** *(max 500 words)*.

Inflammation is an evolutionarily conserved response to both external stimuli (e.g. bacteria) or to internal warning signals generated, for example, by cell damage. Designed to protect the host organism, if unchecked or unbalanced, inflammation can also contribute to disease. Controlled in vivo models in healthy human volunteers, where local inflammation is induced in a safe, consistent way, are useful tools to understand the biological process that regulate the magnitude and duration of the inflammatory response and assess the effect of drugs designed to modify it. The skin, as an easily accessible site, has commonly been employed for this purpose and the most widely used system is blistering (as they may be burst and the exudate collected) induced by either negative pressure (suction) or a chemical (cantharidin).

Whilst both means of producing a blister have been widely employed (including at UCL e.g. 5061/001, 2907/002) and are well tolerated, their comparability is unknown. As such it is unclear whether a) results obtained using one can be extrapolated to the other b) whether one is better suited to certain purposes (e.g. exploring the acute or resolution phase) and c) which demonstrates greater intra and inter subject variability (vital for drug development). It is also unclear what biophysical properties of the skin contribute to this variability and whether these can be controlled for. To answer these questions we intend to conduct - for the first time - side-by side analysis of the two methods of inducing skin blisters in the same subjects (healthy male volunteers) at different time points (Study A) along with prior quantification of their skin barrier function. We further intend to assess the blistering methods relative ability to detect the effect of known topical anti-inflammatory drugs (administration of 1% hydrocortisone cream or 2.32% diclofenac gel to the skin) (Study B).

It is anticipated that comparison and characterisation of these models will inform the design of future experimental medicine and early phase drug discovery studies, allowing selection of the optimal approach.

B2 **Briefly characterise in simple lay person's prose the research protocol, type of procedure and/or research methodology (e.g. observational, survey research, experimental). Give details of any samples or measurements to be taken** *(max 500 words).*

Non-smoking, healthy male volunteers aged 18 to 50 years will be recruited. Participants will be excluded if they have any medical problems or take regular medication (prescription or over-the-counter). Patients with tattoos, damaged skin, existing scars (all at the blistering site) or darker skin tone (Fitzpatrick scale V-VI) will also be excluded, the latter due to a higher risk of lasting skin discoloration following blistering.

The workplan will be composed of two studies: Study A, intra and inter-individual comparison and characterisation including over time, and Study B, detection of pharmacological effect. Participants will not be allowed to volunteer for both Studies.

Study A

10 volunteers will participate in three near-identical sessions over a 3 week period. In session 1, 2 blisters will be induced on the volar (hairless) surface of each forearm; one suction, one cantharidin (4 total). Suction blisters will be created using negative pressure equipment (NP-4, Electronic Diversities, USA) and a validated step-wise protocol. Chemical blisters will be raised using cantharidin (Cantharone - Dormer Laboratories, Inc.), a vesicant extracted from beetles (medically employed in the treatment of warts) using an established technique. Blisters will develop on the day (suction) or overnight (chemical), and will be protected by a dressing. On the second day of the session (24hrs post-blister induction), the blister will be punctured with a sterile needle and its contents collected for analysis of both the cells and the fluid. In session 2 and 3 (7 and 14 days post session 1 respectively) blisters will again be induced but on only one arm at each timepoint (2 per timepoint, 5 particpants right then left arm, 5 left then right, 8 blisters/participant in total). Blood (~10mLs) will be collected at each time point to assess for systemic

effect of the intervention (not anticipated) or inflammation (illness) which is not clinically reported.

Study B

12 volunteers will be asked to apply both a known anti-inflammatory treatment and control agent to their forearms prior to blister induction (as per Session 1). 6 will apply 1% hydrocortisone cream (a steroid) to one forearm (3 left, 3 right) and moisturiser (white soft paraffin) to the other for a week. 6 will apply 2.32% diclofenac diethylammonium cream [Voltarol Emulgel] (a non-steroidal anti-inflammatory) instead of the hydrocortisone. Both active agents are regarded as safe, are available over-the-counter without prescription and will be applied on the same schedule (twice-daily, as recommended). Both the particpant and investigator undertaking the blistering process and subsequent analysis will be blinded to treatment allocation, the topical agents being supplied in tubes obscuring their contents and labelled A and B (by the PI).

Both studies will additionally include a) laser doppler measurement of local blood flow at all time points, b) characterisation of the skin barrier function via some or all the following methods i) tape stripping (ii) transepidermal water loss measurement (TEWL) (iii) Confocal Raman Spectroscopic (CRS) measurment of skin thickness and skin hydration c) recording of anatomical changes to skin and vasculature by high definition multi-spectrum photography d) auto assessment of blister healing and any clinical symptoms or concomitant medication on diary cards and (e) participant-performed photography of the site (days 1, 3, 5, 7, 14, 28, 56, 84) f) questionnaire for participant feedback for each of the methods. Laser doppler, tape stripping, TEWL and CRS measurements in healthy human subjects all represent safe, established techniques that have previously been approved by UCL REC for use in previous studies (e.g. 13271/001, 14109/001).

Attach any questionnaires, psychological tests, etc. (a standardised questionnaire does not need to be attached, but please provide the name and details of the questionnaire together with a published reference to its prior usage).

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B3 **Where will the study take place (please provide name of institution/department)?**
If the study is to be carried out overseas, what steps have been taken to secure research and ethical permission in the study country? Is the research compliant with Data Protection legislation in the country concerned or is it compliant with the General Data Protection Regulation 2018?

Division of Medicine, UCL; School of Pharmacy, UCL and the UCL Digitation Suite (UCL Special collections, science library)

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B4 **Have collaborating departments whose resources will be needed been informed and agreed to participate?**
Attach any relevant correspondence.

N/A

B5 **How will the results be disseminated, including communication of results with research participants?**
The results will be published in peer-reviewed medical/scientific journals and/or presented at scientific conferences. Participants will have the option to have the finalised manuscript sent to them by email.

