CONSENT FORM
Adult Consent Form

Title of this Research Study
Pilot Evaluation of the Empower Neuromodulation System for Anxiety Treatment

Invitation and Summary

You are invited to be in this research study. Taking part in this research is voluntary. You do not have to take part. For the purposes of this document: "You" can refer to:

- Yourself
- The person for whom you are the Legally Authorized Representative (LAR)
- Your child under the age of 19.

"Organization" can refer to: University of Nebraska Medical Center (UNMC), Nebraska Medicine (NM), University of Nebraska at Omaha (UNO) or Children's Hospital & Medical Center (CH&MC).

Here is a summary of the purpose, methods, risks, benefits, and alternatives, to help you decide whether or not to take part in the research.

The purpose of this study is to evaluate the feasibility and acceptability of the Empower Neuromodulation System as a treatment for adults with anxiety. The Empower Neuromodulation System is not approved for marketing by the FDA and is considered an investigational device. This is a small, portable device that works by stimulating nerves under the skin. The device is made up of a controller (electrical signal generator), electrodes, extension cable, and smartphone with the Empower app. The two electrodes (called the stimulation and return electrodes) are connected by the extension cable to the 9-volt battery powered controller. During treatment sessions, you will attach the electrodes to your skin. Study investigators will tell you where to apply the electrodes. You will do the treatment on each side of your body for 15 minutes (30 minutes total) twice a day.

You will be in this study for about six weeks. You will have three visits in the clinic during which you will talk with the study investigators and answer questions about your mental health. At home, you will wear the device twice a day for 30 minutes each time (15 minutes on each side of your body). You will answer questions on a smart phone app about your anxiety, mental health, and medication use. We will track how often you use the device. At the end of the study you will be asked how you liked using the device and if you think you got the real treatment or sham (fake) treatment.

Using the device may cause tickling, tingling, burning, pricking or numbness of the skin (the feeling of "pins and needles" or of a limb "falling asleep"). It could also cause spasms/twitching of the arm and hand muscles, mild discomfort or pain . Completing the surveys and answering questions about your mental health and mood could make you uncomfortable. There is a risk that your anxiety may get worse during the course of the six weeks.

You could have improvement in your anxiety. This study may lead to a non-medication treatment for anxiety.

If you choose not to be in this study, you may continue to see your provider at UNMC or Nebraska Medicine. You may also choose to see your primary care provider or another mental health provider in the community. There are also a variety of apps and on-line tools for use to help your anxiety.

Why are you being asked to be in this research study?
You are being invited to take part in this study because you are at least 19 years old and you have generalized anxiety disorder (GAD).

What is the reason for doing this research study?
The purpose of this research study is to evaluate the Empower Neuromodulation System as a daily therapy for generalized anxiety disorder (GAD). The study may help determine the device's feasibility, acceptability (usability), safety and effectiveness. The Empower Neuromodulation System is not approved for marketing by the FDA and is considered an investigational device.

What will be done during this research study?
A maximum of 30 subjects will participate in this study at UNMC.

You will participate in this study for approximately six weeks. During these six weeks, you will have three in clinic visits during which you will talk with an investigator and complete some assessments. You will do the treatment sessions at home twice a day for 30 minutes and also complete some questionnaires in the Empower app on the smartphone you are given. This study is sham-controlled, meaning there are two groups - one that will receive the real treatment and one that will receive the sham (fake) treatment. You can an equal chance of being in the sham (fake) or real treatment group.

Visit 1 (enrollment): This visit will take about 2 hours. At this visit, someone from the research team will explain the study to you and answer any questions. If you agree to participate, you will do an interview with one of the study investigators to see if you have GAD (generalized anxiety disorder). You will be asked questions and fill out some questionnaires about your mental health, any suicidal thoughts you may have or have had, and your anxiety. If you are a female, you will have a urine pregnancy test.

