UF Institutional Review Board
UNIVERSITY of FLORIDA

INFORMED CONSENT FORM
to Participate in Research, and

AUTHORIZATION
to Collect, Use, and Disclose Protected Health Information (PHI)

INTRODUCTION

Name of person seeking your consent:_____

Place of employment & position: _____

Please read this form, which describes the study in some detail. A member of the research team will describe this study to you and answer all of your questions. Your participation is entirely voluntary. If you choose to participate you can change your mind at any time and withdraw from the study. You will not be penalized in any way or lose any benefits to which you would otherwise be entitled if you choose not to participate in this study or to withdraw. If you have questions about your rights as a research subject, please call the University of Florida Institutional Review Board (IRB) office at (352) 273-9600.

GENERAL INFORMATION ABOUT THIS STUDY

1. Name of Participant ("Study Subject")

_____

2. What is the Title of this research study?

A Phase 2, Exploratory Study to Investigate Safety and Efficacy of Doxycycline Monohydrate Hydrogel (NANODOX® HYDROGEL 1%) In Atopic Dermatitis

3. Who do you call if you have questions about this research study?

Principal Investigator: Anna De Benedetto, MD – Department of Dermatology, UF

Phone Number: (352) 594-1500, a 24-hour number that can be used after hours and on weekends and holidays

Other research staff:

Mary Bohannon, CCRA - Research Coordinator

Phone Number: (352) 594-1547

Email: mebohan@ufl.edu

Lenise Thomas, LPN - Research Nurse

Gregory Schultz, PhD – Co-Investigator

Kiran Motaparthi, MD – Sub-Investigator

Kathryn Potter, MD - Sub-Investigator

Alex Owens, MD– Sub-Investigator

Jennifer Harb, MD – Sub-Investigator

Jennifer Schoch, MD- Sub-Investigator

Bahram Dideban, MD- Sub- Investigator

Michael Montuno, MD- Sub-Investigator

Sanjuana Rodriguez, PA-C- Sub-Investigator

Gina Martorana – EPIC specialist and technology support

Peter Nadeau – Laboratory Bioscientist

4. Who is paying for this research study?

The sponsors of this study include University of Florida Clinical and Translational Science Institute, College of Medicine Department of Dermatology, and Alchem Laboratories Inc.

5. Why is this research study being done?

Atopic Dermatitis (AD), also known as eczema, is the most common inflammatory skin disease, affecting about 17% of children and 6% adults in the United States of America. AD is characterized by skin barrier disruption/open sores, an exaggerated inflammatory response to environmental triggers, susceptibility to skin bacterial infections and hard to control itch. The intense itch and skin infections contribute to the disease and are major drivers of the reduced quality-of-life. So far, AD treatments have targeted inflammation with the widespread use of topical (applied directly to the skin) and more intermittent use of systemic (taken by mouth or injection)

corticosteroids. Despite its high prevalence, effects on quality-of-life and economic burden – there are few effective treatments for AD.

Doxycycline are tetracycline antibiotic, commonly used to treat inflammatory-dermatologic conditions and are often prescribed as oral pill. Several studies in human and animal models have shown doxycycline has anti-inflammatory and pro-healing properties, mainly by blocking activity of certain proteins in the skin.

The purpose of this research study is to investigate the safety and clinical efficacy of a novel 1% topical Doxycycline Monohydrate (NanoDOX® Hydrogel 1%) in Atopic Dermatitis (AD). This investigational drug has been approved by the FDA for use in this study but is not yet commercially available. We are investigating whether the daily application of NanoDOX® Hydrogel 1% blocks activity of specific proteins (cutaneous proteases) in the skin in patients with AD and reduces severity of the disease, by restoring skin barrier function and reducing skin driven inflammation. Throughout the remainder of this form, NanoDOX® Hydrogel 1% will be referred to as Study Drug. Importantly, during the study we will also monitor the anti-microbial activity of this product on AD skin, as colonization with *Staphylococcal aureus* is typically associated with disease severity.