B6 **Please outline any ethical issues that might arise from the proposed study and how they are be addressed.** *Please note that all research projects have some ethical considerations so do not leave this section blank.*

a) Reimbursement. Participants will be recruited by email (using generic UCL mailing lists), local advertising through posters and word-of-mouth. Payment has been set at £200/subject to offer adequate compensation for time (estimated to total ~5-15 hours inc. travel), inconvenience and the interventional nature of the study. Whilst participants in Study B require fewer visits they experience greater inconvenience due to twice daily application of the topical drug for a week. Participants may only partake in one Study so as to avoid harm and over-volunteering.

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b) Cosmetic. The volunteers may develop a hyper or hypopigmented area on the forearm at the site of blister induction. It is expected that for subjects with darker skin pigmentation, a transient discoloration could persist for a longer period of time and be more noticeable. Given this risk, volunteers with Fitzpatrick scale V-VI skin will be excluded. Previous studies have demonstrated that altered pigmentation normally resolves within 4-6 weeks, however may take several months to fully return to normal. In our experience scarring does not occur but this risk will be stated explicitly. These aspects have been clearly identified in the participant information leaflet, and all participants will be verbally informed of this well in advance of the study.

c) Health risk. Venupuncture and blister induction carry a small risk of infection (as the skin is broken). This may be increased via prior hydrocortisone application due to its anti-inflammatory properties. Venupuncture may additionally cause mild discomfort. All procedures will be carried out using aseptic non-touch technique where possible by experienced practitioners, trained in their performance. Participants will be followed up to ensure adequate healing and the research team includes a qualified clinician (PI). If any complications are suspected they will be referred to their GP or acute medical services as appropriate.

d) Medication exposure. Cantharidin is a recognised medical treatment and has been safely employed for induction of skin blisters for >20 years. It will be obtained from Dormer Laboratories Inc. - as in previous studies - where it has been manufactured to GMP standards. Hydrocortisone 1% cream and diclofenac 2.32% gel are commonly used topical anti-inflammatory medications. The proposed regimen (twice daily application for 1 week) is the standard recommended course for both treatments. Both are over-the-counter medication and will be purchased from Boots Pharmacy. No systemic consequences or side effects are anticipated from either agent, however they will be provided with their standard information leaflets and allergy status (re: diclofenac) confirmed prior to provision.

e) Data protection. All data will be pseudo-anonymised and linkable only via a master document to which the study team has access. Individuals will not be able to be identified via the forearm photos they are asked to submit.

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SECTION C DETAILS OF PARTICIPANTS

C1 **Participants to be studied**

C1a. Number of volunteers:	22 completed subjects (10 Study A, 12 Study B), 10 reserve
Upper age limit:	50
Lower age limit:	18

C1b. Please justify the age range and sample size:

In Study A, we are intending to characterise the inter- and intra-subject variability of the blistering methods. The sample size selected is based upon previously published experimental work and our group's experience of the blister models (more than 500 raised). Given the ability to perform within-subject statistical comparisons and large signal size, 10 participants will provide sufficient power.

In Study B, data from animal models (cantharidin-induced ear inflammation) indicate that topical steroids elicit a profound effect on the inflammatory response. As such, we estimate that 6 subjects per treatment arm (steroid/control vs. diclofenac/control) will provide sufficient data to reliably detect an effect.

To account for the possibility of a) drop-out b) volunteer acute illness c) inadvertent blister damage and d) treatment non-compliance (in B) we may require recruitment of up to 10 additional volunteers to obtain the requisite 22 complete datasets (i.e. up to 32 volunteers total)

C2 **Accessing/Using Pre-Collected Data:**
If you are using data or information held by a third party, please explain how you will obtain this. You should confirm that the information has been obtained in accordance with the General Data Protection Regulation 2018.

N/A

C3 **Will the research include children or vulnerable adults such as individuals with a learning disability or cognitive impairment or individuals in a dependent or unequal relationship?** ☐ **Yes** ☒ **No**

How will you ensure that participants in these groups are competent to give consent to take part in this study? *If you have relevant correspondence, please attach it.*

C4 **Will payment or any other incentive, such as gift service or free services, be made to any research participant?**

☒ **Yes** ☐ **No**

If yes, please specify the level of payment to be made and/or the source of the funds/gift/free service to be used.

Payment will be £200 for completion of either Study.

Please justify the payment/other incentive you intend to offer.

Payment will compensate the subject's time and travel expenses taken for participating in the study plus the mild discomfort and transient cosmetic changes caused by the procedure. We estimate that the first visit to obtain consent will take approximately 1 hour, a visit to generate blisters should take approximately 4 hours and a visit to harvest the blisters and collect blood to take another hour. In total the subjects will be present in the unit for approximately 15 hours in Study A (~17 hours with travel and follow-up) and 5-6 hours in Study B. For Part B, subjects will also be asked to comply with a strict regime of drug application. Both studies will also require the completion of a self-report of blister healing and photo diary, taking additional time.

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C5 **Recruitment**

(i) Describe how potential participants will be identified:

Self-identification and word-of-mouth. Posters will be placed around UCL, an advertising email will be sent to UCL students via generic lists describing the study and potentially eligible individuals working in the Division of Medicine will be directly approached.

(ii) Describe how potential participants will be approached:

Contact details of study investigators are included on the advertising poster and email. Interested participants will be encouraged to email the PI and Applicant. Once contact is made and eligibility ascertained the PIS will be provided and a formal meeting arranged.

(iii) Describe how participants will be recruited:

Participants will be asked to read the PIS and consider whether they want to take part in the study. At a subsequent meeting the study will be explained in detail to include design, timelines, potential side effects, commitments, expenses and the right not to participate and to withdraw at any time without penalty. If they are happy to proceed, an informed consent form will be signed and an appointment made to commence the study interventions.

Attach recruitment emails/adverts/webpages. A data protection disclaimer should be included in the text of such literature.

C6

Will the participants participate on a fully voluntary basis? ☒ **Yes** ☐ **No**

Will UCL students be involved as participants in the research project? ☒ **Yes** ☐ **No**

If yes, care must be taken to ensure that they are recruited in such a way that they do not feel any obligation to a teacher or member of staff to participate.

