Participant Information Sheet

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. 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?
In brief, after assessment and consent, you will need to attend a participating pharmacy twice (once when your cold sore begins and once when it has healed), complete an online diary once a day for up to 14 days and complete a satisfaction survey when your cold sore has completely healed. If the cold sore turns into an ulcer, you will be asked to take a swab sample of the cold sore at home and post the swab sample back to our laboratory in a prepaid envelope.

- First pharmacy visit (30 minutes): after eligibility screening, and your written consent to participate in the study, you will be randomly allocated to be in either a treatment or placebo group. You will have the choice of who will apply the treatment. You can choose to apply it yourself, or a trained pharmacist or pharmacy technician can apply it for you. Application is done at the pharmacy, in a private consultation area. Application takes around one minute and only one treatment is required. You will not be able to take any of the treatment vials with you when you leave the pharmacy.
- Swab sample at home (for some participants only: 10-20 minutes): If the cold sore turns into an ulcer/starts to look ulcerated, we will ask you to take a swab sample of the cold sore at home with the supplied swab kit and post the swab sample back to the identified laboratory in a prepaid envelope.
- Last pharmacy visit (20 minutes): when you indicate via your online diary that your cold sore is healing, you will need to visit the same pharmacy within 24 hours for the final healing

assessment by the trained pharmacist or pharmacy technician. 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 (not including travel time to pharmacy visits).

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 pharmacist know if you have received the active or placebo treatment.

You will have the choice of who will apply the treatment. You can choose to apply it yourself, or a trained pharmacist or pharmacy technician can apply it for you. Application is done at the pharmacy, in a private consultation area. Application takes around one minute and only one treatment is required. You will not be able to take any of the treatment vials with you when you leave the pharmacy.

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 the costs of travel to your local participating pharmacy, you will receive a $60 gift voucher (that covers petrol or food) after you complete your second pharmacy visit.

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 last pharmacy 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?
Please be assured that only the researchers will have access to the raw data you provide. However, 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.

Consent Form

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

I hereby consent to participate in the above named research project.

I acknowledge that:

- I have read the participant information sheet (or where appropriate, have had it read to me) and have been given the opportunity to discuss the information and my involvement in the project with the research team.
- The procedures required for the project and the time involved have been explained to me, and any questions I have about the project have been answered to my satisfaction.

I consent to:

☐ *Providing data such as my age, gender and relevant medical history.*

☐ *Having a single vial of topical treatment applied to my cold sore at the pharmacy*

☐ *Coming back to the pharmacy within 24 hours of my lesion healing for visual confirmation*

☐ *If my lesion ulcerates, using a swab at home to take a sample and posting the sample in the envelope provided*

☐ *Providing daily information in an online diary*

I consent for my data and information provided to be used in this project and other related projects for an extended period of time.

Participation is entirely voluntary and you are not obliged to be involved. If you do participate you can withdraw at any time without giving reason.

I understand:

- that my involvement is confidential and that the information gained during the study may be published and stored for other research use but no information about me will be used in any way that reveals my identity but will only be used after additional ethical review.
- that I can withdraw from the study at any time without affecting my relationship with the researcher/s, and any organisations involved, now or in the future.

I would like to receive a summary of the study results when they are available.

Please tick: ☐Yes ☐ No

Participant to sign:

Signed: _____

Name: _____

Date: _____

Pharmacist/researcher to sign:

Signed: _____

Name: _____

Date: _____

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