The study drug will be provided to you in single-dose package containing 1.5 cc of hydrogel with 1% nanodoxy (equal to 15mg Doxycycline). Of note, for systemic use doxycycline is taken orally at doses of 40 mg to 100 mg twice a day, for 2 weeks to several months; this is about 3-14 times the amount that is in the skin gel . We want you to apply the study drug on the target area that will be described to you during your study examination. This target area will include an area with an active dermatitis lesion and the surrounding area. We will be testing both areas throughout the study.

You are being asked to be in this research study because you have previously been diagnosed with atopic dermatitis and may meet the inclusion criteria.

WHAT CAN YOU EXPECT IF YOU PARTICIPATE IN THIS STUDY?

6. What will be done as part of your normal clinical care (even if you did not participate in this research study)?

All the study procedures will be for research purpose only. We will schedule the research visits at a different time than your routine dermatologic visits.

7. What will be done only because you are in this research study?

If you agree to be in this study, we will ask you to come to the Department of Dermatology for at least four visits.

Study Design: Evaluation of NanoDOX Hydrogel 1% in AD subjects.

(Vp)	V1	V2	V3	V4
Pre-Screening <28days	Day 0	Day 14 +/-2	Day 28 +/- 2	Day 42 +/- 5
Clinical & itch score, Skin barrier, photographs	X	X	X	X
Swab, Blood & Skin biopsy	X		X	

Pre-Screening visit (optional, <28days from Day 0):

This visit will take approximately 30 minutes. We will review this consent form with you. If you agree to participate, you will be asked to sign this consent form. A copy of the form will be given to you. We will review your medical history medical history including medications and you will have a dermatology exam (a physician from the study team will look at your skin). If you meet the inclusion criteria, the use of certain medications will be discussed with you, including stopping the use of these medications if necessary until your participation is complete. You will be scheduled to return to the clinic for Visit 1.

Visit 1 (Day 0): This visit will take approximately 2 hours.

At Visit 1, we will review the consent form with you and address any questions or concerns that you may have. If you continue to agree to participate in this study, we will confirm that you still meet the study requirements. The following study related procedures will be performed as part of this visit.

1) Urine Pregnancy test for woman of childbearing potential
   We will ask you to provide a urine sample for a urine pregnancy test. This test will need to be negative to be enrolled on the study. The study doctor will counsel you on acceptable birth control measures to use throughout treatment period (28 days) and until 30 days after stopping the study drug.

2) General History, Physical Exam, and Skin Exam (including review of medications)
   We will do a short exam to make sure that you qualify for the study. We will ask you to wear a gown for the skin exam. This will take about 15 minutes. During this exam, we will ask you questions about your skin. The Doctor will score different areas of your skin for redness, scratch-marks, thickness and other clinical signs of skin disturbance and signs of eczema (atopic dermatitis). You will be asked to describe your skin's itchiness.

3) Target Area Identification
   An area of your body will be identified as the target area to be treated with the study drug and skin biopsy locations will be selected. Arms will be the preferable areas if lesions are present, otherwise legs or torso areas may be chosen.

4) Digital Photographs
   We will take digital photographs of the target area and area used for biopsy.

5) Skin Barrier Measurements

The study team will apply special tools/probes on your skin to measure your skin. These tools measure water loss from the skin:

TransEpidermal Water Loss, (TEWL), the pH of the surface of skin, and how moisturized the skin may be (Stratum Corneum Hydration). This procedure will be repeated at each visit. We call this testing Skin Barrier Measurements.

6) Tape Stripping

The study team will also place circular tape (approximately the size of a quarter) onto your skin. This tape has a special adhesive (glue-like) material that will remove some of the cells of your skin. Tapes will be placed and removed multiple times one after another to remove the uppermost layer of cells and debris that may be on the surface of your skin. These tapes will be placed in an area of an eczema lesion and in an area that does not have a lesion. We will repeat the TEWL skin barrier measurement tool on the areas where the tape was removed.

7) Skin Swab

The study team will use a cotton swab to collect a sample from the surface of your skin in the target lesion area.

8) Optional Skin Biopsy

A 5mm punch biopsy approximately the size of pencil eraser will be taken from an area of skin that is similar to the location of the target lesion. For example, if the target lesion is on the right arm, we would ask to take the first biopsy from the left arm. The area will be numbed with numbing medicine before to reduce any pain in the area. The numbing medicine will be injected into the skin. You will have the option to have this biopsy performed at Visit 3 at the same time as the optional post-treatment biopsy.

