The University of Texas Medical Branch at Galveston
More Than Minimal Risk Consent Form

Protocol Title:	Novel Strategies for Reducing Burn Scar Itch
IRB Number:	24-0180
Funding Source:	Univ of Texas Health Science Center- San Antonio / Trauma Research and Combat Casualty Care Collaborative
Principal Investigator:	Celeste C. Finnerty, PhD Department of Surgery, UTMB (409) 692-9036 ccfinner@utmb.edu

Why am I being asked to take part in this research study?
You are being asked to take part in this study because you have a burn scar that is itchy. Your participation in this study is completely voluntary. You may refuse to participate or stop your participation in this research study at any time without penalty or loss of benefits and without jeopardizing your medical care at UTMB.

Study Summary:
When recovering from a burn, the scar may become itchy, and interfere with sleep, concentration during work or school, and activities (e.g. sports, exercise). Even more than 10 years after a burn, 58% of surveyed survivors report itch that remains a problem. There are not many effective therapies. One of the most used therapies is the H1 antihistamine diphenhydramine (Benadryl). Other strategies for reducing itch include H2 antihistamines and mast cell stabilizers, which are effective for other types of itch. We think that these therapies together will decrease itch better than diphenhydramine (Benadryl) alone. To see if this is true, we will compare the recommendation of diphenhydramine (Benadryl) use with administration of placebo capsules and lotion to the recommendation diphenhydramine (Benadryl), plus famotidine (Pepcid), and topical cromolyn sodium together. You will be asked to take the provided medications and use the provided lotion twice a day for three months, and then record when you take the medicine, how itchy you are before and after, and at 2 different times, we will assess your scar physically and ask for you to answer questions about your scar and activities.

The following things you should know about this research study:

- The purpose of the study is to see whether using diphenhydramine (Benadryl), famotidine (Pepcid), and cromolyn sodium will decrease itch. We think adding these medications will lead to better outcomes compared to using diphenhydramine (Benadryl) alone.

- If you chose to participate, you will be asked to: 1) *take or apply the medication in the morning and evening for 3 months*; 2) *to write down on the log every day when you take or apply the medication in the morning and evening*; 3) *Once a week, you will be asked to rate the itch on a scale of 0 (no itch) to 10 (worst imaginable itch) for your average itch*

level for the past 24 hours and the worst itch level for the past 24 hours and 4) undergo a series of measurements, fill out questionnaires, and have a skin swab sample taken before starting the study and again at about 3 months after starting the medication; these measurements and questionnaires will take about 3 hours. Six months after starting the medication, you will be called to complete questionnaires; this will take about 20 minutes. You have the option to complete another skin swab sample six months after starting the study.

- Risks or discomforts from this research include:
    - Risks related to medication: these risks exist when using cromolyn sodium or famotidine (Pepcid). Cromolyn sodium: Rarely cromolyn sodium may induce an allergic reaction. As the typical administration routes are inhaled, nasal, or oral, additional side effects are specific to those routes of administration. Famotidine (Pepcid): Side effects can include headache, constipation, diarrhea, dizziness, weakness, insomnia, muscle pain/cramps, dry mouth, nausea, vomiting. Should these occur, the events are likely to be mild to moderate in severity.
    - Risks related to loss of your confidentiality. The researchers will try to minimize these risks by not using your name or other identifiable information in the study records. Electronic records will be kept on password-protected computers or servers. With respect to the Fitbit, because of the nature of the data and collection method, we cannot guarantee that your data will be kept confidential, and it may be possible that others will know what you have reported.
    - Risks associated with photography: no different than risks for other forms of photography.
    - There are no known risks associated with measuring blood flow and changes in temperature of your skin using specific devices designed for this purpose. Similarly, there are no known risks for filling out the questionnaires.
    - As with any research study, there may be additional risks that are unknown or unexpected.
- The study may have benefits associated with participation, including decreased itch, improved function/mobility, and/or increased independence.
- Taking part in this research study is voluntary. You do not have to participate, and you can stop at any time.

Please take your time to read this entire form and ask questions before deciding if you want to take part in this research project.