You will be randomized (like tossing a coin) to be in the sham (fake) group or treatment group. You have an equal chance of being in the sham group or the treatment group. You will be trained how to use the device and app. You will then do a treatment session and be asked about any side effects or problems. You will be given the device and smartphone so that you may do the treatments at home. Study investigators are available by phone if you need help with the device.

Visit 2: This visit will take about 20-30 minutes. Approximately two weeks later, you will have a second visit, which may be completed in person or via phone or video call. You will be asked questions about any suicidal thoughts you have had since you started the study, and you will be asked which treatment you think you are receiving. The study investigators will also ask you about any problems you are having and you may ask any questions that you might have.

Visit 3 (completion): This visit will take about 1- 1 1/2 hours. This visit will occur approximately six weeks after the enrollment visit. You will complete some interviews and surveys again. You will discuss with the study investigators any side effects or problems you experienced. You will be asked questions about which treatment you think you received, how usable the device was, and how satisfied you are with the treatment.

At-Home Treatment Sessions: During the at-home treatment sessions, you will complete the treatment on each side of the body for 15 minutes (the total treatment session will last 30 minutes). You will do this twice per day. You will then use the empower app to complete daily questionnaires about medication use, anxiety severity and interference, and skin tingling. You will also complete a rating scale in the app once a week about anxiety.

What are the possible risks of being in this research study?
Risks Associated with Device:
The most likely risks associated with using this device include: experiencing a

sensation of tickling, tingling, burning, pricking or numbness of the skin along the stimulated nerve (paresthesia, generally known as the feeling of "pins and needles" or of a limb "falling asleep"); Spasms/twitching of muscles at or near the stimulation site; involuntary contraction of muscles (tetany) during stimulation at or near the stimulation site; and mild discomfort or pain at or near the stimulation site or along the course of the stimulated nerve.

Less likely risks associated with the device are: skin irritation, redness or inflammation at or near the stimulation site (temporary); skin reaction or hypersensitivity to the electrode gel; moderate-to-high discomfort or pain (including a throbbing pain) at or near the stimulation site or along the course of the stimulated nerve; numbness along the course of the stimulated nerve (temporary); nausea; and headache.

A rare risk of this study is possible interactions with other electrical and/or neurostimulator device, including but not limited to cardiac pacemaker or defibrillator, vagal neurostimulator, deep brain stimulator, spinal stimulator, sacral stimulator, bone growth stimulator, or cochlear implant. Because of this risk, participants who have an implanted electrical or neurostimulator device will be excluded from the study to reduce risk of possible interactions.

Risks Associated with Questionnaires/Surveys/Assessments:
There is a risk that the questions you are asked will make you uncomfortable because they are about your mental health and mood.

Worsening Anxiety:
There is a risk that your anxiety may get worse during the course of the study. Clinicians with experience in treating anxiety disorders will assess you during the clinical visits and direct you as clinically appropriate. If necessary, you may be referred to your current mental health provider or primary care provider. You will also be given information on community resources.

Risks to Those Pregnant or Breastfeeding:
A TENS device has the potential to cause contractions of the uterus (like labor). It is possible that this would injure the mother or fetus by causing pre-term labor. You have been told what is known about this possibility, and you are encouraged to ask further questions.

You may want to discuss this with others before you agree to take part in this study. If you wish, we will arrange for a doctor, nurse or counselor who is not part of this

study to discuss potential risks and benefits with you and anyone else you want to have present.

Because of the potential risks, you must not become pregnant while you are participating in this study. Women must have a negative pregnancy test before entering the study.

If you are sexually active and can get pregnant, you must use two appropriate methods of birth control every time you have sex, or you must not have sex.

Because of the risk to the fetus (or unborn child), methods of natural family planning are not, by themselves, reliable enough to avoid pregnancy.

You can get additional information about methods to avoid pregnancy by calling the UNMC Research Subject Advocate's Office at (402) 559-6941.