9) Blood Draw

Approximately 1 teaspoon (5mL) of blood will be drawn from a vein.

In the **Study procedures & method** section of this consent form you will find more detailed information about the study procedures. Please feel free to ask any of the study team member any question you might have.

10) Study Drug Instructions

The study team will give you enough study drug until your next visit (approximately 14 day supply)

- Instructions will be provided on how and where to apply the product including an at home diary to be completed and special instructions for the morning of upcoming appointments. The target lesion location will be identified on a body map for reference.
- You will be instructed to keep the study drug refrigerated (40°F); We will will be provided with a cooler and ice pack for transport of the study drug so that it remains in a refrigerated environment.
- You will be asked to bring the cooler with you to your next visit and to return the study drug packages, empty or unused.

At home, we will ask you to apply the study drug once daily at bedtime on the chosen target lesion and on the surrounding area (to cover an area of approximately the size of an index card). In the morning rinse the area with water and soap to remove possible leftover study drug. When taken orally, doxycycline can make your skin more sensitive to the sun, during the day when you are exposed to sun make sure you keep the area covered or apply sunscreen (SPF 30 or higher).

If you take any topical treatment for your current skin condition you will be asked to discontinue the use of those medications only in the target lesion and perilesional area for one week before starting the study (washout period) and until study completion. During the study, you will be allowed to stay on anti-histamine and any topical treatment in other lesional areas (except for the target area) as long as the dose of medication does not change. If you have any worsening change in the target area (intense itch, increase redness, pain or oozing) you will be asked to contact the study doctor using the 24-hour number provided. The study doctor will discuss with you what rescue medication you can use (e.g. topical steroid that you have used before the study). You may be asked to return to the clinic.

Visit 2 (Day 14 +/-2): This visit will take approximately 1 hour.

1) Review subject diary and address any questions, concerns, or missed doses

2) Brief Physical Exam and Skin Exam

3) Suture removal at pre-treatment biopsy site, if applicable

4) Digital photographs of the targeted area

5) Skin Barrier Measurements: TEWL, +/- pH and SC hydration

6) Repeated tape strippings and repeat TEWL.

7) Dispense the study drug for two following weeks and provide at home diary with study instructions and next visit date.

In case of complete resolution of the treated area at V2, post treatment biopsy and swab and Venous blood draw will be performed at this visit (instead V3) and subject's final visit will be performed at Day 28.

Visit 3 (Day 28 +/-2): This visit will take approximately 1 hour and 30 minutes.

1) Review subject diary and address any questions, concerns, or missed doses

2) Brief Physical Exam, and Skin Exam

3) Digital photographs of the targeted area

4) Skin Barrier Measurements: TEWL, +/- pH and SC hydration

5) Tape strippings and repeat TEWL

6) Skin swab of treatment area

7) 2 Optional skin biopsies (5 mm punch) 1) from treatment site and 1) from not treated site

8) Venous blood draw

9) Provide at home diary with study instructions and next visit date

Visit 4 (Day 42 +/-5): This visit will take approximately 45 minutes**.**

1) Review subject concerns or questions since last visit

2) Brief Physical Exam and Skin Exam

3) Suture removal at biopsy site

4) Take digital photographs of the targeted area

5) Skin barrier Measurements: TEWL, +/- pH and SC hydration

6) Repeated tape strippings and repeat TEWL

7) Discharge from study, including counseling on birth control measures through 30 days after last application of study drug.

Study procedures & method-

Clinical Score: Subjects will be assessed by:

1) Investigator Global Assessment (IGA), which will provide information of the overall disease (four point scale: clear, mild, moderate, severe).

2) Eczema Area and Severity Index (EASI), It is the sum of the intensity scores for four signs (0 to 3): erythema, induration (hardening), excoriation (scratch-like marks on the skin), lichenification (thickening of the skin) and it is recorded for targeted treatment areas as well as four regions of the body (i.e., head, trunk, lower and upper extremities). The presence or absence of skin irritation will be noted at each study visit.

