# PARTICIPANT INFORMATION SHEET

# Understanding Pain

We would like to invite you to take part in a Children of the 90s study which is looking at how common variation in a key pain sensing gene affects our sensitivity to pain.

This leaflet explains why the project is being done and what will happen during the study. It is important that you read this if you would like to participate so that you understand what is involved. Feel free to discuss it with friends, family and your GP. Also, please do contact us if you have any questions.

**What is the purpose of this research?**

Why do some people suffer with long term pain after an accident or surgery whilst other people recover without incident? We believe that part of the answer lies in the subtle differences in people's genes. We are interested in how these little differences can add up to make an individual more or less likely to suffer from pain. Unfortunately, we don't know which gene differences are important. We plan to invite members of the Children of the 90s cohort, with known common variants in a gene that have been linked to pain detection, to come for testing of their sensitivity to mildly painful stimulation. We call this a Recall by Genotype study, please see attached leaflet explaining the nature of research studies of this type.

Children of the 90s participants are being asked to take part in this study as we already have information about your genetic make-up, obtained from blood samples that you gave us previously. By collecting information about pain perception in this new study we will be able to learn more about how specific gene variants influence the experience of pain.

If we can better understand why some people feel more pain than others, we hope that we will be able to anticipate and treat people's pain on an individual basis. This is called *personalised medicine*. We also hope that this new knowledge will help in the development of new pain-relieving drugs.

We plan to induce mild pain in our participants using tests that have been used in previous studies. We've found that these tests are acceptable and tolerable to participants. Most of our tests look at pain "threshold" e.g. the change from warm to hot. We use the lowest temperature that causes pain to be felt. We will also ask participants to rate how much pain they feel when their skin is pressed with controlled forces. We believe that these tests are less painful than giving blood, for example. Participants may stop the tests at any time if it is too uncomfortable.

**What exactly would I have to do?**

We would like you to come to **CRICBristol (Clinical Research and Imaging Centre), which is located at 60 St Michael's Hill, Bristol BS2 8DX**. You will be asked to take part in a sensory testing session which will take about 1.5 hours plus some time for discussion and questions. The whole visit will last approximately 2.5 hours. During this session we will assess your pain sensitivity to hot and cold temperatures; apply bristles

against the skin (to provoke a mild pricking sensation); and apply a cream that contains a small amount of the ingredients that gives cinnamon its hot taste.

Before your visit

If you return your reply slip indicating that you wish to take part, we will contact you by phone to ask you some questions to check that you are eligible for the study. If you are eligible, we will book you an appointment, and then ask you to follow these restrictions:

- No over the counter painkillers on the day before the study and the day of the study.

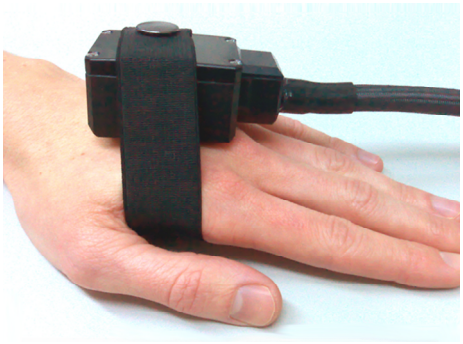
N.B. You should take your normal prescription medications (apart from painkillers), but please inform the researcher on the day of your visit of any medication taken.

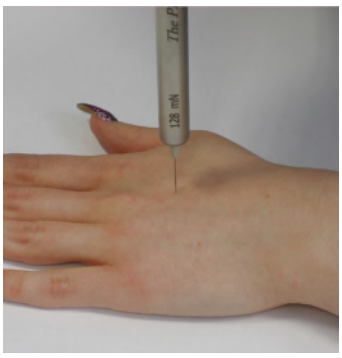
At the clinic visit

On arrival at CRIC, you will be met by a researcher who will ask you some questions to check there have been no changes to your health or eligibility for the study since we spoke to you on the phone. We will ask you some questions about your general health, and allergies. We will explain the study in detail and you will be able to ask questions. We will also provide you with the information sheet to read again. If, after our discussion, you are still happy to take part, we will ask you to provide consent for the study.

