Micropore closure kinetics

PI: Nicole Brogden
IRB ID #: 201806039

Project Details

I. Project Introduction

I.1 ***Project to be reviewed by:***
IRB-01

I.2 ***Project Title:***
Characterizing epidermal response and micropore closure following micropatch application at various body sites in human subjects of varied racial/ethnic skin types

I.3 ***Short Title (optional):***
Micropore closure kinetics

I.4 ***Provide a short summary of the purpose and procedures of the study proposed in this IRB application.***

- ***DO NOT include information on studies not proposed in this application.***
- ***Use LAY terminology only. This must be easily understandable by IRB community members and nonscientists.***
- ***DO NOT cut and paste technical abstracts from funding applications that may not be understood by a general audience.***

The purpose of this study is to determine how skin recovery differs at various body locations in subjects of different racial/ethnic skin types after disruption of the skin barrier by application of a micropatch. Healthy, consenting volunteers ages 18-50 years will be enrolled into 1 of 5 self-identified groups: African American/Black, Asian, Hispanic or Latino, Caucasian/White, and bi- or multiracial/other. Each racial group will receive the same microneedle treatment and measurements at each of three locations: the upper arm, the volar forearm, and the abdomen. At each location five sites will be identified. Noninvasive baseline measurements of hydration, water loss, electrical impedance, and color will be taken at each site. Three of these sites will receive treatment with a micromicropatch (also known as a microneedle) containing 50 tiny projections (or microneedles) that are 800 um in length. Water loss and impedance measurements will be repeated immediately following removal of the patch, and the sites will be covered with occlusive material secured with medical tape. One site will be covered with occlusive material but will remain untreated, and the remaining site will remain untreated and uncovered. The noninvasive measurements (except for water loss) will be repeated at 24, 48, and 72 hours, and new occlusive coverings will be applied at each visit.

I.5 ***Specify your research question(s), study aims or hypotheses (do not indicate "see protocol")***
This study aims to identify differences in micropore closure rates when microneedles are applied, through a micropatch, to different anatomical locations in volunteers of varied racial/ethnic groups. We hypothesize that there will be differences in micropore closure at the different body sites as well as among racial groups, as assessed by electrical impedance measurements. Micropore closure is indicative of skin barrier recovery.

I.6 ***Background and significance and/or Preliminary studies related to this project. (do not indicate "see protocol")***
The skin is an ideal drug administration route (called transdermal delivery) because it overcomes many physiological limitations encountered with oral administration. Unfortunately, the number of topical products and patches currently available is limited because few drugs contain the necessary properties to pass through the hydrophobic, cohesive skin barrier. Many studies have demonstrated that pre-treatment with minimally invasive microneedles can bypass this barrier by creating micropores through which a drug can pass. Importantly, microneedles are well tolerated due to painless application and ease of use.

Microneedles create aqueous micropores in the epidermis that serve as channels for drug delivery. Micropore lifetime corresponds to drug delivery, and is therefore important in determining dosing and frequency of administration to achieve a desired therapeutic effect. Micropores are short-lived, healing within 2 hrs, but this lifespan can be extended to 48-72 hrs by occluding the site with a patch. Many structural and molecular skin characteristics, such as hydration, water loss, sebum content, skin cell size and maturity, and cohesion may affect micropore healing and other aspects in transepidermal drug delivery. These characteristics vary by anatomical site as well as race/ethnicity of the individual.

There are almost no data comparing microneedle response at different anatomical sites, and there are limited data available describing the variation in skin characteristics at different sites. The skin on the abdomen and forearm is more mature than skin on the cheek and wrist. Hispanic/Latino individuals and Caucasian/White individuals have higher water content on one surface of the forearm compared to another. There are also differences in skin thickness, water loss, and protein and lipid composition across sites that can impact drug migration to the systemic circulation. All commercially available transdermal patches are approved for application only at specific body sites because of the variation in drug absorption that can occur from application on other locations on the body. Though direct comparisons of skin response to microneedle application at various sites are lacking, it is reasonable to expect that these differences will affect the rate at which micropores close, thus also affecting the drug absorption at that site.

Data characterizing racial/ethnic structural differences in the skin barrier are also limited. When comparing African American/Black, Asian, and Caucasian/White individuals, skin maturity and barrier strength is greatest in the African American/Black population and weakest in the Asian population. African American/Black individuals also have greater electrical resistance compared to Caucasian/White individuals. Highly pigmented skin exhibits faster recovery compared to lighter pigmentation. These differences are important considerations in micropore closure across populations. A study is currently underway in this lab to explore the differences in microneedle response in various racial/ethnic groups, but that study will only address differences at a single anatomical site.

In this study we will apply microneedles to the abdomen, forearm, and upper arm, by using a micropatch, in five racial groups. These sites were chosen in consideration of patient-accessibility for future self-application of a micropatch. We will measure electrical impedance to evaluate micropore closure and water loss to represent skin barrier integrity. We will also measure hydration, and redness/color to

characterize skin differences in both location and race. The results of this study will provide insight into the optimal locations for microneedle-assisted transepidermal drug delivery in a diverse population.

