CONSENT FORM

An open-label study to evaluate DPCP ointment for the treatment of alopecia areata

Site:	Department of Dermatology University of Minnesota
Sponsors:	National Alopecia Areata Foundation, San Rafael, CA
Study Drug Manufacturer:	Ferndale Laboratories, Inc., Ferndale, MI for Hapten Pharmaceuticals, LLC, Grosse Pointe, MI
Principal Investigator:	Maria Hordinsky, MD
Co-Investigator:	Ronda Farah, MD

What is research?

Doctors and investigators are committed to your care and safety. There are important differences between research and treatment plans:

- The goal of research is to learn new things in order to help groups of people in the future. Investigators learn things by following the same plan with a number of participants, so they do not usually make changes to the plan for individual research participants. You, as an individual, may or may not be helped by volunteering for a research study.
- The goal of clinical care is to help you get better or to improve your quality of life. Doctors can make changes to your clinical care plan as needed.

Research and clinical care are often combined. One purpose of this informed consent document is to provide you clear information about the specific research activities of this study.

Why am I being asked to take part in this research study?

You are invited to participate in a research study to assess the effect that topical (applied to the skin) treatment of an ointment containing the drug diphenylcyclopropenone (DPCP) has on hair loss in patients with extensive alopecia areata. You were selected as a possible participant because you have been diagnosed with extensive alopecia areata. We ask that you read this form and ask any questions you may have before agreeing to be in this study.

This study is being conducted by Maria Hordinsky, MD, Department of Dermatology, University of Minnesota. Other members of the study team are Ronda Farah, MD Co-Investigator, and Research Assistants in the Department of Dermatology at the University of Minnesota.

Why is the study being done?

Alopecia areata is caused by the immune system attacking the hair follicle, which prevents hair growth. DPCP is a contact sensitizer that causes an allergic reaction in the skin. This allergic reaction is thought to draw the immune system away from the hair follicle, allowing new hair to grow. DPCP ointment is an investigational drug. It has been used for decades throughout the world for the treatment of alopecia areata, but has not been approved by the FDA for treatment of this disease.

The purpose of the study is two-fold. First, we will see whether treating alopecia areata with an ointment containing DPCP is safe and causes hair to regrow. Second, we will take blood and scalp biopsy samples and analyze them for biomarkers. The biomarkers in this study are molecules related to DNA that tell us whether certain genes are turned on or off. Those markers may help us predict whether or not patients respond to this type of treatment. The testing for biomarkers will also help us to better understand what causes alopecia areata.

How long will the study last?

This study requires you to make a minimum of forty-two (42) visits to the study site (up to 46) over a course of approximately five to six months.

What is involved in the study?

If you agree to participate in this study, we would ask you to do the following:

You will be asked **not to use prescription or over-the-counter products to treat your alopecia areata during the study without checking first with the study doctors.** In addition, you should not use any other investigational drugs while participating in the study.

If you are currently taking medications/treatments for your alopecia areata, you will be asked to stop taking them for long enough for the effects of the medications/treatments to leave your body before you will be given the study drug. This is called a "washout period". ~~Depending on which medication or treatment you were taking, this "washout period" may be between 4-12 weeks~~. Each medication has a different "washout period" but the study team can tell you what the "washout period" would be for your specific medication. You will be asked not to use any other medication/treatment during the study without alerting the investigative team.

<u>Screening & Physical Examinations</u>
Your first visit is for determining if you are ready to take part in the study. At this visit, we will review this consent form and a HIPAA form. You will be asked questions to see if you meet criteria for taking part in the study. The study doctor will review your medical and medication history with you, and complete a physical examination. Less than half a tablespoon of blood will be collected for regular laboratory tests and to test for low levels of thyroid hormone and vitamin D, and anemia (low levels of red blood cells). If you are a woman who is able to become pregnant, a pregnancy test will be performed. All lab test results will be recorded in your medical record.

At some of your visits, your weight and vital signs (pulse rate, blood pressure) will be measured. After you begin treatment, you will be asked to report any changes in your health or medications, or any symptoms that have occurred since the previous visit.

Measuring your Alopecia Areata

At the beginning and end of the study the study doctor will measure your hair loss and you will complete a survey to report your symptoms. A research coordinator will also take photographs of your scalp on those days to record what your hair loss looks like. The photographs that will be collected will not disclose your identity.

The study doctor will also measure your hair loss and the study coordinator will photograph your scalp at visits once per month while you are being treated with DPCP.