We will then begin testing your pain sensitivity. This will start by placing the temperature tester against your arm (please see photo on the left in Figure 1 showing the equipment on the hand). It is licenced for use in patients and research volunteers. It is very safe, with in built regulation that prevents extremes of temperature that could lead to burns. It is not possible to get a skin burn from this equipment. Please see medoc-web.com for more information. We will slowly increase or decrease the temperature and ask you to click a mouse button when you detect the temperature change, or when you perceive the temperature as painful.

Figure 1.





Left: Thermal sensory testing using Medoc TSA II Neurosensory analyser.

Right: mechanical sensory testing (using fine bristles)

We will then test your sensitivity to fine 'bristles' like those shown in the photograph in Figure1, above, on the right. This is called mechanical sensory testing. We will ask you when you can feel these against your skin, when it becomes painful and how painful it feels. We will also brush your skin gently and ask if that is painful.

We will then put a small amount of liquid onto a dressing that we will then place on your arm. This will be in a slightly different location to the first set of tests, and we will mark

a 4cm x 4cm square on your arm to guide the application of the dressing. This contains cinnamaldehyde which gives cinnamon its hot taste. This liquid will cause a hot sensation similar to having mustard or chilli on your hands. It will also cause your skin to become temporarily red. We will then repeat the pain sensitivity tests whilst also measuring any redness. The discomfort and redness from the cream may persist for some hours afterwards. If this is troubling you, cooling the area will help with the discomfort.

We expect that the testing session will take about 1.5 hours and the whole visit about 2.5 hours. Once again, it is important to remember that you can stop taking part at any point during the study, without having to give a reason. At the end of the visit we will reimburse your out of pocket travel expenses and as a thank you for your time will give you shopping vouchers or cash / bank transfer for £25.

**Are there any reasons why I can't take part?**

You won't be able to take part if you:

- Are, or may be, pregnant
- Are diagnosed with acute or chronic pain conditions
- Are diagnosed with neuropathy – problems with your nerves
- Are severely affected by anxiety or depression
- Are taking pain killers regularly
- Are allergic to cinnamon, mustard, rubber, alcohol / chlorhexidine wipes or latex
- Use non prescribed or recreational drugs
- Are unable to understand verbal and written instructions given in English

When we receive your reply form, if you indicate that you would like to take part, we will phone you to ask you some questions to make sure that you are eligible to participate in the research. If you are eligible, we will then book an appointment that is convenient for you.

**Do I have to take part?**

No, it is your decision whether to take part or not. If you choose to take part, you are free to withdraw from the research at any time without giving a reason. This will not affect your involvement in other Children of the 90s research.

**What are the benefits of taking part?**

The current research project is investigating why people have different sensitivity to pain. There are no direct health benefits for you. Taking part in this study will help us understand how to better predict and treat pain.

However, during testing we may detect a sensory abnormality. If we detect an abnormality, with your consent, we will tell you and give you a letter to take to your GP so that they can discuss this with you, and arrange further tests with a neurologist, if necessary.

**Are there any disadvantages to taking part?**

The stimulation of the skin, either with the thermal sensory testing equipment (TSA-II – Figure 1 [left]), the bristles (Figure 1 [right]) or the cinnamaldehyde will almost certainly cause the skin to redden and be more sensitive to touch and temperature. The

skin on your arm will likely feel hot which may be painful. This sensation will last for a few hours after the testing. It may be "re-started" later that day by changes in temperature, like having a hot bath or shower. We do not expect any effects to last more than 24 hours, but if discomfort is still present after 24 hours, please do contact Children of the 90s for advice on 0117 331 0010.

It is necessary to evoke pain as part of this research. We will minimise pain at all times, though it is important to realise that you will experience short periods of discomfort, particularly with the application of the cinnamaldehyde cream. Some discomfort and reddening will remain after the cream has been removed, for a few hours afterwards. Remember, you are in control at all times, you can tell us to stop if it is too uncomfortable.

It is advisable for people with private healthcare insurance to inform their insurers about participation in research studies.

**Do I have to fast (not eat or drink) before the tests?**
No, you can eat and drink as normal.

**Do I have to wear special clothes?**
Please wear short sleeved or loose clothes so that we can test the skin on the inside of your forearm.