I.7 ***Literature cited / references (if attaching a grant or protocol enter N/A).***
N/A

II. Research Team

II.1 ***Principal Investigator***

Name	E-mail	College
Nicole Brogden	nicole-brogden@uiowa.edu	College of Pharmacy

II.2 ***Team Members***

UI Team Members

Name	E-mail	College	Contact	Key Prsn	UI COI	VAMC COI	Consent Process Involvement	Deactivated
Nicole Brogden, PharmD, PHD	nicole-brogden@uiowa.edu	College of Pharmacy	Yes	Yes	No		No	No
Jamie Carr, BA	jamie-carr@uiowa.edu	Inst Clinical & Translational	Yes	Yes	No		Yes	No
Valeria Cota, BA	valeria-cota@uiowa.edu	Graduate College	No	No	No		Yes	No
Nkanyezi Ferguson, MD, MD	nkanyezi-ferguson@uiowa.edu	Carver College of Medicine	No	Yes	No		No	No
Patrick Ten Eyck, MS	patrick-teneyck@uiowa.edu	Inst Clinical & Translational	No	No	No		No	No

Non-UI Team Members

Name Institution Location FWA Role DHHS Contact Key Prsn UI COI VAMC COI Consent Process Involvement Email

Nothing found to display.

II.3 ***The Principal Investigator of this study is:***
Faculty

II.6 ***Identify the key personnel. The system will automatically designate the PI and all faculty members on the project as "key personnel." For information about other team members who should be designated as "key personnel" please click on the help information.***

Name	Is Key Personnel
Nicole Brogden, PharmD, PHD	Yes
Jamie Carr, BA	Yes
Valeria Cota, BA	No
Nkanyezi Ferguson, MD, MD	Yes
Patrick Ten Eyck, MS	No

II.5 ***Select research team member who is the primary contact for study participants.***
Jamie Carr

III. Funding/Other Support

III.1 ***Funding Sources***

Type	Source	Grant Title	Name of PI on Grant
Federal Agency	US Department of Health & Human Services, National Institutes of Health	The effects of pharmacologic and physiologic variables on the pharmacokinetics of microneedle drug delivery	Nicole Brogden
Private Foundation/Association	American Foundation for Pharmaceutical Education	Characterizing epidermal response and micropore closure following microneedle application at various body sites in human subjects of varied racial/ethnic skin types	Christine Lawson

* new source name

III.2 ***What type of funding agreement would be completed?***

Federal/State/Local Agency/Non-Profit Funded/Other

III.3 ***Does any member of the research team have a financial conflict of interest related to this project according to the Conflict of Interest in Research policy? If yes, please indicate which members below.***

Name	Has Conflict of Interest
Nicole Brogden, PharmD, PHD	No
Jamie Carr, BA	No
Valeria Cota, BA	No
Nkanyezi Ferguson, MD, MD	No
Patrick Ten Eyck, MS	No

III.5 ***What is the current status of this funding source?***

Source	Status	Other Status Description
US Department of Health & Human Services, National Institutes of Health	Awarded	
American Foundation for Pharmaceutical Education	Awarded	

IV. Project Type

IV.1 ***Do you want the IRB to give this project***
Regular (expedited or full board) review

IV.2 ***Enter the date you will be ready to begin screening subjects/collecting data for this project. (If you do not have a specified date, add "upon IRB approval")***
Upon IRB approval

IV.3 ***Are you requesting a waiver of informed consent/authorization (subjects will not be given any oral or written information about the study)?***
No

V. Other Committee Review

V.1 ***Does this project involve any substance ingested, injected, or applied to the body?***

- ***Do not answer yes, if the involvement includes a device, wire, or instrument***

No

V.2 ***Are any contrast agents used for any purpose in this study?***
No

V.9 ***Will any subject be asked to undergo a diagnostic radiation procedure (including radiographic, nuclear medicine, DEXA)?***
No

V.14 ***Will any subject be asked to undergo a radiation therapy procedure (including external beam therapy, brachytherapy, or nuclear medicine therapy)?***
No

V.20 ***Does this project involve the deliberate transfer of recombinant or synthetic nucleic acid molecules, or DNA or RNA derived from recombinant or synthetic nucleic acid molecules, into one or more human research participant?***
No

V.21 ***Will any portion of this project be conducted in the CRU, or does it use any CRU resources?***
Yes

V.22 ***Will this project use:***

- ***any resource/patients of the Holden Comprehensive Cancer Center***
- ***involve treatment, detection, supportive care, or prevention of cancer***

No

V.25.a ***Will the study involve any of the following activity at UI Health Care, even if subjects or their insurance will not be billed for the item or service, and regardless of the study funding source (including studies with departmental or no funding)?***

- ***Procedures, tests, examinations, hospitalizations, use of Pathology services, use of clinic facilities or clinical equipment, or any patient care services, including services conducted in the Clinical Research Unit; or***
- ***Physician services or services provided by non-physicians who are credentialed to bill (ARNPs, Physician Assistants, etc.)***

No

V.26 ***The study involves Department of Nursing Services and Patient Care nursing, nursing resources or evaluates nursing practices at UI Health Care.***
No

VI. Subjects

VI.1 ***How many adult subjects do you expect to consent or enroll for this project?***
70

VI.2 ***What is the age of the youngest adult subject?***
18.0

VI.3 ***What is the age of the oldest adult subject?***
50.0

VI.4 ***What is the percentage of adult male subjects?***
50

VI.5 ***What is the percentage of adult female subjects?***
50

VI.6 ***How many minor subjects do you expect to consent or enroll for this project?***
0

VI.13 ***Describe EACH of your subject populations***

- ***Include description of any control group(s)***
- ***Specify the Inclusion/Exclusion criteria for EACH group***

Subjects will be healthy volunteers between the ages of 18 and 50 years. Our target enrollment is 14 subjects in each of 5 groups, with the expectation that some subjects will be consented but not complete the study. We expect that 10 subjects in each group will complete the entire study.

