Participant Information Sheet – Remote recruitment

Project Title: The effect of a topical treatment containing *Hypericum perforatum* (St John's Wort), *Calendula officinalis* (calendula) and *copper sulfate* on cold sores.

Project Summary:
You are invited to participate in a research study being conducted by Dr Mike Armour and Dr Carolyn Ee from NICM Health Research Institute, Western Sydney University, and Dr Alex Semprini from the Medical Research Institute of New Zealand. The study will explore the effects of a topical treatment containing St John's Wort, calendula and copper sulfate on cold sores (herpes simplex).

If you are aged 18-65 years with and have had cold sores at least three times previously, you may be eligible to participate in the study. You don't need to currently have a cold sore to participate. To confirm your eligibility, we will need to ask you more questions before you start.

How is the study being paid for?
This study is sponsored by Sci-Chem International Pty. Ltd.

Why is this study being done?
Herpes simplex virus (HSV) is a common infection that causes painful sores in and around the mouth ("cold sores"). Current topical treatments like creams need to be applied regularly to slightly reduce the symptoms and duration of cold sores. The topical treatment used in this study (currently sold in Australia under the name *Dynamiclear™)* contains herbs (*Hypericum perforatum* and *Calendula officinalis*) and a mineral (*copper sulfate*) that could potentially reduce the severity of symptoms and duration of cold sores with the application of a single vial. This study will examine if a single application of the topical treatment, compared to a placebo (a treatment that looks the same but doesn't contain any active ingredients) , can reduce the time it takes for your cold sore to heal and to reduce the amount of pain you may have during the episode.

What will I be asked to do?

The recruitment and administration of this trial is all done online and via phone to comply with all social distancing guidelines due to COVID-19. No face to face contact is required with any member of the research team.

- Screening via phone or zoom (10 minutes): In brief, after a telephone assessment and digital consent, if you are eligible you will be randomly allocated to one of two groups, either the active treatment or placebo. You are twice as likely to get the active treatment as the placebo treatment. You will receive your topical treatment by Australia Post courier service to your home or other location of your choice. Once it arrives you will be asked to upload a photo of the box that contains the treatment vial so we can ensure you have received the correct box and it is intact.
- First phone or zoom 'visit' (10 minutes): When you next get a cold sore you will need to contact the research team either via text message or email within 48 hours of the start of your cold sore. You will need to upload a photo of your cold sore which you can take via your cell phone, tablet or laptop camera. A member of the research team will contact you via phone as soon as possible, double check your eligibility to continue in the study, re-confirm your consent, and explain how to apply the treatment. Once you have applied the treatment you will need to return the rest of the vial (which may or may not be completely empty) to us via a

pre-paid envelope.

- Daily diary (2-3 minutes per day): You will be asked to fill in an online diary each day about your symptoms. This can be done from your cellphone, tablet or computer and takes around 2-3 minutes each day.
- Second phone or zoom 'visit' (20 minutes): When you indicate via your online diary that your cold sore is healing, you will be contacted by a member of the research team to confirm your cold sore has healed, and check for any side effects of treatment. You will need to upload another photo of where your cold sore was. You will also be asked to answer a 5-10-minute online exit survey.
- Follow up phone call (5 minutes): a researcher will ring you two weeks after the last pharmacy visit to follow up in case of any adverse events.

How much of my time will I need to give?
The total time you will need to give in this study is approximately 1-2 hours over one to two weeks.

What kind of treatment will I receive?
This study is testing a product that contains St John's Wort (*Hypericum perforatum*), Calendula (*Calendula officinalis*) and copper sulfate as active ingredients. This is called the 'active treatment'. These ingredients have been traditionally used to treat skin infections, however we don't know how well this combination of ingredients might work in the treatment of cold sores.

We will be testing this treatment against a cream that looks, smells and tastes the same but doesn't have any of the active ingredients (called the 'placebo treatment').

Whether you get the active or placebo treatment is based on randomisation. This means the research team don't know in advance which treatment you will get and your allocation to a treatment group is based purely on chance. There is a two-thirds chance (66%) you will receive the active treatment and a one third (33%) chance you will receive the placebo treatment.