By signing this and being in the study, you are agreeing to not get pregnant while you are on the study. Should you become pregnant while on this study, you should immediately notify the study personnel. The investigator will assist you in finding appropriate medical care. The investigator also may ask to be allowed to continue getting information about your pregnancy. You can refuse to provide this information.

You could have other side effects that we do not know about yet.

What are the possible benefits to you?
This Empower device may reduce your anxiety. However, you may not get any benefit from being in this research study.

What are the possible benefits to other people?
This study could lead to a non-pharmacological (non-medication) intervention for anxiety.

What are the alternatives to being in this research study?
Instead of being in this research study, you can choose not to take part. You can continue to see provider and be treated at UNMC without participating in the research study. You may also choose to see a mental health provider outside of UNMC. You have access to various apps and online resources that may assist with the management and treatment of anxiety disorders.

What will being in this research study cost you?

There is no cost to you to be in this research study.

Will you be paid for being in this research study?
You will be paid with Amazon gift cards for your time and expenses associated with the study. You will be compensated $100 for the first visit, $100 each for the remaining two visits, and $25 for returning the study equipment (Empower controller and smartphone). Compensation at visits 2 and 3 includes compensation for the time and effort for conducting the twice daily treatment sessions at home. You will be paid $25 for returning the study equipment even if you do not complete the study.

Who is paying for this research?
The sponsor of the research is Theranova, LLC. TheraNova, LLC gives us money to do this study. Theranova has a financial interest in the Empower device.

What should you do if you are injured or have a medical problem during this research study?
Your health and safety is our main concern. If you are injured or have a medical problem because of this study call someone listed at the end of this consent form. You can get emergency medical treatment at Nebraska Medicine. You can also go to your doctor, the nearest emergency room or call 9-1-1.

If your skin becomes too irritated to comfortably carry out the treatment sessions, you will be instructed by research personnel to refrain from administering a treatment session until the skin is no longer irritated. If your skin becomes too irritated to comfortably carry out the treatment sessions, and after refraining from administering a treatment session until the skin is no longer irritated, the irritation returns upon administering another treatment session, the principal study investigator (PI) may withdraw you from the study.

Adverse events and changes in symptoms will be monitored frequently during the study at each clinical visit. Trained clinicians will assess you and direct you as clinically appropriate. In addition, you will have site contact information in case you have a question or need to report problem.

We have no plans to pay for your treatment or give you any other money or compensation. The sponsor has no plans to pay for care of research related injuries.

Signing this does not mean you have given up any of your legal rights.

How will information about you be protected?

In the course of this research we may collect information about you. This can be things that could be used to find out who you are (like your name, phone number, birthdate, address). We call this "identifiable private information". We will keep this information as confidential as possible.

During the study, information on how often and how long you are using the device and daily survey data will be upload by the smartphones cellular data plan to a cloud-based, password-protected, secure server (Amazon Web Services). Your personal smart phone is not used for this purpose.

Who can see information about you?

We also will get medical information about you (like medical record number, medical history, or the results of physical exams, blood tests, x-rays or other medical or research procedures). We call this "protected health information" or PHI. PHI is protected by a law called the HIPAA Privacy Rule. We will collect the smallest amount of PHI that we can. We will keep your PHI as confidential as possible.

By signing this consent form, you are letting us (the researchers listed on this consent form and other people involved in this research at the Organization) have access to your PHI. Your PHI will be used only for the purposes described in the section "What is the reason for doing this research study?"

You can change your mind and tell us to stop collecting your PHI for use in this research at any time by writing to the principal investigator. We can still use the PHI we have already collected. If you tell us to stop collecting your PHI, you will have to stop being in this research.

We may share your PHI with other groups listed below:

- The UNMC Institutional Review Board (IRB)
- Institutional officials designated by the UNMC IRB
- The HHS Office for Human Research Protections (OHRP)

We may share your PHI with other groups listed below. The HIPAA Privacy Rule requires these groups to protect your PHI.