Please state how you will bring to the attention of the participants their right to withdraw from the study without penalty?

The right to withdraw will be emphasised verbally during the consenting process as well as in the PIS. Awareness of this right will be indicated on the consent form.

C7

CONSENT

Please describe the process you will use when seeking and obtaining consent.

After confirmation of eligibility, potential volunteers will be provided with a copy of the PIS in advance (>24hrs) of a formal meeting where the study will be explained and - if they are happy to proceed - consent taken. This will allow time to read the details of the study, formulate questions and seek external advice if needed. At the meeting, all details of the study will be discussed including procedures, timelines, required visits to UCL as well as the potential side effects of participation. It will be highlighted that volunteers are under no obligation to participate and that they can withdraw at any time without penalty. Potential participants will be encouraged to ask the Investigators any questions. If they are willing to participate they will be asked to sign a consent form. If they want more time to consider participation this will be provided along with the opportunity to seek further clarification/more information.

A copy of your participant information sheet(s) and consent form(s) must be attached to this application. For your convenience proformas are provided in Appendix I. These should be filled in and modified as necessary.

In cases where it is not proposed to obtain the participants informed consent, please explain why below.

N/A

C8

Will any form of deception be used that raises ethical issues? If so, please explain.

No. Subjects will be blinded as to which arm they are applying the active compound but they will a) be aware of which drug they are applying and b) the possible side effects

C9

Will you provide a full debriefing at the end of the data collection phase? ☐ **Yes** ☒ **No**

If 'No', please explain why below.

The outputs for this study will relate to group-level data on each model rather than individual responses. These data are not likely to be of interest to the volunteers taking part on the study as they have no direct clinical or health relevance. All data is expected to be disseminated in the scientific literature and participants will be offered the chance to receive a copy of these manuscripts.

C10

Information Sheets And Consent Forms: Appendix I

A poorly written Information Sheet(s) and Consent Form(s) that lack clarity and simplicity frequently delay ethics approval of research projects. The wording and content of the Information Sheet and Consent Form must be appropriate to the age and educational level of the research participants and clearly state in simple non-technical language what the participant is agreeing to. Use the active voice e.g. "we will book" rather than "bookings will be made". Refer to participants as "you" and yourself as "I" or "we". An appropriate translation of the Forms should be provided where the first language of the participants is not English. If you have different

	participant groups you should provide Information Sheets and Consent Forms as appropriate (e.g. one for children and one for parents/guardians) using the templates provided in Appendix I. Where children are of a reading age, a written Information Sheet should be provided. When participants cannot read or the use of forms would be inappropriate, a description of the verbal information to be provided should be given. Where possible please ensure that you trial the forms on an age-appropriate person before you submit your application.

SECTION D: APPROPRIATE SAFEGUARDS, DATA STORAGE AND SECURITY

D1

Will the research involve the collection and/or use of personal data?
☒ **Yes** ☐ **No**

Personal data *is data which relates to a living individual who can be identified from that data OR from the data and other information that is either currently held, or will be held by the data controller (the researcher).*

This includes:

- *any expression of opinion about the individual and any intentions of the data controller or any other person toward the individual.*
- *sensor, location or visual data which may reveal information that enables the identification of a face, address, etc (some postcodes cover only one property).*
- *combinations of data which may reveal identifiable data, such as names, email/postal addresses, date of birth, ethnicity, descriptions of health diagnosis or conditions, computer IP address (if relating to a device with a single user).*

If yes, is the research collecting or using special category data as defined by the GDPR 2018, for example participants' :

- sexual behaviour or orientation
- political opinions or philosophical beliefs
- violence towards them
- abuse or exploitation
- mental or physical health
- gender or ethnic status
- trade union membership

- **data which might be considered sensitive in some countries, cultures or contexts?**

If yes, state whether explicit consent will be sought for its use and what data management measures are in place to adequately manage and protect the data.

A statement of good health i.e. denial of diagnosed medical conditions and lack of regular medication taking will be required for eligibility along with indication of known drug allergies but not formally recorded or verified. No additional details of health status or other SCPD will be taken.

D2

<u>During the Project</u> (including the write up and dissemination period)

State what types of data will be generated from this project (i.e. transcripts, videos, photos, audio tapes, field notes, etc).

Data will consist of 4 types: i) Personal (age, name, email address, brief medical history [statement of good health and lack of medication use]) ii) biological (derived from blood and blister fluid) iii) questionnaire/self-report on blister healing and iv) photos of the forearms

How will data be stored, including where and for how long? This includes all hard copy and electronic data on laptops, share drives, usb/mobile devices.

Electronic data will be stored on secure UCL servers, or where needed, password-protected, firevault encrypted personal laptops. Paper records (questionnaire/diary card) will be kept in locked filing cabinets on secure UCL premises. All data will be pseudo-anonymised via allocation of a study number and only linkable to an individual via a password protected master list kept on secure UCL servers. Only the PI and Applicant will have access to this document

After completion of the study the master sheet will be deleted to fully anonymise both the raw and analysed data. This will be stored indefinitely for future comparison and any necessitated retrospective analysis.

	Biological samples will retained for a maximum of 5 years after completion of the study (est. 2025) **Who will have access to the data, including advisory groups and during transcription?** Only the study team - and if required - the Sponsor will have access to the data

D3	**Will personal data be processed or be sent outside of the European Economic Area (EEA)*?** **If yes,** please confirm that there are adequate levels of protection in compliance with the General Data Protection Regulation 2018 and state what these arrangements are below. No

D4	**<u>After the Project</u>** **What data will be stored and how will you keep it secure?** As above. All data will be fully anonymised after completion of the study and kept indefinitely. After transcription of the paper records to an electronic format they will be destroyed **Where will the data be stored and who will have access?** UCL servers with access only by the study team. There may be the need to share fully anonymised data with collaborators in the future **Will the data be securely deleted?** **If yes,** please state when will this occur: Paper records at the end of the study, following transcription. Electronic records will not be deleted but instead fully anonymised

D5	**Will the data be archived for use by other researchers?** ☒ **Yes** ☐ **No** If **Yes**, please describe provide further details including whether researchers outside the EEA will be given access. Whilst this is not anticipated (this being a small, discrete study) we will store the anonymised data for future comparison, necessitated retrospective analysis or to enable collaborative research.