DETAILED RESEARCH CONSENT

What is the purpose of this research study?
The purpose of this study is to examine the effect of a new approach to treating burn scar itch. In other patient populations experiencing itch, H2 antihistamines and/or topically applied cromolyn sodium have decreased itch. We believe that these medications will reduce itch from burn scars. To test this idea, we will compare two methods of treating itch: 1) recommended oral diphenhydramine (Benadryl) with placebo capsule and placebo lotion and 2) recommended oral diphenhydramine (Benadryl) with administration of oral famotidine (Pepcid) and topically applied cromolyn sodium.

We expect that the results may lead to a change in how burn scar itch is treated. Our studies may demonstrate that the addition of famotidine (Pepcid) with topical cromolyn sodium is a simple, but effective addition to the Standard of Care already in use.

How many people will take part in this study?
About 44 people will take part in this study at UTMB.

What procedures are involved as part of this research study?
If you agree to take part, you will be asked to sign this consent form and have the following tests and procedures. All the procedures in this study are being done only because you are taking part in this research study. You might have a regular clinic visit for your burn care during the time you are in the research study. The timing of the regular clinic visit may overlap with the timing of your research visit. If that happens, we will conduct all procedures for this study after the regular clinic visit. If you do not have any regular clinic visits for your burn care, you will still need to return to the clinic to have the research visits.

If you participate you will have a start of study assessment and then a total of 1 study visit, that will take place about 3 months following the start of the trial. There will be a final phone call / virtual follow-up around 3 months after completion of the medication, which is 6 months after the start of the trial.

Screening and enrollment: You were approached for enrollment after you reported having an itchy scar by your treating physician, who may be a doctor of this study. If you decide to participate, you will be asked to sign the consent form and then will be assigned a study ID.

Group assignment: You will then be randomized (assigned by chance like the flip of a coin) to one of these groups:

- A Placebo group (recommended active H1 antihistamine, plus administration of placebo famotidine and placebo cromolyn sodium)
- A group recommended to take active H1 antihistamine, and administered active H2 antihistamine and using cromolyn sodium PLUS (-PLUS active H1 antihistamine, plus active famotidine and active cromolyn sodium)

Study interventions: For both the placebo and the PLUS group, the research staff will review the instructions for using the prescribed medications with you. They will review how to record the information in the logbook. They will also review how to record use of diphenhydramine.

Procedures and evaluations during research: The first assessment will be performed before beginning the therapy to obtain baseline measurements and photos, and you will be given instructions to follow at home. You will be given a 3-month supply of medication. You will be

asked to write down when you use the medication and to rate the itch before and after taking the medication. When you return to clinic at about 3 months, the outcomes listed below will be assessed. Final survey questions will be asked 6 months after study start.

	Pre-study	Study Start	Twice Daily for 3 months	Weekly for 3 months	~1 month (+/- 15 days)	~2 months (+/- 15 days)	~3 months (+/- 15 days)	~6 months (+/- 15 days)
Informed consent	X							
Randomization		X						
Demographics		X						
Study Staff Medication Administration		X					X	
Participant Medication Administration and Logbook			X					
Physical Exam (clinical visit)		X					X	
Visual Analog Scale (VAS itch)		X		X			X	X[1]
3D photography		X					X	
Questionnaires (POSAS, BBSIP, PROMIS-29, PGIC, VAS Pain)		X					X	
DermaLab Combo		X					X	
Laser Doppler		X					X	
Skin swab microbiome collection		X					X	X[2]
Fitbit Sync					X[1]	X[1]	X	X[1]
Post-study Questionnaires (PGIC and VAS Itch and Pain)								X[1]