3) Pruritus Scale (5-D): The pruritus (itch) categorical scale is a 4-point scale commonly used in clinical studies of AD. The scale is rated as follows: 0: absence of pruritus; 1: mild pruritus (occasional slight itching/scratching); 2: moderate pruritus (constant or intermittent itching/scratching that does not disturb sleep) and 3: severe pruritus (bothersome itching/scratching that disturbs sleep).

4) Digital photographs: A digital picture will be taken with a dedicated digital camera. The photographs will be labeled with the subject's study ID and date. Photographs will not include identifying information (e.g. facial features, tattoo, etc.). Photographs will be taken at a distance for easy identification of the anatomical area and closer to better capture clinical changes. Digital photographs will be used to record the location and monitor the size of target lesions. At conclusion of the study, two medical doctors on the study team will be asked to score (0-4 scale, clear, mild, moderate, severe) in a blind fashion (i.e., photographs will be de-identified and presented randomly/ not inchronologic order). This would allow objective confirmation of the clinical score taken during the study.

Skin swab: Skin swabs will be collected for microbiologic analysis to look for bacteria on your skin, including S. aureus spp. and to determine antibiotic sensitivity. Skin swabs are performed by swiping and rolling a sterile cotton-tipped applicator 4-5 times across the target area. Swabs will be obtained from target lesion areas pre and post treatment. These swabs may be repeated as needed throughout the study to monitor bacterial growth.

Optional Skin biopsy: The biopsy will consist of removing a piece of skin with a sterile 5-mm skin biopsy punch. One skin biopsy sample (5 mm ≈ pencil eraser size) will be obtained within the surrounding area of the target lesion (if possible) or on the contralateral side before and after treatment with study drug. Biopsy will be performed after injecting a local anesthetic (Lidocaine +/- epinephrine) to minimize pain and bleeding. At the biopsy sites, one or two sutures will be placed to ensure better healing, minimize blood loss and to provide a more aesthetic scar formation. A pressure bandage will be applied to the biopsy site to minimize the risk of bleeding and infection. We will provide each subject with a wound care instruction sheet.

Each biopsy will be used for analysis of proteins that are typically upregulated in inflammatory skin. Secondarily, we will evaluate changes in inflammatory and pro-inflammatory pathways in study-drug treated and non-treated skin. The biopsies are optional.

Tape stripping: The most superficial layers of the skin will be collected by tape stripping using D-squame and Cuderm™ tape. Tapes will be applied and removed immediately one after the other: 0, 5, 10, and 15 tape-strippings. This is a well-established method used in clinical research to gently disturb the skin barrier. The first tape will be discarded to eliminate dirt and remnants of skin products. Each tape will be gently pressed against the skin using a standardized pressurizer instrument (D-squame). Non-lesional skin samples will be collected from the volar side of the forearm and lesional skin samples will be collected from the target area in an easily accessible area, such as arms or lower legs.

This method collects most superficial layer of the skin to analyze for the presence of proteins important in skin inflammation.

Skin barrier measurements: Transepidermal water loss (TEWL), pH and skin hydration measurements will be obtained on treatment area at a non-lesional site and on a site of inflammation. For each of the specific measurements, a probe will be gently applied on the skin surface for up to 90 seconds. We will perform all measurements in a climate-controlled examination room with consistent temperatures humidity after the patient has become comfortable in the room to ensure that perspiration due to stress or acclimatization does not alter the TEWL. TEWL will be measured at baseline and after tape stripping at each visit. Optional measurements: Skin hydration and surface pH will be assessed on non-lesional and lesional skin before tape stripping at each visit when equipment is available. These measurements should provide data to determine if the treatment has an effect on skin barrier integrity.

Blood Sample: A blood sample (4 ml, approximately 1 teaspoon) will be obtained to evaluate biomarkers of disease severity. This blood sample will be drawn at 2 visits: Day 0 before treatment and Day 14 (if lesion is resolved) or Day 28 after treatment period is complete.

Test Results: Results of the tests will not be shared with you since it is not known what importance they would have for your medical care. Knowing the test results would not change your medical care.

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 can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

8. How long will you be in this research study?

This study consists of up to 5 visits, including the screening visit, during an approximate 70-day time period. The study treatment period is expected to be 42 days (6 weeks). Some subjects may complete the study in approximately 28 days if resolution of lesion is noted at the 14-day visit.