Inclusion criteria: Subjects will be healthy, non-obese men and women between 18 - 50 years of age who identify as African American or Black, Asian, Hispanic or Latino, Caucasian/White, bi-/multiracial or other.

Exclusion criteria: Unable to give consent; severe general allergies requiring chronic treatment with steroids or antihistamines; previous adverse reaction to microneedle insertion; previous history of keloids, known allergy or adverse reaction to medical tape/adhesive or aloe vera; any inflammatory diseases of the skin; psoriasis, atopic dermatitis, and blistering skin disorders; diseases associated with altered immune function (including but not limited to: rheumatoid arthritis, diabetes, lupus, HIV/AIDS); any subjects taking medication that impairs the immune system (including but not limited to corticosteroids, TNF inhibitors, monoclonal antibodies, chemotherapy agents); any current malignancy or history of malignancy present at the treatment site; eczema or scaling present at the treatment site; any current inflammation or irritation present at the treatment site (including but not limited to: rash, inflammation, erythema, edema, blisters); BMI>29.9. Uncontrolled mental illness that would, in the opinion of the physician, affect the subject's ability to understand or reliably participate in the study will also be an exclusion criteria.

Subjects taking medications in the following therapeutic classes will be excluded: HMGCoA reductase inhibitors ("statins"), oral or topical steroids, oral antibiotics, topical antibiotics at the local treatment site, topical antihistamines at the local treatment site, beta-blockers, and systemic or topical NSAIDS/analgesics. A subject who has recently used oral or topical steroids, antibiotics, antihistamines, or analgesics may be enrolled if more than 5 elimination half-lives of the drug have passed since the last dose (this is a typical parameter in pharmacokinetics, when it is assumed that 99% of drug in the systemic circulation is eliminated after 5 half-lives). The estimated elimination half-life for any specific drug will be obtained from standard pharmacy references such as Micromedex or other comparable references.

Any subjects that are pregnant/nursing will be excluded from participation. Subjects will also be excluded for any condition that would, in the opinion of the PI or physician, place the subject at an unacceptable risk of injury or render the subject unable to meet the requirements of the protocol.

VI.14 ***Provide an estimate of the total number of subjects that would be eligible for inclusion in each of your study populations (include your control population if applicable)***
It is somewhat difficult to know the total number of subjects that would be eligible for the study because we are recruiting generally healthy, non-obese individuals (of which there will be a large number in the local community). However, it is reasonable to estimate that perhaps several hundred to a few thousand subjects in this local area may be eligible.

VI.15 ***Describe how you will have access to each of your study populations in sufficient number to meet your recruitment goals.***
This is a relatively small study with low numbers of subjects per group, so we do not anticipate significant challenges with recruitment. We have had excellent enrollment in our previous studies, including one with very similar inclusion and exclusion criteria. For these studies, we used the following methods of advertisement, and will do the same for this study: mass emails, Noon News, advertisement at UIHC outpatient dermatology clinic, and advertisement on the University Cambus system.

VI.16 ***Do you <u>plan</u> to recruit/enroll non-English speaking people?***
No

VI.18 ***Do you propose to enroll any of the following in this study as subjects?***

- ***Employee of the PI or employee of a research team member***
- ***Individual supervised by PI or supervised by member of research team***
- ***Individual subordinate to the PI or subordinate to any member of the research team***
- ***Student or trainee under the direction of the PI or under the direction of a member of the research team***

Yes

VI.19 ***Provide justification for why these subjects must be included in the study.***

Individuals working in Dr. Nkanyezi Ferguson's Dermatology clinic (residents, fellows) and individuals within our own research group (post-doctoral fellows and graduate research assistants) that meet the inclusion requirements may be enrolled if there are unanticipated challenges with recruitment of our subject population.

VI.20 ***Will subjects provide any information about their relatives?***
No

VI.23 ***Will anyone (other than the subject) provide you with information about the subject (e.g. proxy interviews)?***
No

VI.26 ***Is this project about pregnant women?***
No

VI.27 ***Will this project involve fetuses?***
No

VI.28 ***Does this project involve adult subjects who may be incompetent or have limited decision-making capacity on initial enrollment into the study?***
No

VI.32 ***Does this project involve subjects whose capacity to consent may change over the course of the study?***
No

VI.37 ***Does this project involve prisoners as subjects?***
No

VII.A. Project Description (A)

VII.A.1 ***Where will project procedures take place (check all that apply)?***

- Other UI campus site - Upon closure of the study any hard copy study materials will be stored in the office of the Clinical Coordinator 558 CPB or in B105 and B109 ML.
- CRU

VII.A.2 ***Is this project also being conducted by other researchers at their own sites (e.g. a multi-site collaborative project)?***
No

VII.B. Project Description (B)

VII.B.1 ***Does this project involve any of the following (Check all that apply):***