1. Completed virtually.
2. Optional.

Event	Timing	Included procedures	Included patients
Consent & randomization	At enrollment		All
Data collection from EMR	Throughout study		All
Medication Administration	Twice daily for 3 months	Call to participant to check on compliance	All
Itch measurement	At study start, weekly for 3 months, at 3 and 6 months after start of study	Visual analog scale (VAS) Itch, monthly call to remind participant to record medication use and itch evaluation in logbook	All
Measurements	At study start, and at clinic visit approximately 3 months after study start (±15 days)	Photographs, Physical properties of the scar, Blood flow, Questionnaires (POSAS, BBSIP, PROMIS-29, PGIC, VAS Pain)	All
Sample Collection	At study start, at 3 and 6 months after study start (±15 days each timepoint). 6 month swab collection will be optional.	Skin Swab Collection	All
Fitbit Sync	Month 1, 2, 3 (+15 days, each timepoint)	Call to patient to remind to sync Fitbit data on app.	All
Post-study questionnaires	6 months (± 15 days) after study start (end of the study)	Questionnaires (PGIC, VAS Itch and VAS Pain)	All

A combination of the following study procedures will be performed;

- We will ask you to rate your pain and itch
- We will take photographs to measure wound &/or scar size and volume
- We will collect a microbiome skin swab sample from two areas; the scar and an unscarred skin
- We will measure elasticity (stretchiness), color, temperature, scar thickness, and transepidermal water loss (water loss through the skin)
- We will measure blood flow through your burn
- We will measure changes in skin temperature

- We will assess your scars
- We will ask you to fill out the following questionnaires:
    - Patient and Observer Scar Assessment Scale v3.0
    - Brisbane Burn Scar Impact Profile
    - PROMIS-29
    - Patient's Global Impression of Change

We will ask you to:

- Fill out a log at home with when you take the medications.
- Record your itch once a week for 3 months.
- Wear an activity monitor (e.g., Fitbit): The Fitbit Inspire will be given to you and the application will be downloaded onto your preferred device after enrollment. It provides physical activity measurements such as activity counts, energy expenditure, steps taken, distance travelled, and activity intensity levels. A mock email account will be set up in the study doctors name. Only your height, weight, sex assigned at birth, and age will be entered. If a name or date of birth is requested, a randomly generated entry will be provided. The activity monitor for estimation of daily activity should be attached to your clothing in a location that is comfortable to you. It should be always worn, including when sleeping but may be removed during wound care. The activity monitors are water resistant, not waterproof (do not submerge / place in water) and can be disinfected with hospital grade solution/spray. You will not be required to return the Fitbit when you complete the study. Study staff will assist in syncing the device data at all in-clinic visits or will call you at month 1, 2, 3, and 6 to remind you to sync the data.

These tests will be done before you begin the medication, and at approximately 3 months after study start.

What extra tests and procedures will I have if I take part in this study?
There are some extra tests that you will need to have if you take part in this study.

You will have the following extra tests:
- We will ask you to rate your pain and itch.
- We will take photographs of your wound and scar.
- We will measure skin and scar elasticity (stretchiness), color, temperature, scar thickness, and transepidermal water loss (water loss through the skin).
- We will measure blood flow in the skin and scar.
- We will measure changes in skin temperature.
- We will assess your scars.
- We will collect a skin swab sample of your microbiome from your itchy burn scar and unscarred skin.
- We will ask you to fill out the following questionnaires:
    - Patient and Observer Scar Assessment Scale v3.0
    - Brisbane Burn Scar Impact Profile
    - PROMIS-29
    - Patient's Global Impression of Change

The skin swab sample we will collect will be of your microbiome. The microbiome is the collection of tiny living things—like bacteria, viruses, and fungi—that live in and on your body, especially in places like your gut (intestines), skin, and mouth.

Even though the word "bacteria" often sounds bad, most of these microbes are actually good for you. They help you digest food, fight off harmful germs, and keep your body healthy and

balanced. We will collect a skin swab sample of your microbiome of the itchy burn scar, and of unscarred skin. This will help us determine if there is a change in your microbiome from the itchy burn scar, and of unscarred skin. The collection of the skin swab sample is completed by rubbing a swab (like a q-tip) lightly on your skin. This should not cause you any pain or discomfort.

The research study will pay for all the extra tests.

What are the possible risks for choosing to participate in this research study?