9. How many people are expected to take part in this research study?

We hope 15 subjects will complete all protocol-required visits. Up to 30 subjects will be recruited from the University of Florida Department of Dermatology.

WHAT ARE THE RISKS AND BENEFITS OF THIS STUDY AND WHAT ARE YOUR OPTIONS?

10. What are the possible discomforts and risks from taking part in this research study?

Risks Associated with Digital Photographs

There are no known risks for the digital photographs. The image will not include identifying features and will be labeled with study subject ID and date. Photographs will be taken with a dedicated camera, stored on a secure server and transferred into secure database.

Risks Associated with Barrier Assessments

There are no known risks for the barrier assessments.

Risks Associated with Tape Stripping

The risks associated with tape stripping, theoretically, include the rare possibility of an allergic reaction to the tape and infection. The tape used is approximately the size of a quarter and is a gentle adhesive specifically designed for this measurement. Each tape is removed 10seconds after application, thus the risk of reaction is extremely low. We will exclude study subjects with known allergy to tapes or adhesive material. In previous and ongoing studies involving tape stripping, it has been noted that a very mild erythema may develop immediately after a series of tape stripping on one localized area of skin, presumably due to the mild mechanical disturbance. The erythema is expected to resolve within 12 hours without further effect. The risk of skin infection is extremely low since only superficial skin layers are removed. Subjects will be provided with wound care information and a department phone number to contact should they have any concerns.

Risks of blood draws

The risks of drawing blood from a vein include discomfort at the site of puncture; possible bruising and swelling around the puncture site; rarely an infection; and, uncommonly, faintness from the procedure.

Subjects will be encouraged to drink plenty of water prior to the blood draw. Phlebotomy will be performed on the interior side of the elbow to minimize pain and bruising. Subjects will be seated during the blood draw to minimize dizziness and any risk of falling. Pressure will be applied to the site after the draw and a Band-Aid will be applied to minimize the risk of bleeding and infection.

Risks of punch biopsy and injection of local anesthesia

The biopsies will be no larger than 5 mm in diameter (about a pencil eraser head). At the biopsy site, one or two sutures will be placed to ensure better healing, minimize

blood loss and to provide a more aesthetic scar formation. A pressure bandage will be applied to the biopsy site to minimize the risk of bleeding and infection. A small scar will remain at the site. The scar will be smaller than the initial biopsy but may also be hypo- or hyper-pigmented. Sutures will be removed in 14 days. The risks of this procedure include adverse reaction to anesthesia (lidocaine), pain, bleeding, infection and hypertrophic scars. Biopsy will be performed after injecting a local anesthetic to minimize pain. Patients with a history of Novocain or lidocaine allergy or a history of keloid formation will not be allowed to participate in order to minimize the risk of adverse reactions. Written wound care instruction will be provided for at home care after the procedure. In case of increased redness, pain or oozing of the sites subjects will be instructed to call the dermatology department and if appropriate, subjects will be asked to come to clinic in the next 24-48 hours for wound check.

Risks of NANODOX® HYDROGEL 1% ®

Some patients may experience some irritation from the NANODOX® hydrogel especially in areas of open skin from scratching. Subjects may experience local irritation including redness, pain, stinging or burning sensation in the area. Some subjects might also experience a blistering rash or swelling. Some subjects may experience increased dryness from the hydrogel formulation. All patients will be advised to moisturize in the morning and use gentle body wash to minimize these potential side effect. Preclinical studies have shown that over time (12-24 hours) the color of leftover products in the package might change from a white transparent tone to a more yellow-brown color. Change in color has not been associated with change in efficacy. To minimize risk of skin discoloration we will advise the subjects to rinse off the site in the morning.

As with any antibiotic, long term use might increase the risk of developing antibacterial resistance.

Subjects with sensitivity to doxycycline might develop an allergic drug reaction, which could vary from local irritation to more severe systemic reaction. Subjects with known sensitivity/allergy to tetracycline will not be enrolled in the study.

In case of any abnormal reaction, we will instruct the subjects to call the dermatology office and stop using NanoDOX® Hydrogel 1% until discussing symptoms with study team.

Risks to children or pets are not known and subjects will be instructed to keep the products out of reach from children and pets. Because this is an investigational medication/formulation, some side effect may not yet be known. Any adverse reaction will be accounted.