- National Institutes of Health (NIH)

We may share your PHI with other groups listed below. These groups are NOT required by HIPAA to protect your PHI. If we share your PHI with these other groups they may share it with others who also do not have to protect it under HIPAA.

- Theranova LLC, which sponsors this research and may pay the Organization

to do this research
- Independent Monitoring Committee (IMC)

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. A Certificate of Confidentiality means that the researcher in most cases cannot reveal identifiable information about you to others without your permission. He or she can report things like potential child abuse or intent to hurt self or others. He or she can report contagious diseases, and can share information with agencies paying for the research or with the Food and Drug Administration. He or she can also share the information with other scientific researchers, as allowed by federal regulations protecting research subjects. A Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research.

You are letting us use and share your research data for as long as the research is going on.

How will results of the research be made available to you during and after the study is finished?
Information obtained in the course of the research that will not be shared with you is which treatment you receive. By signing this authorization, you are temporarily giving up your right to see this research-related information while the research is going on. You will be able to see this information if you wish after the research is completed.

In most cases, the results of the research can be made available to you when the study is completed, and all the results are analyzed by the investigator or the sponsor of the research. The information from this study may be published in scientific journals or presented at scientific meetings, but your identity will be kept strictly confidential.

If you want the results of the study, contact the Principal Investigator at the phone number given at the end of this form or by writing to the Principal Investigator at the following address:

Lauren Edwards MD
510 S. 42nd Street
Omaha, NE 68198-5575

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.

What will happen if you decide not to be in this research study?
You can decide not to be in this research study. Deciding not to be in this research will not affect your medical care or your relationship with the investigator or the organization. Your doctor will still take care of you and you will not lose any benefits to which you are entitled.

What will happen if you decide to stop participating once you start?
You can stop being in this research (withdraw) at any time. Just call the researcher or any research staff.

If you stop being in the research study it will not affect your care or your relationship with the investigator or the organization. You will not lose any benefits to which you are entitled.
You may be taken off the study if you do not follow instructions of the investigator or the research team.

You may also be taken off the study if:

- you or your medical provider request withdrawal from the study.
- the Principal Investigator (PI) decides it is in your best interest to withdraw you from the study. This could be to worsening depression and/or anxiety, thoughts of suicide or homicide, and adverse event, need for alternative treatment, or other reasons.
- the Principal Investigator (PI) decides to stop your participation due to medical, safety, regulatory, or other reasons consistent with applicable laws, regulations, and good clinical practice (GCP). Good clinical practice helps to ensure the integrity of clinical data to help protect the rights, safety, and welfare of human subjects in research.
- You are not completing the procedures, which includes not completing at least one at-home treatment session in each two week period.
- the research team is unable to reach you for follow-up; you have not been in contact with the research team for at least two weeks after three attempted contacts.
- a protocol violation occurs (you, the investigator, or the sponsor fails to adhere to important protocol requirements for the study).
- the sponsor decides to end the study.
- you receive a positive pregnancy test.
- you response "yes" to question 4 or question 5, or to question 6 in the last

three months on the C-SSRS-R assessment during a clinic visit. The C-SSRS-R is used to assess suicidal thoughts and behavior.
- the your skin becomes too irritated to comfortably continue the treatment sessions after stopping treatment until the skins is no longer irritated and then trying again.

You may be taken off the study at any time if you, the investigator, or the sponsor feels it is not in your best interest to continue. Any research data we have already collected can still be used in the research.

Will you be given any important information during the study?
We will tell you right away if we get any new information that might make you change your mind about being in the study.

What should you do if you have any questions about the study?
We gave you a copy of *"What Do I Need to Know Before Being in a Research Study?"*

If you ever have any questions about this study, call the Principal Investigator or anyone else listed on this consent form.