• Medication: Cromolyn sodium: Rarely cromolyn sodium may induce an allergic reaction. As the typical administration routes are inhaled, nasal, or oral, additional side effects are specific to those routes of administration. Famotidine (Pepcid): Side effects can include headache, constipation, diarrhea, dizziness, weakness, insomnia, muscle pain/cramps, dry mouth, nausea, vomiting. Should these occur, the events are likely to be mild to moderate in severity. For females- The medication may involve risks to a fetus or embryo if you become pregnant which are currently unknown.

Loss of confidentiality: Any time information is collected; there is a potential risk for loss of confidentiality. Every effort will be made to keep your information confidential; however, this cannot be guaranteed. The researchers will try to minimize these risks by not using your name or other identifiable information in the study records. Electronic records will be kept on password-protected computers or servers. With respect to the Fitbit, because of the nature of the data and collection method, we cannot guarantee that your data will be kept confidential, and it may be possible that others will know what you have reported.

• Risks associated with photography: no different than risks for other forms of photography.

• There are no known risks associated with measuring blood flow and changes in temperature of your skin using specific devices designed for this purpose.

• There are no known risks for filling out these questionnaires.

• As with any research study, there may be additional risks that are unknown or unexpected.

What are the potential benefits for participating in this research study?
If you agree to take part in this study, there may be direct benefits to you. We hope the information learned from this study will benefit others with itchy burn scars in the future. The potential benefits that may result from participating in the study include reduction in itch, improved function/mobility, and/or increased independence. Based on the results of this study, benefits to other burn survivors may result due to changes in the standard of care following burn or benefits from increased knowledge regarding new ways to treat burn scar itch.

Will I be paid for participating in this research study?
You will be reimbursed $100 dollars for each of the in-person study visits (study start and at 3 months), and $20 for completion of the 2 surveys by phone at 6 months for a total of up to $220. You will be reimbursed for each visit that you complete, even if you do not complete the overall study. You will be issued a UTMB Clincard, which is a debit card that your funds are loaded onto following completion of each study visit. When a study visit is completed, funds will be approved and loaded onto your card. The funds will be available within 48 hours and can be used at your discretion. You will be issued one card for the duration of your participation. If your card is lost or stolen, you can contact customer service at 1-866-952-3795. We will collect some information about you, including name, address, telephone number, date of birth, email

address, if applicable, and your social security number (if a US citizen) to issue the debit card. All information is stored in a secure fashion and will be deleted from the system once the study has been completed and the funds on the card have been all used.

Compensation for participation in research may be considered taxable income. The IRS requires that compensation greater than or equal to $600 be reported to the IRS as required by law. Personal information about you, such as your name, address, and Social Security Number (SSN) or Tax Identification Number (TIN), may be provided to the IRS by the participating site for tax purposes. If you receive $600 or more in a calendar year, you may be provided with a 1099 tax form from the Sponsor, site, or vendors working on behalf of the Sponsor for tax purposes. If you prefer to not receive payment for this study, you may alert your study site.

If you have any questions about costs to you from taking part in the study or any questions about reimbursement, please speak with the study doctor or study team.

Is there an alternative treatment/procedure?

You do not have to participate in this research to receive care for your medical problem. Instead of being in this study, you have the following options: to utilize the medication recommended by your care team as is the standard of care, or no treatment at all.

Please talk to the researchers or your personal doctor about these options.

If I agree to take part in this research study, can I be removed from the study without my consent?
Yes. The researchers may decide to take you off this study if:

- Your medical problem remains unchanged or becomes worse.
- The researchers believe that participation in the research is no longer safe for you.
- The researchers believe that other treatment may be more helpful.
- The sponsor or the FDA stops the research for the safety of the participants.
- The sponsor cancels the research.
- You are unable to keep appointments or to follow the researcher's instructions.

Will my insurance provider or I be charged for the costs of any part of this research study?
No. Neither you nor your insurance provider will be charged for anything done only for this research study (i.e., the Screening Procedures, Experimental Procedures, or Monitoring/Follow-up Procedures described above).

However, the standard medical care for your condition (care you would have received whether or not you were in this study) is your responsibility (or the responsibility of your insurance provider or governmental program). You will be charged, in the standard manner, for any procedures performed for your standard medical care.