Based on preliminary data, we do not anticipate any complications associated with the use of topical doxycycline.

Risks related to Oral Doxycycline

Common skin reactions with taking ***oral*** doxycycline include:

- Redness
- Swelling

•Blistering rash

Common allergic reactions with taking ***oral*** doxycycline include:
•Hives
•Shortness of breath
•Swelling of the face, lip, tongue, or throat

Common systemic reactions with taking ***oral*** doxycycline include:
•Headache
•Dizziness
•Fever
•Chills
•Rash
•Nausea
•Vomiting
•Diarrhea
•Thrush
•Vaginitis

General Risks

When participating in any research study there is a possibility for invasion of privacy or breach of confidentiality.

Property damage risks

Objects in contact with the study drug may have discoloration (e.g. bedding, towels, and clothes). Subjects are advised to be careful handling the opened study drug packages and to rinse the excess of product from their skin if they observe change in color to minimize the likelihood of stain on towels, rugs or other clothing.

Reproductive Risks

The effects of topical doxycycline on an unborn fetus or nursing (breast-feeding) infant are unknown. It is possible that use of the study drug may be associated with unanticipated risks to a pregnancy or fetus. Women of childbearing potential will be counseled to use acceptable birth control methods. Women will not be allowed to participate in this study if they are pregnant, become pregnant, or are nursing an infant.

Researchers will take appropriate steps to protect any information they collect about you. However, there is a slight risk that information about you could be revealed inappropriately or accidentally. Depending on the nature of the information, such a release could upset or embarrass you, or possibly affect your insurability or employability. Questions 17-21 in this form discuss what information about you will be collected, used, protected, and shared.

This study may include risks that are unknown at this time.

Participation in more than one research study or project may further increase the risks to you. If you are already enrolled in another research study, please inform Dr. Anna De Benedetto or one of the research team members listed in question 3 of this form at (352) 594-1547 or the person reviewing this consent with you before enrolling in this or any other research study or project.

Throughout the study, the researchers will notify you of new information that may become available and might affect your decision to remain in the study.

If you wish to discuss the information above or any discomforts you may experience, please ask questions now or call one of the research team members listed in question 3 in this form.

11a. What are the potential benefits to you for taking part in this research study?

There are no benefits for the individual participant. The investigational medication may temporally improve or worsen the lesion in the target area of application. The nature of this pilot study does not promise benefit for the individual.

11b. How could others possibly benefit from this study?

We hope that this research will increase our understanding of AD and hopefully this will lead to development of new therapeutics aiming at repairing skin barrier and skin driven inflammation.

11c. How could the researchers benefit from this study?

In general, presenting research results helps the career of a scientist. Therefore, the Principal Investigator Dr. Anna De Benedetto and co-Investigators may benefit if the results of this study are presented at scientific meetings or in scientific journals.

12. What other choices do you have if you do not want to be in this study?

Your participation in this study is voluntary. You may decide not to participate or you may leave the study at any time. Your decision will not result in any penalty or loss of benefits to which you are entitled.

13a. Can you withdraw from this study?

You are free to withdraw your consent and to stop participating in this study at any time. If you do withdraw your consent, you will not be penalized in any way and you will not lose any benefits to which you are entitled. If you decide to withdraw your consent to participate in this study for any reason, please contact Dr. Anna De Benedetto by calling (352) 594-1547 or one of the research team members listed in question 3 of this form. They will tell you how to stop your participation safely. If you experience adverse drug reactions, you will be followed until resolution or stabilization of the adverse event, or until you start a new treatment regimen. If you are removed from the study for unacceptable adverse events, you will be followed in the same manner. In addition, you may have to undergo additional tests, based on the condition of your health.

If you have any questions regarding your rights as a research subject, please call the Institutional Review Board (IRB) office at (352) 273-9600.

13b. If you withdraw, can information about you still be used and/or collected?

If you withdraw from the study samples and data already collected from you may still be used for research. Additional clinical data or samples will not be collected from you.

13c. Can the Principal Investigator withdraw you from this study?