- ☐ **Registry** – The collection and maintenance of data (not including biologic samples) in which: (1) the individuals in the registry have a common or related condition(s), and/or (2) the individuals in the registry are interested in being contacted for future studies by investigators other than those listed in Section II of this project.(UI Guide)
- ☐ **Repository** – The collection, storage, and distribution of human biologic samples and/or data materials for research purposes. Repository activities involve three components: (i) the collection of data and/or specimens such as blood, tissue, saliva, etc.; (ii) the storage of data or specimens, and data management function; and (iii) the sharing of data/specimens with recipient investigators other than the original investigators. (paraphrased from OHRP)
- ☐ **Expanded Access** – A process regulated by the Food and Drug Administration (FDA) that allows manufacturers to provide investigational new drugs to patients with serious diseases or conditions who cannot participate in a clinical trial. Examples of expanded access include non-protocol access to experimental treatments, including protocol exception, single-patient IND, treatment IND, compassionate use, emergency use, continued access to investigational drug, and parallel track (ClinicalTrials.gov & FDA).
- ☐ **Clinical (or Treatment) trial** – A prospective biomedical or behavioral research study of new treatments, new drug or combinations of drugs, new devices, or new approaches to surgery or radiation therapy. (NIH and ClinicalTrials.gov & FDA)
- ☑ **Physiology intervention/study** – A pharmacologic or measurement study aimed at understanding basic mechanisms of disease and/or of normal human physiology, often without any therapeutic intent (though a clinical trial could include such components, often labeled as "translational" or "basic science" aims.) Measurements in such studies could include, but are not limited to, a blood draw, EKG, EEG, MRI, auditory or sensory testing, checking vital signs, DEXA scans, eye tracking, specimen collection, exercise, fasting, special diets, etc.
- ☐ **Behavioral intervention/study** – May be used to refer to studies of individual or group behavior. This option does not include drugs, biologics, or devices but could include psychotherapy, lifestyle counseling, behavior modification, etc.
- ☐ **Diagnostic trial** – Protocol designed to evaluate one or more interventions aimed at identifying a disease or health condition (ClinicalTrials.gov & FDA)
- ☐ **Non-clinical** – any college/department that would regularly submit to IRB-02
- ☐ **Other**

VII.B.1.b ***Provide the NCT (National ClinicalTrials.gov Identifier) number***

VII.B.2 ***Does this project involve a drug washout (asking subject to stop taking any drugs s/he is currently taking)?***
No

VII.B.11 ***Is there a separate, written protocol that will be submitted in addition to this IRB New Project form? (Note: a grant application is not considered to be a protocol)***
No

VII.B.18 ***Does this project involve testing the safety and/or efficacy of a medical device?***
No

VII.C. Project Description (C)

VII.C.1 ***Does this project involve any research on genes or genetic testing/research?***
No

VII.D. Project Description (D)

VII.D.1 ***Check all materials/methods that will be used in recruiting subjects (you will need to attach copies of all materials at the end of the application):***

- Advertisements -
- Posters -
- E-mail -
- Letter -
- Use of any information available to the researchers or their colleagues because this person is a patient OR use of any information considered to be Protected Health Information (PHI) OR review of patient/clinic records - Potential subjects that are seen in the Dermatology clinic at UIHC will be pre-screened by members of the research team using the electronic medical record (EMR). This information will be used only for determining eligibility and will not be collected or stored.
- Existing Registry/database - Subject's that have previously enrolled in other studies related to this application will be sent a letter containing information about new study opportunities available. Specifically at this time individuals that have participated in IRB# 201701708
- Other - A survey generated using the program RedCap will be utilized to recruit and screen potential subject's.
- Website - UIHC Clinical Trials and Research Website
- Referral from colleague - Dermatologists at UIHC seeing patients who they think qualify for the study may refer subjects to the study coordinator for more information.

VII.D.2 ***List the individual data elements you will need to access/use from the patient or clinic records to identify potential subjects for recruitment***
Researchers will review the patients' age, height and weight, current medications, pregnancy/nursing status, and medical conditions (as listed in section VI.13). Patient addresses from their medical record will be obtained in order to send a recruitment letter to inform them of the study opportunity. This information will not be stored or collected as a part of the research data.

VII.D.3 ***Describe why you could not practicably recruit subjects without access to and use of the information described above***
The Department of Dermatology at UIHC consists of 13 dermatologists and numerous ARNPs, PAs, and medical students. Up to 100 patients can be seen in one day at the clinic. In addition, the Department of Dermatology also has an Ethnic Skin Care Clinic that offers specialized services for patients of color (defined as skin types IV-VI in the Fitzpatrick Skin Type Classification). Patients of color are minority populations in the state of Iowa, and working with the EMR for patients in these dermatology clinics allows us to review eligibility for patients who might otherwise be difficult to access through general advertising. It is necessary for our research team to be able to determine eligible potential subjects prior to their visit because it would not be feasible for us to speak with every patient that the dermatology clinic sees in one day. By determining eligibility prior to their appointment we will be able to increase the efficacy of our recruitment and maximize the outcomes of our study.

VII.D.4 ***Describe why you could not practicably obtain authorization from potential subjects to review their patient or clinic records for recruitment purposes.***
Due to the large number of patients seen in the dermatology clinics each day, it is not feasible for us to expect that our research team would be able to meet one on one with each of them every day. None of the information reviewed will be recorded or stored for purposes of the study.

VII.D.5 ***Describe plans to protect the identifiers from improper use or disclosure***
No subject information reviewed using the EMR will be recorded or stored for purposes of this study. All necessary information will be collected from the subject upon consenting in the study.