Skin Biopsy Procedure

Three (3) 4-mm skin biopsies will be collected up to 3 times during the study. All participants will give 3 biopsy samples three times: once at the beginning of the study, once soon after you begin treatment, and once at the end of the study. Some participants may regrow more than 50% of their hair on their scalp. For those participants, we will collect three biopsy samples on a visit when we measure that hair regrowth, rather than at the end of the study.

A skin biopsy is obtained in the following manner. An anesthetic, usually 1% lidocaine with epinephrine, is injected to numb the area to be biopsied. Then, an instrument which looks like a pencil but which has a sharp 1/8 inch opening (i.e.○) at its tip, is applied to the numbed skin using a twisting motion. This removes a piece of skin of the same size. At the conclusion of the procedure, you will have one to two stitches for each biopsy. The stitches will be removed 10-14 days after the biopsy procedure. Study staff will be careful not to apply ointment to the area with the stitches until they are removed.

The skin biopsy specimen collection is not standard of care for alopecia areata. As such research funds will pay for the skin biopsy procedure.

Blood Draw

Approximately 3 tablespoons of blood will be collected from your inner elbow on the same visits as your biopsy. Blood will also be drawn at the screening visit and visit 29.

Treatment with DPCP Ointment

Sensitizing

Before we start treating your scalp with the ointment, we need to create in you an allergic reaction to DPCP. This is called “sensitizing” you to DPCP. We will do this on your second visit. A washable marker will be used to make a small marking on the inner part of your upper right arm. The DPCP ointment will be applied to directly to the skin over that marking.

At the third visit, the study doctor will view the inner part of your upper right arm to see if sensitizing you to DPCP worked. We will know that you are sensitized if redness or itching has occurred in the spot where the DPCP ointment was applied. If you are not sensitized, we will try sensitizing you again one more time. If you are still not sensitized after both tries, you will not be able to participate in this study.

Determining the correct dose for you
After you are sensitized to DPCP, we need to find out how strong the ointment that we apply to your scalp will need to be. We will test up to four (4) different doses on the inner part of your upper left thigh. The four areas where the doses were applied will each be covered with a spot Band-Aid and a clear waterproof dressing. There are four different possible doses that you could be put on. We will apply these one at a time starting with the lowest and getting higher and stop once you have a strong enough reaction to the lowest possible dose. This will be your dose for the duration of the study. Therefore, it is possible that you could have up to 4 different visits to determine your best dose or you could have only one, if you have a strong enough reaction to the lowest dose.

We will look at the areas at your next visit, which we call the "challenge" visit. We will then begin treating you.

Treating your hair loss
After we determine your dose, we will begin treating your scalp with the DPCP ointment. The ointment will be applied to the entire scalp at twice per week visits over a period of four and a half months (18 weeks). In all, there will be 37 visits where the drug will be applied to the scalp.

What does the schedule look like?

	Visit							
Procedure	**1**	**2**	**3**	**4**	**5**	**6-40**	**41**	**42**
Informed consent	X							
Screening for eligibility	X						X	
Blood tests	X					X (1 time at week 12)	X	
Pregnancy test	X					X (1 time a month)	X	
Vital signs	X	X			X	X (1 time a month)	X	X
Adverse events		X	X	X	X	X		X
Assessment of hair loss	X		X			X (1 time a month)	X	
Photographs	X		X			X (1 time a month)	X	
Scalp biopsy procedure		X			X	X (if 50% regrowth)	X	
Suture removal				X		X (as needed)		X
Blood draw		X			X	X (if 50% regrowth)	X	
DPCP ointment - sensitizing		X						
DPCP ointment – dose determination			X					
DPCP ointment - challenge				X				
DPCP ointment - treatment				X	X	X (twice per week For 17 weeks, visit 40 will occur during week 18)		
Study completion								X

What are the possible risks?

The risks of participating in the study include:

Biopsy Procedure
The risks associated with the punch biopsy procedure, although slight, include dizziness or fainting, an allergic reaction to the anesthetic, a stinging sensation when the anesthetic is injected, bleeding at the biopsy site, and the possibility of developing an infection at the biopsy site. Six months or so after the procedure, the biopsy sites should be barely noticeable. However, some individuals may develop a scar at the site where a biopsy was taken.

Blood Draw
The risks associated with donating a blood sample include pain at the site of the blood draw, bruising, and bleeding and rarely, the chance of infection or fainting.

DPCP Ointment

All participants will have a mild dermatitis (redness, itching) because of the DPCP, as that is how the drug works. Other side effects occur in roughly 2-5% of patients, particularly before the correct dose of DPCP is determined. Those possible side effect include: a more severe dermatitis that can involve larger areas of redness, swelling, and/or blistering where the DPCP was applied, dermatitis spreading to areas of the body where the DPCP was not applied, or hive-like reactions and changes in the skin coloring such as darkening of skin in treated areas. Notably, no long term side effects have been reported after 18 years use of DPCP.