You may be withdrawn from the study without your consent for the following reasons:

- Your disease worsens, you experience unacceptable toxicity, or you decide to withdraw from the study.
- Discovery of unexpected, unacceptable risks to participants.
- Your failure to follow the study doctor's instructions.
- You become pregnant.
- If it is in your best interest.
- If you do not later consent to any future changes that may be made in the study plan.

WHAT ARE THE FINANCIAL ISSUES IF YOU PARTICIPATE?

14. If you choose to take part in this research study, will it cost you anything?

Study Drug

NanoDOX® Hydrogel 1% will be provided at no cost to you while you are participating in this study.

Study Services

The Sponsor will pay for all services required as part of your participation in this study as described above in the question *"What Will Be Done Only Because You Are In This Research Study*". If you receive a bill for these services, please contact Dr. Anna De Benedetto and the study team by calling (352) 594-1547

Items/Services Not Paid for by the Sponsor

All other medical services provided to you that are not directly required by this study will be billed to you or your insurance company in the usual manner.

15. Will you be paid for taking part in this study?

You will be paid for each completed study visit, $ 25 for screening and follow up visit, $45.00 each visit, and an additional $45.00 for each biopsy for a total of up to $275.00 (2 biopsies) or $185.00 (without biopsies), according to the following schedule:

Screening visit=$25 (if needed)
Visit 1= $45(+$45 biopsy, or at Day28)= maximum of $90
Visit 14d= $45
Visit 28d= $45+$45post treatment biopsy+($45 for non-treatment biopsy, if not performed at Visit 1)= maxiumum of $135
Visit 42d= $25 (if needed)
Visa cards will be provided at Study Visit 1 and the cards will be loaded with the amount listed above within 7 business days of each completed visit.

If you are paid more than $75 for taking part in this study, your name and social security number will be reported to the appropriate University employees for purposes of making and recording the payment as required by law. You are responsible for paying income taxes on any payments provided by the study. If the payments total $600 or more or you are a nonresident alien, payment will be processed through the University of Florida Accounts Payable department and the University must report the amount you received to the Internal Revenue Service (IRS). The IRS is not provided with the study name or its purpose. If you have questions about the collection and use of your Social Security Number, please visit: http://privacy.ufl.edu/SSNPrivacy.html.

Your payment for participation in this research study is handled through the University of Florida's Human Subject Payment (HSP) Program. Your information which will include your name, address, date of birth, and SSN (depending on amount of money you are paid) is protected. Access to the (HSP) Program site is limited to certain staff with the assigned security role. You will be randomly assigned a specific identification (ID) number to protect your identity.

The study team will provide you with an informational form called the Prepaid Card Facts document. If you have any problems regarding your payment call the HSP Office (352) 392-9057.

University employees are no longer paid through the University payroll system. Instead, UF employees will be paid in a manner consistent with other participants in this research study.

16. What if you are injured because of the study?

If you are injured as a direct result of your participation in this study, only the professional services that you receive from any University of Florida Health Science Center healthcare provider will be provided without charge. These healthcare providers include physicians, physician assistants, nurse practitioners, dentists or psychologists. Any other expenses, including Shands hospital expenses, will be billed to you or your insurance provider.

You will be responsible for any deductible, co-insurance, or co-payments. Some insurance companies may not cover costs associated with research studies or research-related injuries. Please contact your insurance company for additional information.

The Principal Investigator will determine whether your injury is related to your participation in this study.

No additional compensation is offered. The Principal Investigator and others involved in this study may be University of Florida employees. As employees of the University, they are protected under state law, which limits financial recovery for negligence.

Please contact Dr. Anna De Benedetto and the study team by calling (352) 594-1547 or the Department of Dermatology triage nurse at (352) 594-1500 if you experience an injury or have questions about any discomforts that you experience while participating in this study.

17. How will your health information be collected, used and shared?

If you agree to participate in this study, the Principal Investigator or a research team member will create, collect, and use private information about you and your health. This information is called protected health information or PHI. In order to do this, the Principal Investigator needs your authorization. The following section describes what PHI will be collected, used and shared, how it will be collected, used, and shared, who will collect, use or share it, who will have access to it, how it will be secured, and what your rights are to revoke this authorization.