SECTION E: DETAILS OF RISKS AND BENEFITS TO THE RESEARCHER AND THE RESEARCHED

E1 **Please state briefly any precautions being taken to protect the health and safety of researchers and others associated with the project (as distinct from the research participants).**

Risk assessments will be undertaken prior to commencement and any required mitigation activities completed. Cantharidin is not expected to pose significant occupational safety risk to site staff under proposed conditions of use and administration. Adequate precautions will be taken to avoid direct eye or skin contact and the generation of aerosols or mists. Venupuncture will be undertaken by appropriately trained individuals using ANTT. All vaccinations mandated by Occupational Health will be completed. All procedures and visits will take place at UCL in working hours.

E2 **Will these participants participate in any activities that may be potentially stressful or harmful in connection with this research?** ☒ **Yes** ☐ **No**

If **Yes**, please describe the nature of the risk or stress and how you will minimise and monitor it.

As discussed, the blistering process can be associated with minor, temporary skin discoloration. Whilst no scarring has previously been observed we will explicitly state in the PIS that this cannot be guaranteed. There is also a very small risk of infection. Venupuncture can cause mild discomfort. The Investigators are very experienced with all procedures associated with the proposed work and include a Clinician. Appropriate protective equipment, sterile dressings and technique will be employed throughout. All subjects will be followed up to ensure safe resolution and healing of the blister lesions. Laser doppler and measures of skin barrier function are non-harmful. Cantharidin is potentially toxic but not at the dilutions, manner and quantity employed here. Both of the anti-inflammatory drugs employed are available over-the-counter and are being used in the recommended manner. As such we do not anticipate a significant risk of side effects.

E3 **Will group or individual interviews/questionnaires raise any topics or issues that might be sensitive, embarrassing or upsetting for participants?**

If **Yes,** please explain how you will deal with this.

No.

E4 **Please describe any expected benefits to the participant.**

There are no direct benefits for the participants.

E5

Specify whether the following procedures are involved:

Any invasive procedure(s) ☒ **Yes** ☐ **No**

Physical contact ☒ **Yes** ☐ **No**

Any procedure(s) that may cause mental distress ☐ **Yes** ☒ **No**

Please state briefly any precautions being taken to protect the health and safety of the research participants.

There is a limited invasiveness and physical contact during both the blister raising procedure and measurements of skin barrier function. All procedures will be carried out on the forearm on UCL premises by experienced scientists. Phlebotomy will be carried out by qualified clinicians.

E6

Does the research involve the use of drugs? ☒ **Yes** ☐ **No**

If **Yes**, please name the drug/product and its intended use in the research and then complete Appendix II

Hydrocortisone 1% is a commonly used drug, available over-the-counter for treatment of mild skin conditions such as eczema, contact dermatitis, insect bites or stings and rashes. This drug should elicit significant effects on the formation of the blisters and the migration of cells and fluid to the compartment whilst having no systemic effect. Used for the duration described, no harm or side effects from application are anticipated

Diclofenac diethylammonium 2.32% (Voltarol Emulgel) is again widely employed (predominantly for relief of joint aches and pains),is licenced as a safe medicine, and will be used as per standard recommendations and is expected to have a significant biological effect

Soft white paraffin is commonly employed as a moisturizer and is not thought to be 'active' pharmacologically

Does the project involve the use of genetically modified materials? ☐ **Yes** ☒ **No**

If **Yes**, has approval from the Genetic Modification Safety Committee been obtained for work? ☐ Yes ☐ No

If **Yes**, please quote the Genetic Modification Reference Number: N/A

E7

Will any non-ionising radiation be used on the research participant(s)? ☐ **Yes** ☒ **No**

If **Yes**, please complete Appendix III.

E8

Are you using a medical device in the UK that is CE-marked and is being used within its product indication? ☐**Yes** ☒ **No**

If **Yes**, please complete Appendix IV.

CHECKLIST

Documents to be Attached to Application Form (if applicable)	Tick if attached
Section B: Details of the Project	
• Questionnaire(s) / Psychological Tests	☒
• Relevant correspondence relating to involvement of collaborating department/s and agreed participation in the research i.e. approval letters to gatekeepers seeking permission to do research on their premises/ in their company etc.	☐
Section C: Details of Participants	
• Parental/guardian consent form for research involving participants under 18	☐
• Participant/s information sheet	☒
• Participant/s consent form/s	☒
• Advertisement	☒
Appendix I: Information Sheet(s) and Consent Form(s)	☒
Appendix II: Research Involving the Use of Drugs	
• Relevant correspondence relating to agreed arrangements for dispensing with the pharmacy	☐
• Written confirmation from the manufacturer that the drug/substance has has been manufactured to GMP	☐
• Proposed volunteer contract	☐
• Full declaration of financial or direct interest	☐
• Copies of certificates: CTA etc…	☐
Appendix III: Use of Non-Ionising Radiation	☐
Appendix IV: Use of Medical Devices	☐

APPENDIX II RESEARCH INVOLVING THE USE OF DRUGS

1 **Please specify any financial or other direct interest to you or your department arising from this study.**

A full declaration should be included in this space, or on an attached sheet.

Nil

2 **Is the study blinded?** ☒ Yes ☐ No

If the study is blinded, please describe how blinding will be achieved.

In Part B, participants will be allocated to either 1% hydrocortisone or 2.32% diclofenac diethylammonium via toss of a coin (until groups are filled, 6/arm) and provided with a control (moisturiser). One active agent (hydrocortisone or diclofenac) will be applied to one forearm, the control to the other arm (3 participants right/left, active/control respectively). Both the topical active agent and control will be supplied in identical weight (15, 30 or 50g) containers and labelled A or B, obscuring the product label. This task, along with drug arm allocation, will be performed by an investigator separate to those involved in blister creation or data analysis. As such, neither the participant nor the investigator will be aware which arm has been exposed to an active or control agent (double-blind). The participant will be informed which drug they are applying for safety and consent purposes but asked not to inform the investigator undertaking the direct investigations. It is accepted that the formulations of the drugs are non-identical (appearance, consistency, excipients) but this is not expected to adversely effect the study as we are not seeking to make claims of efficacy or utility - merely look for a drug signal.