VII.D.6 ***Describe plans to destroy identifiers at the earliest opportunity consistent with conduct of the research***
No subject information or patient identifiers will be recorded for purposes of this study.

VII.D.7 ***Does the research team agree that the requested information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the study, or for other research for which the use or disclosure of the requested information would be permitted by the HIPAA Privacy Rule***
Yes

VII.D.8 ***Will a member of the research team discuss the study with the subject in person prior to the subject agreeing to participate?***
Yes

VII.D.9 ***Describe the physical location where the consent process will take place:***
The consent process will take place in a private room in the CRU.

VII.D.10 ***Will a member of the research team discuss the study with the subject by phone prior to the subject agreeing to participate?***
Yes

VII.D.11 ***Describe:***
Individuals who call the study site after viewing one of our many advertisements will be provided a brief overview of the purpose and study procedures. If the individual provides permission, they may be asked questions on a pre-screening survey. These questions will help determine if the subject is likely to meet any of the exclusion criteria. If a subject is interested in study participation and passes pre-screening

procedures, they may be emailed a copy of the informed consent and invited to attend an informational session at the CRU where staff will present a detailed discussion of the study rationale, procedures, risks, and benefits. Questions will be solicited.

VII.D.12 ***Who will be involved in the consent process (including review of consent document, answering subjects' questions)?***

Name	Consent Process Involvement
Nicole Brogden, PharmD, PHD	No
Jamie Carr, BA	Yes
Valeria Cota, BA	Yes
Nkanyezi Ferguson, MD, MD	No
Patrick Ten Eyck, MS	No

VII.D.15 ***Check all materials that will be used to obtain/document informed consent:***

- Consent Document

VII.D.16 ***Are you requesting a waiver of documentation of consent (either no subject signature or no written document)?***
No

VII.D.19 ***Before the subject gives consent to participate are there any screening questions that you need to directly ask the potential subject to determine eligibility for the study?***
Yes

VII.D.20 ***List any screening questions you will directly ask the potential subject to determine eligibility.***
Are you between 18 – 50 years of age?
How tall are you?
What do you weigh?
What racial/ethnic group do you self-identify with? (Subject will be provided a list of examples if clarification is required)
Do you have any general allergies that require daily treatment with steroids or antihistamines?
Have you ever had any kind of microneedle patch applied to your skin? If so, did you experience any adverse reactions to it?
Do you have a known allergy or adverse reaction to medical tape, Band-Aids, adhesive or aloe vera?
Do you take prescription medications?
Do you have any chronic or ongoing medical conditions (including skin disorders or pregnancy)?

Screening will be streamlined with the use of a redcap survey found at the following link. https://redcap.icts.uiowa.edu/redcap/surveys/?s=4XJ8CYKNCF

VII.D.21 ***Will you keep a screening log or other record that would include information on people who do not enroll in the study?***
Yes

VII.D.22 ***Describe the information being collected and the purpose for keeping this information.***
A screening log will be maintained that will document the first and last name of the prospective participant that was screened, date of screening, phone number if provided, email address if provided, and whether it was a screen failure or if the subject will continue on to the consent process. This information will be kept until all study activities have been completed for all participating subjects. We will keep the screening information because it is not uncommon for individuals to respond to the same advertisements more than once (for example, Noon News) and we want to know if a subject has previously contacted us about the study. The log will be destroyed when all subjects have finished the study.

VII.D.23 ***Will this information be shared with anyone outside the UI research team members?***
No

VII.D.25 ***After the subject agrees to participate (signs consent), are there any screening procedures, tests, or studies that need to be done to determine if the subject is eligible to continue participating?***
Yes

VII.D.26 ***List and describe screening***
After a subject consents to be in the study, baseline demographic data will be collected including age, sex, height, and weight, race/ethnicity; information regarding current medical conditions/allergies and medications will also be collected. Specifically, the subject's approximate duration of each condition/allergy, what treatments the subject has received, and approximate severity of the conditions, and a current medication list will be collected. All of this information will be collected directly from the subject and the subject's medical record will not be reviewed/abstracted for research data.

VII.D.27 ***Discuss how much time a potential subject will have to agree to consider participation and whether or not they will be able to discuss the study with family/friends before deciding on participation.***
There is no limit on the time a potential subject may take to consider participation. The only restriction on time is that the subject will only be allowed to participate if the study is still enrolling subjects when they provide consent.

VII.D.28 ***How long after the subject agrees to participate do study procedures begin?***
Study procedures can begin immediately after obtaining consent.

VII.D.29 ***Provide a description of the enrollment and consent process for adult subjects***

- ***Describe each study population separately including control population***
- ***Include when recruitment and consent materials are used***
- ***Use 3rd person active voice "The Principal Investigator will identify subjects. For example, the principal investigator will identify potential subjects, the study coordinator will discuss the study with subjects over the telephone and schedule the first study visit, etc..."***
- ***Describe the steps that will be taken by the research team to minimize the possibility of coercion or undue influence during the consent process***

This study will be advertised through the University of Iowa campus-wide email system and through the University of Iowa Health Care "Noon News," a daily announcement flier printed for community and faculty members within the UIHC. We will also be using printed fliers to advertise the study in Dr. Ferguson's Ethnic Skin Care Clinic at UIHC and on the University Cambus System. The UIHC Clinical Trials and Research Website will be utilized for recruiting subjects. Subjects will be recruited through the dermatology clinic based upon screening of the EMR as well as by physician referral. Advertisements will also be hung in the University Services Building and various cultural centers on the University campus (African-American Cultural Center, Latino and Native American Cultural Center, and Asian-Pacific American Cultural Center). Advertisements for this study have been created so that specific subject populations may be better reached via targeted advertisements, in order to meet our enrollment goals. The mass mailing advertisement has been written in this way as well. It is possible that the mass email will be distributed to certain listservs of University students/staff/faculty that meet our specific demographic criteria (specifically race and ethnicity); we will be working with ITS, the registrar and HR to build confidential lists of individuals who will receive this email. These lists will only be exchanged directly between ITS, HR, and the registrar. No member of the research team will have access to any information about individuals being emailed in this manner.