What are your rights as a research participant?
You have rights as a research subject. These rights have been explained in this consent form and in The Rights of Research Subjects that you have been given. If you have any questions concerning your rights, or want to discuss problems, concerns, obtain information or offer input, or make a complaint about the research, you can contact any of the following:

- The investigator or other study personnel
- Institutional Review Board (IRB)
  - Telephone: (402) 559-6463
  - Email: IRBORA@unmc.edu
  - Mail: UNMC Institutional Review Board, 987830 Nebraska Medical Center, Omaha, NE 68198-7830
- Research Subject Advocate
  - Telephone: (402) 559-6941
  - Email: unmcrsa@unmc.edu

Documentation of informed consent
You are deciding whether to be in this research study. Signing means that:

- You have read and understood this consent form.

- You have had the consent form explained to you.
- You have been given a copy of The Rights of Research Subjects
- You have had your questions answered.
- You have decided to be in the research study.
- You have been told you can talk to one of the researchers listed below on this consent form if you have any questions during the study.
- You will be given a signed and dated copy of this consent form to keep.

Signature of Subject_____ Date_____

My signature certifies that all the elements of informed consent described on this consent form have been explained fully to the subject. In my judgment, the subject possesses the legal capacity to give informed consent to participate in this research and is voluntarily and knowingly giving informed consent to participate

Signature of Person Obtaining Consent_____ Date_____

Authorized Study Personnel
Principal
* Edwards, Lauren
phone: 402-552-6002
alt #: 402-552-6002
degree: MD

Secondary
Weeks, Justin
phone: 402-559-5031
alt #: 402-559-5031
degree: PhD

What Do I Need To Know Before Being In A Research Study?

You have been invited to be in a **research study**. Research studies are also called "clinical trials" or "protocols." **Research** is an organized plan designed to get new knowledge about a disease or the normal function of the body. The people who are in the research are called **research subjects**. The **investigator** is the person who is running the research study. You will get information from the investigator and the research team, and then you will be asked to give your **consent** to be in the research.

This sheet will help you think of questions to ask the investigator or his/her staff. You should know all these answers before you decide about being in the research.

What is the **purpose** of the research? Why is the investigator doing the research?

What are the **risks** of the research? What bad things could happen?

What are the possible **benefits** of the research? How might this help me?

How is this research different than the care or treatment I would get if I wasn t in the research? Are there other treatments I could get?

Does **everyone** in this research study get the same treatment?

Will being in the research **cost** me anything extra?

Do I have to be in this research study? Will the doctor still take care of me if I say **no**?

Can I **stop** being in the research once I ve started? How?

Who will look at my **records**?

How do I reach the investigator if I have more **questions**?

Who do I call if I have questions about being a **research subject**?

Make sure all your questions are answered before you decide whether or not to be in this research.

Academic Research & Services Building 3000 / 987830 Nebraska Medical Center / Omaha NE 68198-7830
402-559-6463 / FAX 402-559-3300 / Email: irbora@unmc.edu / http://www.unmc.edu/irb

THE RIGHTS OF RESEARCH SUBJECTS
AS A RESEARCH SUBJECT YOU HAVE THE RIGHT

to be told everything you need to know about the research before you are asked to decide whether or not to take part in the research study. The research will be explained to you in a way that assures you understand enough to decide whether or not to take part.

to freely decide whether or not to take part in the research.

to decide not to be in the research, or to stop participating in the research at any time. This will not affect your medical care or your relationship with the investigator or the Nebraska Medical Center. Your doctor will still take care of you.

to ask questions about the research at any time. The investigator will answer your questions honestly and completely.

to know that your safety and welfare will always come first. The investigator will display the highest possible degree of skill and care throughout this research. Any risks or discomforts will be minimized as much as possible.

to privacy and confidentiality. The investigator will treat information about you carefully, and will respect your privacy.

... to keep all the legal rights you have now. You are not giving up any of your legal rights by taking part in this research study.

to be treated with dignity and respect at all times

The Institutional Review Board is responsible for assuring that your rights and welfare are protected. If you have any questions about your rights, contact the Institutional Review Board at (402) 559-6463.