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3 **Have you had any discussions with Pharmacy about the sourcing, accountability, receipt, storage, distribution, dispensing and destruction arrangements for each drug/substance?** ☐ Yes ☒ No

If yes, please provide email confirmation of arrangements on an attached sheet.

All drugs will be purchased from Boots Pharmacy, Tottenham Court Road and stored as per manufacturers' instructions.

If the answer to question 2 is "Yes" and/or question 3 is "No", please answer the following questions 4-8:

4 **Please name all drugs/substances (e.g. food products) to be used in the study including placebo if applicable.**

A

Approved name*: Hydrocortisone

Strength: 1%

Dosage & Frequency: 1 FTU, twice daily

Route: Topical

Schedule of Administration: One week

Pharmaceutical Form: Cream

**If possible, give the International Non-proprietary name for the drug*

Continue on an attached sheet if required.

4 B	**Please name all drugs/substances (e.g. food products) to be used in the study including placebo if applicable.** Approved name*: Diclofenac diethylammonium Strength: 2.32% Dosage & Frequency: 1 FTU, twice daily Route: Topical Schedule of Administration: One week Pharmaceutical Form: Gel **If possible, give the International Non-proprietary name for the drug* **Continue on an attached sheet if required.**

4 C	**Please name all drugs/substances (e.g. food products) to be used in the study including placebo if applicable.** Approved name*: Soft white paraffin Strength: n/a Dosage & Frequency: 1 FTU, twice daily Route: Topical Schedule of Administration: One week Pharmaceutical Form: Cream **If possible, give the International Non-proprietary name for the drug* **Continue on an attached sheet if required.**

5	**Does the study involve pre-marketing use of a drug/substance/ or a new use for a marketed licensed product?** ☐ Yes ☒ No

6	**If the drug/substance is licensed outside of the UK, but used within the UK, please give the name and full contact details (including the relevant licences to sell and produce medicines) of the manufacturer.** All products are licensed for use in the UK and available over-the-counter Note: You will need to provide confirmation from the manufacturer that the drug/substance has been manufactured to GMP

7	**If the drug/substance is unlicensed, please give details of any arrangements that are in place with a manufacturer (e.g. contractual arrangements). If this is not known, give an indication of where this can be manufactured or identify the Active Pharmaceutical Ingredient (API) as applicable.** N/A

8	**If the drug/substance used in the study is to be modified in anyway, state the nature of the modification (for example, packaging and labelling).** As stated above, the packaging of the tubes containing the creams will be modified to obscure the contents to achieve blinding. The product itself will not be modified.

PLEASE NOTE: A detailed study protocol can be used to give this information if this has been written by the Investigator. Mechanistic Protocol templates are available on the JRO website: www.ucl.ac.uk/jro

Thank you for addressing the above questions. The information provided will be forwarded to the IMP Compliance Manager (Sponsor Pharmacist) for review. Should you have any difficulty in sourcing drugs for this study the Sponsor Pharmacist will be able to assist you.

More information is available on the JRO website:
http://www.ucl.ac.uk/jro

IMPORTANT NOTICE

You may require written confirmation from the Medicines and Healthcare products Regulatory Agency (MHRA) if the study falls outside of the Clinical Trials Regulation.
Please refer to the Clinical Trial Algorithm to establish whether your study falls outside of the Clinical Trials Regulations: http://www.mhra.gov.uk/home/groups/l-unit1/documents/websiteresources/con009394.pdf

Please do not hesitate to contact JRO.Randd@ucl.ac.uk for an opinion regarding the need to approach the MHRA.

DIVISION OF MEDICINE
UNIVERSITY COLLEGE LONDON

Participant Information Sheet For Adult Volunteers

UCL Research Ethics Committee Approval ID Number: 5060/003

YOU WILL BE GIVEN A COPY OF THIS INFORMATION SHEET

Title of Study:
Comparison and characterisation of two skin blister models of inflammation

Department:
Applied Biomedical Engineering Group (ABEG), Division of Medicine, UCL

Name and Contact Details of the Researcher(s):
João Oliveira, Dr James Fullerton and Professor Richard Day, ABEG, Division of Medicine, Rayne Building, 5 University Street, London, WC1E 6JF
Dr Majella Lane, School of Pharmacy, 29-39 Brunswick Square, WC1N 1AX
Professor Adam Gibson, Medical Physics and Biomedical Engineering, London WC1 6BT

Name and Contact Details of the Principal Researcher:
Dr James Fullerton, j.fullerton@ucl.ac.uk, +44 7803 729439

Invitation
You are being invited to take part in a research project conducted by the Applied Biomedical Engineering Group, based at University College London. This consists of a group of scientists and clinicians who are working together to improve human health.

You should only participate if you want to; choosing not to take part will not disadvantage you in any way. Before you decide it is important for you to understand why the research is being done and what participation will involve. Please take time to read the following information carefully and discuss it with others 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. Thank you for reading this.

What is the project's purpose?
We are trying to better understand inflammation and how to study drugs that affect it. Inflammation causes the redness, swelling, heat, and pain you may be familiar with following a wound or an infection. Inflammation can help the body to fight infection and repair damage however, in some cases, the response is abnormal such that it begins to damage the tissues of the body rather than heal them.

To study the inflammatory process in humans, scientists have often created blisters on the skin. This is as the content of blisters can be collected at different times and analysed. They are easy to create, painless for the volunteers and allow insight into the processes that cause disease and the ability of drugs to modify these. At the moment two different methods of creating a blister are commonly

used: negative pressure (suction) and application of a chemical (cantharidin). It is not known if they produce exactly the same information or whether one is better than the other for certain purposes.