Your protected health information may be collected, used, and shared with others to determine if you can participate in the study, and then as part of your participation in the study. This information can be gathered from you or your past, current or future health records, from procedures such as physical examinations, x-rays, blood or urine tests or from other procedures or tests. This information will be created by receiving study treatments or participating in study procedures, or from your study visits and telephone calls. More specifically, the following information may be collected, used, and shared with others:

- Complete past medical history to determine eligibility criteria
- Records of physical exams
- Laboratory and other test results
- Records about study medications or drugs
- Your social security number [for compensation purposes]

This information will be stored in locked filing cabinets or on computer servers with secure passwords, or encrypted electronic storage devices.

Some of the information collected could be included in a "limited data set" to be used for other research purposes. If so, the limited data set will only include information that does not directly identify you. For example, the limited data set cannot include your name, address, telephone number, social security number, photographs, or other codes that link you to the information in the limited data set. If limited data sets are created and used, agreements between the parties creating and receiving the

limited data set are required in order to protect your identity, confidentiality, and privacy.

18. For what study-related purposes will your protected health information be collected, used, and shared with others?

Your PHI may be collected, used, and shared with others to make sure you can participate in the research, through your participation in the research, and to evaluate the results of the research study. More specifically, your PHI may be collected, used, and shared with others for the following study-related purpose(s):

- to study if the study drug is safe and well-tolerated in humans
- to study whether the study drug has an effect on atopic dermatitis

Once this information is collected, it becomes part of the research record for this study.

19. Who will be allowed to collect, use, and share your protected health information?

Only certain people have the legal right to collect, use and share your research records, and they will protect the privacy and security of these records to the extent the law allows. These people include:

- the study Principal Investigator (listed in question 3 of this form) and research staff associated with this project.
- other professionals at the University of Florida or Shands Hospital that provide study-related treatment or procedures.
- the University of Florida Institutional Review Board (IRB; an IRB is a group of people who are responsible for looking after the rights and welfare of people taking part in research).

20. Once collected or used, who may your protected health information be shared with?

Your PHI may be shared with:

- The study sponsor, Alchem Laboratories will review your research records for quality assurance and data analysis purposes. Alchem will not give out any information which will let researchers know who you are.
- Alchem needs to review your PHI in order to analyze the information to find out whether the drug that is being tested if effective and to monitor your safety.
- United States governmental agencies who are responsible for overseeing research, such as the Food and Drug Administration, the Department of Health and Human Services, and the Office of Human Research Protections.

- Government agencies who are responsible for overseeing public health concerns such as the Centers for Disease Control and federal, state and local health departments.

Otherwise, your research records will not be released without your permission unless required by law or a court order. It is possible that once this information is shared with authorized persons, it could be shared by the persons or agencies who receive it and it would no longer be protected by the federal medical privacy law.

21. If you agree to take part in this research study, how long will your protected health information be used and shared with others?

Your PHI will be used and shared with others until the end of the study.

You are not required to sign this consent and authorization or allow researchers to collect, use and share your PHI. Your refusal to sign will not affect your treatment, payment, enrollment, or eligibility for any benefits outside this research study. However, you cannot participate in this research unless you allow the collection, use and sharing of your protected health information by signing this consent and authorization.

You have the right to review and copy your protected health information. However, we can make this available only after the study is finished.

You can revoke your authorization at any time before, during, or after your participation in this study. If you revoke it, no new information will be collected about you. However, information that was already collected may still be used and shared with others if the researchers have relied on it to complete the research. You can revoke your authorization by giving a written request with your signature on it to the Principal Investigator.

SIGNATURES

As an investigator or the investigator's representative, I have explained to the participant the purpose, the procedures, the possible benefits, and the risks of this research study; the alternative to being in the study; and how the participant's protected health information will be collected, used, and shared with others:

Signature of Person Obtaining Consent and Authorization	Date

You have been informed about this study's purpose, procedures, possible benefits, and risks; the alternatives to being in the study; and how your protected health information will be collected, used and shared with others. You have received a copy of this Form. You have been given the opportunity to ask questions before you sign, and you have been told that you can ask questions at any time.

You voluntarily agree to participate in this study. You hereby authorize the collection, use and sharing of your protected health information as described in sections 17-21 above. By signing this form, you are not waiving any of your legal rights.

Signature of Person Consenting and Authorizing	Date