**What will happen if I don't want to carry on with the research?**
You are free to withdraw at any time, without giving a reason. We will support you in this choice. This will not affect your involvement in other Children of the 90s research.

**Will my identity be protected?**
Your data will be stored with an individual ID number but not with your personal information (such as your name, address or date of birth). Files that link this ID number to your personal details will be securely stored and only named Children of the 90s staff on the study will have access to this data. The data will be used for research purposes only and will be analysed by Children of the 90s approved researchers. Selection of participants will be done by Children of the 90s. Researchers will not know which genotype variant each individual participant belongs to. Analyses are done using codes for participants to protect the identity of participants and ensure that any personal information cannot be linked directly to an individual. All information collected about you during the course of the research will be kept strictly confidential.

We will keep your personal details confidential and separate from your research data. Your personal details will not be shared with third parties except for certain service providers working on our behalf, for example VCars if you ask us to book a taxi for your visit.

Children of the 90s is compliant with GDPR (General Data Protection Regulation) and with the Data Protection Act (2018) about the collection, processing, storage and disclosure of personal information. If you would like to find out more, please see our privacy notice here: http://www.bristol.ac.uk/alspac/participants/privacy/

**What will happen to the results of the study?**
The results will be reported in professional publications and at scientific meetings, but you will not be identified by name. We will also include summaries of research results in participant newsletters and other participant communications.

**Who is funding and organising the study?**
This research is funded by University Hospitals Bristol Above and Beyond Fund. Children of the 90s receives core funding from the Wellcome Trust, the UK Medical Research Council and the University of Bristol.

This project is organised by Dr Jim Dunham, Academic Clinical Lecturer, University of Bristol and Professor Tony Pickering, Professor of Anaesthesia and Neuroscience, School of Physiology and Pharmacology, University of Bristol, and Children of the 90s.

Dr Dunham and Professor Pickering have an on-going collaboration with Eli Lilly UK across several projects. Eli Lilly UK, Erl Wood Manor, Windlesham, Surrey, GU20 6PH are developing new medicines to target specific gene variants with the hope that they will provide better pain relief.

Our collaborators at Lilly, Dr Keith Phillips and Dr Laura Addis, have helped in the design of the study. They are also providing the equipment that will allow us to accurately measure the area of redness that is caused by the cinnamaldehyde. We expect that Dr Keith Phillips and Dr Laura Addis, will be involved in discussions around the summary results of the study in preparation for publication. We anticipate that Dr Keith Phillips and Dr Laura Addis, will be co-authors on the publications that follow this study.

Eli Lilly UK will not have access to your name or any other personalised information that you have provided to the Children of the 90s project. Neither Eli Lilly UK, nor the academic research team, will know your individual genotype. Eli Lilly UK will not be performing independent analysis on these data. They are not paying for access to these data.

**Who has reviewed the study?**
The study has been reviewed by the ALSPAC Executive Committee, the ALSPAC Ethics and Law Committee and the Children of the 90s original cohort advisory panel (OCAP) and adheres to approved safety and ethical procedures at the Clinical Research and Imaging Centre (CRIC).

**Will I receive any compensation for taking part in this study?**
Yes, we will give you £25 as a thank you for taking part in this visit, of approximately 2.5 hours. This can be provided in shopping vouchers or in cash. / bank transfer, depending on your preference. We will also reimburse your out of pocket travel expenses (either as cash on the day, if less than £30, or via a fee form). We can book overnight accommodation if you need this. Please keep all your receipts and we will reimburse you at your visit. We'll also give you a letter for your employer asking them to give you paid time off work, if you need it.

**What do I do now?**

If you are interested in taking part please return the enclosed reply slip, we will then telephone you to ask you some questions to make sure that you are eligible to take part. If you are eligible, we will then book an appointment that is convenient for you.

**Who do I contact for further information?**

For further information about the study please contact:

Children of the 90s
Tel: 0117 331 0010
Email: info@childrenofthe90s.ac.uk
Web: www.childrenofthe90s.ac.uk
Children of the 90s, Oakfield House, Oakfield Grove, Bristol, BS8 2BN

*Thank you for reading this and for considering whether you would like to take part in this research.*