We hope to answer these questions by simultaneously raising blisters on your skin (forearms) using both methods and collecting the resulting fluid the following day. If you are enrolled in Study A we will do this on three separate occasions. If you are enrolled in Study B we will do this on one occasion but you will have been asked to apply one of two commonly used anti-inflammatory drugs (along with a control: moisturiser) to the skin for 1 week prior. We will tell you which study you are being asked to participate in before you provide your consent.

Why have I been chosen?
You have been approached because you are male, between 18 and 50 years of age, have mark-free forearms (no skin damage, tattoos or scars on the hairless part of either arm) and have a lighter skin tone (Fitzpatrick scale I-IV, pale to moderate brown). The latter is to avoid the risk of lasting skin discolouration in individuals with darker skin tone. If you tell us you are healthy, don't take any regular medications and don't smoke then you can participate. If you take part in Study B we will need to confirm that you are not allergic to the medication being applied or any related to it.

Do I have to take part?
It is up to you to decide whether or not to take part. Please feel free to discuss the study with us or anyone else to arrive at this decision. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you change your mind you can withdraw at any time without giving a reason and without penalty. If you decide to withdraw from the project we will not approach you again but any samples we have already stored, or data we have produced from these samples, will be retained.

What will happen to me if I take part?
Before any interventions occur you will be asked to sign a consent form indicating your understanding of what the study involves, and your willingness to participate. This acceptance and your understanding will also be confirmed verbally. After agreeing to take part in the study, we will arrange the study dates according to your availability and clarify what will happen at each. We are running two Studies and you will be enrolled in only one of these. In both Studies you will have the same fundamental procedures carried out (as described below) however they are different:

a) Background information:
To calibrate our blister assessments we want to conduct the following tests:

i) Evaluation of your blood for signs of inflammation. You will have ~10mls of blood taken from your arm by an experienced doctor using aseptic non-touch technique at each time point (before blister induction and before blister fluid collection).

ii) Measurement of local blood flow in the arm. This will be measured using laser doppler flowmetry, a painless technique that takes 5-10 minutes and involves you sitting still and wearing protective eyeglasses. Again, this will be performed at each timepoint

iii) Understand your skin 'function'. This will involve application and removal of tape to your forearm to 'strip' the very top layer for assessment, application of a probe to quantify water loss through the skin and finally placement of a Confocal Raman Spectroscopic probe on your forearm to visualise the skin. All measurements are quick and pain free and have been used for many years to understand skin health.

iv) Multispectral imaging to photograph the forearm under different illumination wavelengths and determine whether this can provide a means of non-invasively monitoring the formation of blisters in human volunteers.

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b) Raising of blisters:
A patch of skin about 10cm x 5cm on the bottom (hairless side) of one or both your forearms will be cleaned with an alcohol wipe to make it sterile, and any small hairs removed with a safety razor. We will then induce 2 small circular blisters (circa 1cm diameter) on either one or both of your forearms using two different methodologies:

i) Chemical. Cantharidin solution (a treatment for warts) will be applied to the skin. We will mark a suitable area by making a circle/ring imprint using Vaseline and add the cantharidin. This will then be covered with a protective dressing. Over the next 24hrs the cantharidin will evaporate and a blister will form.

ii) Negative pressure (suction). A suction device will be attached to both your arms and held in place with Velcro. The negative pressure will gradually be increased then decreased (according to a protocol, but modified on an individual basis) to gradually form a blister over approximately 2 hours. The suction cup will then be removed and the blister covered with a protective dressing.

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c) Collection of blister fluid:
The following day you will be asked to re-attend UCL. All blisters will be punctured with a sterile needle, and the fluid aspirated with a pipette. A dressing will again be placed over your arms. This visit should take less than an hour to complete.

If you are taking part in Study A: we will ask you to re-attend UCL ideally on the same two days on the following 2 weeks after the first visit (total 6 visits, 2/session). On the first visit we will raise 2 blisters on each of your forearms. In the second and third weeks we will raise blisters (one chemical, one suction) on only one of your arms (left then right or vice versa). As a result you will have 8 blisters created in total (4 then 2 then 2). This is to allow us to see if the inflammatory response detected by blisters is consistent within individuals over time. If you have become unwell in the interim we will discuss whether you can continue in the Study.

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If you are taking part in Study B: after providing your consent, we will ask you to apply one of two topical anti-inflammatory drugs (1% hydrocortisone cream or 2.32% diclofenac diethylammonium) to one of your forearms twice a day for seven days. You will be provided with two tubes labelled A and B. One will contain one of the above drugs (you will be told which) and the other moisturiser. Both need to be applied to one arm each in the same manner and you will be told which goes on the right or left. After this, you will attend for the creation of blisters on both arm simultaneously (2/arm, 4 total) as above. This is to allow us to see if the two blister methods can detect the effect of the drug as well as each other.

Hydrocortisone is a commonly available, over-the-counter (non-prescription) medication (steroid) used for dermatitis, eczema and insect bites. Diclofenac gel [Voltarol] is also available over-the-counter and used for joint aches and pains. As compliance with the medication is *very* important you will receive a phone message reminding you to apply 1 fingertip unit of cream (the amount of medication needed to squeeze a line from the tip of your finger down to the first crease) in the morning and evening.

d) Follow-Up
We wish to chart the comparative healing of both blister methods and to ensure no complications arise. We will ask you to complete a diary card for 3 months following the first set of blisters (Study A) or only blisters (Study B). In addition we would like you to take photos of your arms on set days (1, 3, 5, 7, 14, 21, 28, 56, 84) so we can see how they are resolving. You will be sent text reminders of the above. The photographs taken during this research will be used only for analysis and for illustration in scientific publications, presentations and lectures. No other use will be made of them

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without your written permission, and no one outside the project will be allowed access to the original photos. In addition, you will be sent an online questionnaire on completion of the procedures to obtain your feedback on both methods used to raise the blisters.