Who will apply the treatment?
This trial is double-blinded, which means neither you nor the research team know if you have received the active or placebo treatment.

Application takes around one minute and only one treatment is required. The research team will advise you how to apply the treatment when you get a cold sore. You will need to return the vial to us even if it is not empty. We will provide you a pre-paid envelope for this.

What benefits will I, and/or the broader community, receive for participating?
Depending on whether you receive the active or placebo treatment, you may have a reduction in the duration of your cold sore, and your pain and other symptoms (like burning or tingling) may be reduced, however there may be no benefit at all from the treatment.

To cover your time in participating in the study, you will receive a $60 gift voucher (that covers petrol or food) after you complete your second

You will be helping to advance medical research, which could assist in the development of effective treatments in the future for people who suffer from cold sores.

Will the study involve any risk or discomfort for me? If so, what will be done to rectify it?

The topical treatment used in this study is considered safe to apply to cold sores. There is a small risk that a minority of people may experience minor skin irritation from the treatment.

To monitor for side effects, study staff will monitor participants' daily online diary for symptom severity ratings and two weeks after your second phone visit to make sure you haven't had any delayed reactions. If your diary input shows signs of higher than expected discomfort or side effects, the study staff will contact you and, if necessary, refer you to your general practitioner.

If you have any side effects that you are concerned about at any time, you should contact your general practitioner directly or the study staff via the contact details in your online diary or at the end of this sheet.

How do you intend to publish or disseminate the results?
We anticipate that the results of this research project will be published and/or presented in a variety of forums. In any publication and/or presentation, we will present information in such a way that a participant can't be identified, such as tables and graphs showing the overall information.

If you would like to receive a summary of research results, please tick the box on the Consent Form.

Will the data and information that I have provided be disposed of?
Your health records and any information obtained during the research project are subject to inspection (for the purpose of verifying the procedures and the data) by the relevant authorities and authorised representatives of the Primary Sponsor including monitor(s), auditor(s), NICM Health Research Institute, Western Sydney University, or as required by law. By signing the Consent Form, you authorise release of, or access to, this confidential information to the relevant study personnel and regulatory authorities as noted above.

Your data may be used in other related projects for an extended period of time. If you provide us with a swab of your cold sore this will be destroyed at the end of the study once the analysis is complete. In accordance with the Australian privacy and other relevant laws, you have the right to request access to your information that we have collected and stored by the research team.

Please contact the chief investigator, Dr Mike Armour, m.armour@westernsydney.edu.au, 0415 363 201, if you would like access to your information.

We will store all information collected for this study securely and destroy it 15 years after the results are published in accordance with university policy and the Australian Code for the Responsible Conduct of Research.

Can I withdraw from the study?
Participation is entirely voluntary, and you are not obliged to be involved. If you do participate you can withdraw at any time.

If you choose to withdraw, the study investigator or other staff may ask you for your reason for withdrawing to ensure we follow up on any unresolved issues. If you withdraw, you can advise us that you do not consent for us to use the data we collected up until your withdrawal. We will only use the information that you give consent for us to use.

Whatever your decision, it will not affect your medical treatment from the pharmacy or your relationship with the medical or other staff involved in the study.

Can I tell other people about the study?
Yes, you can tell other people about the study by providing them the contact details of the Clinical Trial Coordinator on 0410 522 980 who will give them the appropriate information.

What if I require further information?
Please contact the Clinical Trial Coordinator on 0410 522 980 if you want to discuss the research further or before deciding whether or not to participate.

What if I have a complaint?
If you have any complaints or reservations about the ethical conduct of this research, you may contact the Ethics Committee through Research Engagement, Development and Innovation (REDI) on Tel +61 2 4736 0229 or email humanethics@westernsydney.edu.au.

Any issues you raise will be treated in confidence and investigated fully, and you will be informed of the outcome.

If you agree to participate in this study, you may be asked to sign the Participant Consent Form. This Information Sheet is for you to keep and the consent form is retained by the researcher/s.

This study has been approved by the Western Sydney University Human Research Ethics Committee. The Approval number is H12776.