Individuals who call the study site will be provided a brief overview of the purpose and study procedures. Prospective participants may be pre-screened through a telephone survey or a survey link created by researchers using a data collection tool called RedCap. If a subject is interested in study participation and passes pre-screening procedures, they will be invited to sign an informed consent with a study team member (where they will again be provided overview of the study rationale, procedures, risks, and benefits). An informed consent document will be provided to the subject for review prior to any meeting. If the prospective participant cannot receive an informed consent by email, the individual will be invited to review the document with the study coordinator at UIHC, and must be given the option to schedule a separate meeting to sign the document. This ensures that the individual has the chance to review the material in the informed consent on their own time.

Individuals who contact Dr. Ferguson for information about the study will be provided with a brief description of the study. They will also be provided with an informed consent document for them to review on their own time and will be instructed to contact the study coordinator for more information. Individuals identified prior to their appointment in the dermatology clinic will be invited by their physician or a member of the study team to meet with the study team to learn more about the research opportunity. Prior to their appointments individuals that have been screened by members of the study staff will receive a letter in the mail giving them information about the study and notifying them that they may be eligible to participate in the study. The principal investigator of this study is planning to conduct multiple onsite studies involving microneedles; currently a similar study in production is 201701708. Participants from this study will be sent a letter or email with information about this study instructing them to reach out to the study team if they are interested in participation. There will be no follow up to anyone who is sent a letter or email that does not respond.

Screening for this study will be streamlined with the use of a survey created by the research team (link provided in VII.D.20). The link to this survey will be sent to potential subjects via the Noon News, Mass Email, and the Letter to prior subjects. Participants who complete the survey will provide their email address, and the study team will contact them in response to their answers. The information provided by the individual will be used to determine eligibility and will not be kept or stored by the researcher. All information collected for purposes of this study will be collected during an in-person visit with the potential subject.

It is recognized that the consent process must be carried out in an environment where no coercion is applied and where subjects can be adequately informed of the purpose, nature, procedures, risks and hazards of the study. One of the important features of our screening process is the ability for the prospective participant to review the informed consent on his/her own time, outside of the study site. This additionally demonstrates the reliability of the subject if they schedule a follow-up meeting to sign the informed consent.

VII.D.37 ***Does the study include any form of deception (e.g., providing participants with false information, misleading information, or withholding information about certain study procedures)?***

Examples:

- ***Procedure includes a cover story that provides a plausible but inaccurate account of the purposes of the research.***
- ***Participants will be provided with false information regarding the particular behaviors of interest in the research.***
- ***Procedures include a confederate pretending to be another participant in the study.***
- ***Participants will be told that the research includes completion of a particular task, when in fact, that task will not be administered.***
- ***Study is designed to introduce a new procedure (or task) that participants are not initially told about.***
- ***If yes, a waiver of informed consent must be requested under question IV.3.***

No

VII.E. Project Description (E)

VII.E.1 ***Will subjects be randomized?***
No

VII.E.3 ***Will any questionnaires, surveys, or written assessments be used to obtain data directly from subjects in this study?***
Yes

VII.E.4 ***List all questionnaires, surveys, written assessments and ATTACH each one to the application. (NOTE: You are NOT prohibited from attaching copyrighted materials to this application)***
There will be a pre-screening questionnaire and a screening questionnaire to collect information from the subjects. File name: Pre-Screening Questionnaire MCK, Screening Questionnaire MCK

A survey will be utilized to help determine an individuals eligibility to participate in the study. This survey can be found at https://redcap.icts.uiowa.edu/redcap/surveys/?s=4XJ8CYKNCF

VII.E.5 ***Does this project involve creating any audiotapes, videotapes, or photographs?***
No

VII.E.6 ***Provide a detailed description in sequential order of the study procedures following the consent process - DO NOT cut and paste from the Consent Document.***

Describe study populations separately if they will be participating in different procedures - include CONTROL population if applicable.

DESCRIBE:

- ***What subjects will be asked to do/what happens in the study (in sequential order)***
- ***The time period over which procedures will occur***
- ***The time commitment for the subject for individual visits/procedures***
- ***Long-term followup and how it occurs***

Following consent, a member of the study team will obtain the following demographic information directly from the subject: age, height, weight, and gender. A member of the study team will also identify the subject's Fitzpatrick skin type, and obtain a list of current medications and ongoing medical conditions. The subject will be asked to elaborate on the duration and severity of medical conditions and any treatments received. No medical records will be consulted to obtain or confirm this information. A member of the research team will use this information to screen out subjects meeting any of the exclusion criteria defined in VI.13. Subjects who pass the screening may proceed to the next step described below. Consent and screening procedures will take approximately 1 hour.