Please note, that if you chose to take part in the study, we will ask you to avoid the following in the 24 hours preceding blister formation and whilst the blister is present:

- Heavy exercise using your hands or arms
- Putting any creams or lotions on your forearms
- Taking medication including anti-histamines, anti-inflammatories (e.g. aspirin, ibuprofen), pain killers (e.g. paracetamol) and steroids. If these are required please inform the study team as it is likely you cannot take part.
- Alcohol (any) and significant (>2 beverages/day) caffeine consumption

In addition to the above we will give you advice on how to protect the blister and help it's healing e.g. not getting the blister dressing wet during bathing

What are the possible disadvantages and risks of taking part?

Cantharidin is used clinically to treat warts. Cantharidin application is usually well tolerated but can cause skin irritation or burning if not used appropriately. The concentration used for the study is more dilute than employed clinically, and has been safely employed in multiple other studies. The investigators will check your skin to see if it is suitable for having cantharidin applied.

Suction blister formation will be performed using a set protocol and under the direct observation of an investigator so that individual adjustments can be made. The process is not painful but can lead to a mild 'tugging' sensation. Again, this procedure has been successfully carried out many times before.

Potential risks of blister formation include:

- Infection at the blister site. This will be minimised via the use of sterile technique and the provision of protective dressings
- Skin discolouration / pigmentation at blister site. Previous studies have demonstrated that discolouration is normally temporary and usually resolves completely in 6-8 weeks. Rarely discolouration took longer to resolve or did not resolve completely in some people. The blisters formed are superficial and expected to heal without leaving a permanent scar but this cannot be guaranteed. We will provide you with appropriate information on skin care.
- Premature rupture. Despite the dressing blisters may occasionally burst. This should result in no harm to you although the information we could have obtained will be lost.

Blood taking may cause slight discomfort and can lead to minor bruising around the area where the needle is inserted. There is also a very small risk of infection. The chance of these occurring will be minimised by experienced professionals performing the procedure with appropriate precautions and equipment. The tests we will be performing are not intended to be diagnostic of any medical conditions nor are able to confirm a diagnosis. If however a significant abnormality were seen we would refer you to your GP for further investigation.

Those enrolled in Study B will apply 1% hydrocortisone or 2.32% diclofenac to a patch of skin for one week. Both medications are available without prescription and are not anticipated to cause any systemic or local complications, however we encourage you to read the Patient Information Leaflets provided with the drugs prior to application. The effect of these drugs on subsequent blister formation and healing is unknown. We will monitor you as above and you will have the ability to contact the investigators at any time.

What are the possible benefits of taking part?
Whilst there are no immediate benefits for those people participating in the project. It is hoped that this work will lead to new tools for monitoring clinical conditions and creating treatments for disease. You will be offered £200 as compensation for the time, inconvenience and any discomfort resulting from taking part in this study. This will only be payable upon completion of all elements of either Study A or B (whichever you enrolled into).

What if something goes wrong?
If you have any complaint or concern about the way in which this research project has been or is being conducted, please, in the first instance discuss them with the researcher. If the problems are not resolved or you wish to comment in any other way, please contact Professor Richard Day or Dr. James Fullerton using the contact details above. If you feel your complaint has not been handled to your satisfaction then you can contact the Chair of the UCL Research Ethics Committee at ethics@ucl.ac.uk.

We believe that the study is very low risk. We carry insurance (through UCL) to make sure that if you suffer bodily injury as a result of being in this study, then you can be compensated. In such a situation, you will not have to prove that the bodily injury arose from the study but you must agree to abide by the Conditions of Compensation. If you are not happy with any proposed compensation, you may have to pursue your claim through legal action and will have to prove that the bodily injury arose from the trial.

Will my taking part in this project be kept confidential?
Yes. We will not inform anyone that you are taking part. You will not be able to be identified in any ensuing reports or publications.

What will happen to the results of the research project?
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 also be used as part of a PhD project and presented in the thesis. You will not be able to be identified in any of these. Should you wish to be notified of any published outputs please inform the researcher.

Your biological samples will be retained for up to 5 years after the end of the study (estimated 2025). Data obtained from this study will be retained indefinitely in fully anonymised (cannot be linked in any way to you) so that it may be used for additional or subsequent research.

As we are keen to maximise the value of your contribution we would like to share, where appropriate, either the samples themselves or data obtained from them with other academic groups and/or industrial partners who we are working with. You will have the option to indicate whether you agree to this or not on the consent form. If these are outside the European Economic Area we will seek approval from UCL Research Ethics Committee and the Data Protection Officer for this to occur. This will always occur in a fully anonymised fashion and these individuals or organisations will not be able to identify you.

Local Data Protection Privacy Notice
The data controller for this project will be University College London (UCL). The UCL Data Protection Office provides oversight of UCL activities involving the processing of personal data, and can be contacted at data-protection@ucl.ac.uk. UCL's Data Protection Officer can also be contacted at data-protection@ucl.ac.uk**.** Further information on how UCL uses participant information can be found here:
www.ucl.ac.uk/legal-services/privacy/participants-health-and-care-research-privacy-notice

Your personal data will be used for the purposes outlined in this notice. The categories of personal data used will be as follows:

Name, Age at time of participation, Contact details (email and phone number), Health status: declaration of lack of medical conditions, medication use and allergy status

The legal basis that will be used to process your *personal data* will be performance of a task in the public interest. The legal basis used to process *special category personal data* will be for scientific and historical research. We will pseudonymise the personal data you provide us with (only the listed study team having access to the database linking your name to study number) and fully anonymise it (deleting the linking database) upon completion of the study. We will endeavour to minimise the processing of personal data wherever possible.

You have certain rights under data protection legislation in relation to the personal information that we hold about you. These rights apply only in particular circumstances and are subject to certain exemptions such as public interest (for example the prevention of crime). They include:

- The right to access your personal information;
- The right to rectification of your personal information;
- The right to erasure of your personal data;
- The right to restrict or object to the processing of your personal data;
- The right to object to the use of your data for direct marketing purposes;
- The right to data portability;
- Where the justification for processing is based on your consent, the right to withdraw such consent at any time; and
- The right to complain to the Information Commissioner's Office (ICO) about the use of your personal data.