What will happen if I am harmed as a result of taking part in this study?
It is important that you report any illness or injury to the research team listed at the top of this form immediately.

Compensation for an injury resulting from your participation in this research is not available from the University of Texas Medical Branch at Galveston.

You or your insurance company or health care plan will be billed and you will be responsible for any charges.

You will be responsible for paying any costs related to illnesses and medical events not associated with being in the study. There are no plans to provide other forms of compensation. However, you are not waiving any of your legal rights by participating in this study.

If I agree to take part in this research study, will I be told of any new risks that may be found during the course of the study?
Yes. You will be told if any new information becomes available during the study that could cause you to change your mind about continuing to participate or that is important to your health or safety.

How will my information be protected?

All results obtained in this study will be kept confidential and only available to the research study team. Your individual information will not be reported, only the results of all participants as a group.

With respect to the Fitbit, because of the nature of the data and collection method, we cannot guarantee that your data will be kept confidential, and it may be possible that others will know what you have reported.

Data collected in this research might be deidentified and used for future research or distributed to another investigator for future research without your consent.

Clinicaltrials.gov Registration Information
A description of this clinical trial will be available on www.clinicaltrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

How will my privacy be protected?
We have rules to protect information about you. Federal and state laws and the federal medical Privacy Rule also protect your privacy. By signing this form, you provide your permission, called your “authorization,” for the use and disclosure of information protected by the Privacy Rule.

The research team working on the study will collect information about you. This includes things learned from the procedures described in this consent form. They may also collect other information including your name, address, date of birth, and information from your medical records. This could include information about HIV and genetic testing, or treatment for drug or alcohol abuse or mental health problems.

The research team will know your identity and that you are in the research study. Other people at UTMB, particularly your doctors, may also see or give out your information. We make this information available to your doctors for your safety. If you think this study might affect your clinical care, please inform your doctor.

People outside of UTMB may need to see or receive your information for this study. Examples include government agencies (such as the Food and Drug Administration), safety monitors, and entities that sponsor the study.

We cannot do this study without your authorization to use and give out your information. You do not have to give us this authorization. If you do not, then you may not join this study.

We will use and disclose your information only as described in this form; however, people outside UTMB who receive your information may not be covered by this promise or by the

federal Privacy Rule. We try to make sure that everyone who needs to see your information keeps it confidential – but we cannot guarantee that your information will not be re-disclosed.

The use and disclosure of your information has no time limit. You may revoke (cancel) your permission to use and disclose your information at any time by notifying the Principal Investigator of this study by phone or in writing. If you contact the Principal Investigator by phone, you must follow-up with a written request that includes the study number and your contact information. The Principal Investigator's name, address, phone number, and information are on page one of this consent form.

If you do cancel your authorization to use and disclose your information, your part in this study will end and no further information about you will be collected. Your revocation (cancellation) would not affect information already collected in the study, or information we disclosed before you wrote to the Principal Investigator to cancel your authorization.

Who can I contact with questions about this Research study?

If you have any questions, concerns, or complaints before, during or after the research study, or if you need to report a research related injury or bad side effect, you should immediately contact Dr. Celeste Finnerty at 409-692-9036 or Dr.Steven Wolf at 210-787-0507.

This study has been approved by the Institutional Review Board. If you have any complaints, concerns, input or questions regarding your rights as a subject participating in this research study or you would like more information about the protection of human subjects in research, you may contact the Institutional Review Board Office via email irb@utmb.edu.

CONSENT TO PARTICIPATE:

The purpose of this research study, procedures to be followed, risks and benefits have been explained to you. You have been given the opportunity to ask questions, and your questions have been answered to your satisfaction. You have been told who to contact if you have additional questions. By signing this form, you are confirming that you have read this consent form and voluntarily agree to participate as a subject in this study.

_____ _____

Signature of Participant Date

_____

Printed Name of Participant

FOR PERSON OBTAINING CONSENT TO COMPLETE:

Using language that is understandable and appropriate, I have discussed this project and the items listed above with the subject.

_____ _____

Signature of Person Obtaining Consent Date

_____

Printed Name of Person Obtaining Consent