On Day 0 (may be the same day as consent is obtained), the subject will sit in a study room at the CRU for 30 minutes prior to any procedures. This allows the subject's skin to acclimate to the ambient environment in the study room (temperature, humidity). Following this acclimatization, the researcher will identify and mark with a marker 5 sites at each of the following 3 locations (for a total of 15 sites): upper arm, volar forearm, and abdomen. Hair may be clipped (but not shaved) at the sites if necessary. Noninvasive baseline measurements will be taken at each of the 15 sites as follows:
• Hydration will be measured by gently pushing a corneometer probe against the skin. The measurement will take less than 30 seconds at each site.
• Transepidermal water loss (TEWL) will be measured by resting a probe gently against the skin. This measurement will take 1- 3 minutes at each site. (TEWL will only be measured on Day 0.)
• Electrical resistance (impedance) will be measured with an impedance meter by applying gel electrodes to each site and a reference electrode at a nearby site. The measurement will be repeated 3 times at each site, and will take less than 2 minutes total at each site.
• Skin color and redness will be measured by placing a colorimetry probe gently against each site. This measurement will take less than 30 seconds at each site.

Following baseline measurements on Day 0, micropatches will be applied to three of each set of five sites. The sites will first be cleansed with an alcohol swab. A sterilized micropatch containing 50 tiny projections, each 800 um in length, will be placed perpendicular to the skin, and the researcher will apply gentle pressure to the back of the patch for 10 seconds. The researcher will then remove the patch, rotate it 45 degrees, and apply it again at the same site for another 10 seconds. This will create 100 micropores at each site. Micropatch application will only occur on Day 0.

Immediately after treating a site with a micropatch, TEWL and impedance measurements will be repeated. The site will then be covered with a sterile occlusive cover, and the researcher will apply a new micropatch array to the next site. Two sites at each location will not receive micropatch treatment. An occlusive covering will be placed over one of these two sites, and the other untreated site will remain uncovered. The 4 covered sites will be secured with medical tape. Note that all baseline measurements, micropatch applications, Day 0 post-micropatch measurements, and covering and medical tape placement will be performed at one anatomical location (5 sites) before proceeding to the next location. Day 0 procedures will require 3 - 4.5 hours.

Subjects will be asked to return to the CRU every 24 hours for 3 days. On each day hydration, impedance, and color measurements will be repeated at all sites. New occlusive material will be applied on Days 1 - 2. On Day 3 (the final day), covering will be removed, but not replaced. Procedures on Days 1-3 will last 2 - 3 hours.

Within 3-4 days after the Day 3 visit (or the last completed visit if a participant decides to drop out early) a study team member will contact the subject via phone or email to determine if the subject is experiencing any redness or irritation at the treatment site. No long-term follow-up will be necessary. The overall time commitment for this study is 9 - 13.5 hours in one week, across 4 study days if consent is obtained on Day 0, or 5 study days if consent is obtained before Day 0; consent may occur any time prior to study procedures.

VII.E.7 ***Will you attempt to recontact subjects who are lost to follow-up?***
No - those lost to followup will not be recontacted

VII.E.9 ***Will subjects be provided any compensation for participating in this study?***
Yes

VII.E.10 ***Cash***
No

VII.E.11 ***Gift Card***
No

VII.E.12 ***Check***
Yes

VII.E.13 ***Who will be providing the research compensation check to the subject?***
Accounting Services directly via the e-Voucher system

VII.E.16 ***Other***
No

VII.E.19 ***Describe the compensation plan including***

- ***Compensation amount and type per visit***
- ***Total compensation***
- ***Pro-rating for early withdrawal from study***

Compensation will be provided as follows:

Day 0- $100

Day 1- $40
Day 2- $40
Day 3- $40
Total - $220

Compensation will be prorated for any subject who does not complete all days of the study. Subjects will only be paid for the study days they complete. Subjects will be paid in one check.

VIII. Risks

VIII.1 ***What are the risks to subjects including***
- emotional or psychological
- financial
- legal or social
- physical?
In general, microneedle treatments are well tolerated. However, the skin could become irritated or inflamed from the microneedle insertion or from the adhesives (either on the patches used to apply the microneedles and make measurements, or the medical tape used to hold the occlusive patches in place). There may be mild discomfort, itching, redness, bruising, inflammation, or hyper-/hypopigmentation at the treatment sites or where adhesives were in contact with the skin. Loss of confidentiality is also a risk.

VIII.2 ***What have you done to minimize the risks?***

- ***If applicable to this study ALSO include:***
  - ***How you (members of your research team at Iowa) will monitor the safety of individual subjects.***
  - ***Include a description of the availability of medical or psychological resources that subjects might require as a consequence of participating in this research and how referral will occur if necessary (e.g. availability of emergency medical care, psychological counseling, etc.)***

During the consent process the subjects will be counseled about the micropatch. The skin will be cleansed thoroughly with alcohol wipes prior to applying the micropatch treatments (cleaning technique similar to that used for insertion of a typical hypodermic needle). They will also be counseled about the possibility of local skin irritation and redness from the adhesive tape. Subjects will be closely observed during the measurements and during treatment with the micropatches; emergency facilities and staff will be available if necessary. Subjects will be instructed to contact a member of the study team if problems arise at any time during their participation in the study (all pertinent contact information will be provided to the subjects). Within 3 - 4 days following study completion, a member of the research team will call or email the subject to follow-up and be sure that no irritation or infection has occurred. The risk of loss of confidentiality will be minimized by keeping all documents in a locked cabinet that is only accessible to members of the research team. All electronic forms of data will be kept on a secure-server supported by the University of Iowa that allows only members of the research team access.