If you are concerned about how your personal data is being processed, or if you would like to contact us about your rights, please contact UCL in the first instance at data-protection@ucl.ac.uk. If you remain unsatisfied, you may wish to contact the ICO. Contact details, and further details of data subject rights, are available on the ICO website at: https://ico.org.uk/for-organisations/data-protection-reform/overview-of-the-gdpr/individuals-rights/

Who is organising and funding the research?
This project is funded by the National Institute of Health Research (NIHR) Surgical MedTech Cooperative. Dr James Fullerton is a Clinical Lecturer who's salary is funded by the NIHR. João Oliveira is a part-time PhD student, but an employee of GlaxoSmithKline. Additional charitable or government funds may also be used to analyse the samples you provide in the future. As part of either existing or new collaborations other academic organisations or industrial partners may either acquire or be sent your samples or data. We cannot predict the funding sources available to these individuals or organisations.

Contact for further information
Please contact Dr James Fullerton 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 to take part in this research study.

DIVISION OF MEDICINE
UNIVERSITY COLLEGE LONDON

VOLUNTEERS WANTED

If you are *male, aged 18-50, healthy and a non-smoker* please get in touch

We are offering **£200** to take part in a study comparing methods of investigating skin inflammation

The study will require between 5-15 hours of your time and take place at UCL.

If you are interested please email:
João Oliveira: joao.oliveira.18@ucl.ac.uk
Dr James Fullerton: j.fullerton@ucl.ac.uk

Be quick - Recruitment limited to <25 individuals

Division of Medicine, UCL
Rayne Building, 5 University Street
London WC1E 6BT
Tel: +44 (0)20 7679 6351
j.fullerton@ucl.ac.uk
www.ucl.ac.uk/medicine

Email Advert:

VOLUNTEERS WANTED

If you are *male, aged 18-50, healthy and a non-smoker* please get in touch

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The study will require between 5-15 hours of your time and take place at UCL.

If you are interested please email:
João Oliveira: joao.oliveira.18@ucl.ac.uk
Dr James Fullerton: j.fullerton@ucl.ac.uk

Be quick - Recruitment limited to <25 individuals

Subject Questionnaire

Please complete the survey below.

Thank you!

Participant feedback for study:

Comparison and characterisation of two skin blister models of inflammation

As part of the comparison between the two approaches to blister formation (suction and cantharidin/chemical methods), we want to understand your experience and opinion on the skin blister models. Please fill in the form in relation to this study, rating the parameters (where appropriate) out of 10 (where 0 is low and 10 high). We would also be grateful if you shared some of your feelings about the procedures.

Subject number	_____
Age when started procedure	_____
Are you currently	◯ In full or part time education (e.g. MSc or PhD) ◯ Employed ◯ Unemployed ◯ Other
Please define	_____
Which option best describes your primary field of work or study?	◯ Science ◯ Arts ◯ Humanities ◯ Clinical practice ◯ Other ◯ N/A
Please describe your field of work	_____
Have you taken part in scientific studies previously (please detail number if yes)?	☐ At an academic institution? ☐ At a company? ☐ Involving skin blistering?
How many studies have you participated at an academic institution?	_____
How many studies have you participated at a commercial institution?	_____
How many studies have you participated involving skin blisters?	_____

What were the main reasons for you participating in this study (e.g. interest, undertaking related research, financial compensation, to help advance science)?

_____

Blistering Techniques

Rate how apprehensive you were regarding participating in a study involving skin blister formation via:

The suction technique

No concerns — Extremely anxious

(Place a mark on the scale above)

The cantharidin technique

No concerns — Extremely anxious

(Place a mark on the scale above)

What aspects of the techniques caused you greatest concern before participating?

Suction method

_____

Cantharidin method

_____

Rate discomfort out of 10 (0- No pain/discomfort to 10- Worst imaginable pain/discomfort) for the suction technique:

During blister formation

No pain/discomfort — Worst pain/discomfort imaginable

(Place a mark on the scale above)

During blister fluid collection

No pain/discomfort — Worst pain/discomfort imaginable

(Place a mark on the scale above)

After blister fluid collection

No pain/discomfort — Worst pain/discomfort imaginable

(Place a mark on the scale above)

Overall

No pain/discomfort — Worst pain/discomfort imaginable

(Place a mark on the scale above)

Please add any comments on discomfort for the suction technique

Rate discomfort out of 10 for the cantharidin technique

During blister formation

No pain/discomfort — Worst pain/discomfort imaginable

(Place a mark on the scale above)

During blister fluid collection

No pain/discomfort — Worst pain/discomfort imaginable

(Place a mark on the scale above)

After blister fluid collection

No pain/discomfort — Worst pain/discomfort imaginable

(Place a mark on the scale above)

Overall

No pain/discomfort — Worst pain/discomfort imaginable

(Place a mark on the scale above)

Please add any comments on discomfort for the cantharidin technique

Please rate inconvenience of the 2 methods used from 0 - No disruption to daily activities to 10 - Major disruption to day

Rate inconvenience out of 10 for the suction technique

No disruption to day — Major disruption to day

(Place a mark on the scale above)

Rate inconvenience out of 10 for the cantharidin technique

No disruption to day — Major disruption to day

(Place a mark on the scale above)

What were the main negative aspects about each approach (if any)

Suction method

Cantharidin method

Rate how willing you would be to participate in a future study involving skin blister formation via

The suction technique

Never again — Without question

(Place a mark on the scale above)

The cantharidin technique

Never again — Without question

(Place a mark on the scale above)

If you were to partake in a further blister study which approach would you prefer

◯ Suction method ◯ Cantharidin method

Given your experience, please rate how well the Patient Information Sheet and accompanying verbal information adequately explained what the study involved (0 not at all, 10 entirely clear)?

0 — 10

(Place a mark on the scale above)

Are there any elements of the study and associated procedures that should be emphasised or additional cautions provided?

Is there anything that could be improved from a participant perspective with the different approaches?

Suction method

Cantharidin method

Final comments or suggestions