Are there any potential benefits?

There are no direct health benefits to you from participating in this study, other than the possibility of hair regrowth where the DPCP is applied. It is possible that the information gained from your participation may help others with alopecia areata.

What other options are there?

You do not need to participate in this study to receive treatment for your alopecia areata. The study doctor will discuss the various treatment options with you. The DPCP ointment is not commercially available, but you may choose not to participate in the study and still receive treatment with a different form of DPCP through your doctor.

What are the costs?

You will not be charged for procedures or clinic visits related to this research. DPCP ointment will be provided free of charge while you are in the study. You will not be compensated for your time spent participating in this study.

What will happen if there is a research-related injury?

In the event that this research activity results in an injury, treatment will be available, including first aid, emergency treatment and follow-up care as needed. Care for such injuries will be billed in the ordinary manner to you or your insurance company. If you think that you have suffered a research related injury, let the study physicians know right away.

What about confidentiality?

The records and photography of this study will be kept private. In any publications or presentations, you will not be identified by name or other recognizable way on any records, results or publications relating to the study. Your record for the study may, however, be reviewed by University of Minnesota (UM), University of Minnesota Physicians (UMP) and University of Minnesota Medical Center (UMMC) personnel who monitor research and UM, UMP and Medical Center personnel who need access to the information to complete the clinical trial. Your record may be reviewed by staff with the Clinical and Translational Science Institute (CTSI) at the University of Minnesota and the FDA for regulatory oversight. Your participation in this study may be recorded in your medical record. To these extents, your confidentiality is not absolute. Study data will be encrypted according to current University policy for protection of confidentiality.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. law. This Web site will not include information that could identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

What will happen with my biological samples?
The blood and biopsy samples you donate will be used for research only. The samples will be processed and stored in dermatology and genomic laboratories at the University of Minnesota. A portion of your sample will also be sent to Dr. James Krueger at the Rockefeller University in New York, NY. You will be assigned a study identification number that will be attached to your samples. No personal identification information will go with your samples, so your identity will not be compromised. Samples taken will be kept indefinitely. The data will become the property of the Clinical Research Division, Maria Hordinsky, M.D., Director.

What about protected health information (PHI)?

Your PHI created or received for the purposes of this study are protected under the federal regulation known as HIPAA. You will be asked to review and sign a separate HIPAA authorization concerning the use of this information.

What are your rights as a research subject?

Your participation in this study is entirely voluntary and you have the right to choose not to participate. Your decision whether or not to participate in this study, or to withdraw from the study, will not affect your current or future relations with the University of Minnesota, the Department of Dermatology, or the University of Minnesota Medical Center, Fairview.

If you decide to participate, you are free to withdraw at any time, even after signing the consent form, without giving a reason. The principal investigator and study team can stop your participation in the study at any time without your consent for any reason.

If you withdraw voluntarily from the study or are taken out of the study, you may be asked questions about your experience in the study. You also may be asked to have laboratory tests and physical examinations, as the study doctor considers necessary.

The study doctors will notify you if there are new findings about DPCP or the ointment in which it is delivered that might affect your willingness to continue to be in the study, or that could affect your health either during or after the study.

Whom do I contact if I have questions, concerns or feedback about my experience?

To reach the research team: Please see the "Investigator Contact Information" section at the beginning of this form.

To reach someone outside of the research team: This research has been reviewed and approved by an IRB within the Human Research Protections Program (HRPP). To share feedback privately with the HRPP about your research experience, call the Research Participants' Advocate Line at 612-625-1650 (Toll Free: 1-888-224-8636) or go to z.umn.edu/participants. You are encouraged to contact the HRPP if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You are having difficulty reaching the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research participant.
- You want to get information or provide feedback about this research.

Will I have a chance to provide feedback after the study is over?

The HRPP may ask you to complete a survey that asks about your experience as a research participant. You do not have to complete the survey if you do not want to. If you do choose to complete the survey, your responses will be anonymous.
If you are not asked to complete a survey, but you would like to share feedback, please contact the study team or the HRPP. See the "Investigator Contact Information" of this form for study team contact information and "Whom do I contact if I have questions, concerns or feedback about my experience?" of this form for HRPP contact information.

You will be given a copy of this form to keep for your records.

Statement of Consent

I have read the above information. I have asked questions and have received answers. I consent to participate in the study.

_____
Subject's Name (Print)

_____
Subject's Signature

_____
Date of Signature

_____
Name of person conducting consent process (Print)

_____
Signature of person conducting consent

_____
Date of Signature