VIII.3 ***Does this study have a plan to have an individual or committee review combined data from all subjects on a periodic basis (such as summary or aggregate safety and/or efficacy data)?***
No

IX. Benefits

IX.1 ***What are the direct benefits to the subject (do not include compensation or hypothesized results)?***
There are no direct benefits to the subjects.

IX.2 ***What are the potential benefits to society in terms of knowledge to be gained as a result of this project?***
Microneedle-assisted drug delivery is a very promising method of administration. It is more tolerable than standard hypodermic needles for injections, and delivery through the skin bypasses many of the shortcomings involved with oral medications. There are several microneedle devices in use around the world, mostly for cosmetic purposes. The first microneedle product cleared by the FDA for influenza vaccine administration is Soluvia, which is marketed by Sanofi as Fluzone Intradermal. As the use for microneedles in drug therapy gains interest, it is very important to understand how therapeutic endpoints will differ with microneedle application at different body sites and in different skin types. The first step in understanding this is to characterize the response to microneedles in various anatomical sites and races. This knowledge is currently lacking, but will be directly related to the micropore closure rate (assessed by impedance), skin hydration, and redness/color data gathered from this study.

X. Privacy & Confidentiality

X.1 ***What are you doing to protect the privacy interests of the subjects?***
No direct patient identifiers will be recorded on data collection material. Instead, subjects will be assigned a subject number on study materials. Only the data necessary to answer the research question will be collected, and all consent processes and study procedures will take place in a private location in the Clinical Research Unit.

X.2 ***Are you collecting the Social Security Number of any subjects for any purpose?***
Yes

X.3 ***Provide the intended usage of SSN:***

- To provide compensation to subjects

X.4 ***How will information/data be collected and stored for this study (check all that apply):***

- Paper/hard copy records (hard copy surveys, questionnaires, case report forms, pictures, etc.) - Hard copies will only be transported by members of the research team. Hard copies will be stored in the office of the Clinical Coordinator in C44-P of the ICTS center of UIHC or in the office of the Clinical Coordinator in 558 CPB in a locked filing cabinet only accessible to members of the study team.  

- Electronic records (computer files, electronic databases, etc.) - Electronic records (computer files, electronic databases, etc.) - Electronic results and data (after direct patient identifiers have been removed) will be kept on a password protected shared drive (College of Pharmacy, University of Iowa) that only members of the research team will be able to access.
  - Name - Greg Schwartz
  - Title - IT Director
  - University Job Classification - Faculty/Staff

X.5 ***Do the confidentiality protections indicated above allow only members of the research team to access the data/specimens?***
Yes

X.7 ***Does your study meet the NIH criteria for a Certificate of Confidentiality or will you be applying for Certificate of Confidentiality?***
No

XI. Data Analysis

XI.1 ***Describe the analysis methods you will use, including, if applicable, the variables you will analyze***
Descriptive statistics will be used for subject demographics. Each subject will serve as their own control, and paired t-tests will determine differences in TEWL (water loss measurements) and impedance from baseline to post-microneedle insertion. This will be used to determine if the microneedles adequately breached the skin barrier, demonstrated by a significant increase in TEWL from baseline and a significant decrease in impedance from baseline. For the colorimetry, and hydration measurements, each daily measurement will be compared to its baseline at that site, as well as to its hydration control (untreated, occluded site), using paired t-tests.
Impedance data will be analyzed using similar methods as our previous study, and will ultimately be used to calculate the half-life of micropore closure. Z-pores values will be calculated from impedance measurements taken immediately following and over the days following microneedle treatment. These values will be converted to admittance (the inverse of impedance), which can demonstrate how “open” the micropores are in a very intuitive manner. If a micropore has a maximum admittance, then the micropore is 100% open. Using this information, we will plot admittance vs. time and calculate a rate constant of micropore admittance (k). The rate constant is then used to calculate the half-life of micropore closure, which thus describes a rate of closure in units of time. This micropore half-life will serve as the primary endpoint and will be compared among locations within a group, among groups within a location, and among locations in all groups.

XI.2 ***Provide the rationale or power analysis to support the number of subjects proposed to complete this study.***
There are no data in any population other than Caucasian individuals and no data directly comparing micropore closure at various anatomical sites to guide a formal power analysis. Our calculation of subject number was based on what is feasible for a pilot study to give enough preliminary data for a power analysis later. We plan to enroll subjects into 5 groups based on self-identified race/ethnicity. Each of the following groups will have 10 subjects each: African American/Black, Hispanic/Latino, Caucasian/White, Asian, and bi-/multiracial. We have selected 70 subjects as the number for enrollment to help account for those who will complete the informed consent but will either be screened out afterwards or will not participate in the study to completion.

XII. Future Research

XII.1 ***Do you wish to keep any information about subjects involved with this research project so that members of the current research team may contact them in the future for your own research projects?***
Yes

XII.2 ***Do you wish to keep any information about subjects involved with this research project so that other researchers may contact them for future research?***
No

XII.3 ***List the data or information you will keep:***
Name and contact information.

XII.4 ***Does this project involve storing any data, tissues or specimens for future research?***
No