Name and Clinic Number
Patient ID Sticker Here

IRB APPROVED
May 19, 2022

RESEARCH PARTICIPANT CONSENT AND PRIVACY AUTHORIZATION FORM

TITLE: A Randomized, Phase II, Open-Label Study Evaluating the Nu-V3 Cranial Nerve Stimulation Treatment Device in Patients with Chronic Pain, Anxiety, Depression, and/or Sleeplessness

PROTOCOL NO.: Nu-V3P2RCT
IRB Protocol #20221817

Protocol Name: Nu-V3 RCT Protocol

SPONSOR: Nu-Life Solutions

Protocol Version: v1.6

SPONSOR: Nu-Life Solutions

INVESTIGATOR: Vipul Kella, MD, BS, MBA, FACEP
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STUDY-RELATED PHONE NUMBER(S): 317-941-6709 (24 hours)

This Informed Consent Form is for adults 18 years and older who suffer from the symptoms of chronic pain, anxiety, depression, and/or sleeplessness.

Please read this information carefully. It tells you important things about this trial. A member of our research team will talk to you about taking part in this research study. If at any time you have any questions, please ask to stop and go through the information for further explanation. If you have questions later, you can always ask your study coordinator, the study doctor, or the staff.

Take your time to decide. Feel free to discuss the study with your family, friends, and healthcare provider before you make your decision.

To help you decide if you want to take part in this study, you should know:

- Taking part in this study is completely voluntary.
- You can choose not to participate.
- If you choose to participate, you are free to change your mind at any time.
- Your decision not to take part or to stop taking part won't cause any penalties or loss of benefits to which you're otherwise entitled.
- If you choose not to participate or discontinue your participation, your decision won't change the access to medical care you receive now or in the future.

You will be given a copy of the full signed Informed Consent Form.

Introduction:
The Nu-V3 device is a miniaturized, lightweight, non-invasive, non-pharmaceutical device used for the possible relief of one or more of the following symptoms: chronic pain, anxiety, depression and/or sleeplessness.

A research study is being conducted to determine the effectiveness of the Nu-V3 device to offer possible relief from chronic pain, anxiety, depression, and/or sleeplessness. You are being asked whether you want to be in a research study because you have one or more of these symptoms. The Nu-V3 device is investigational, which means that it has not been approved by the Food and Drug Administration (FDA) or any other agency and is currently being studied. The device is similar to other devices such as a TENS machine, but differs in treatment, delivery, and patient experience.

At the beginning of the study, half of the subjects will receive the Nu-V3 device; the other half will not. Subjects who do not receive the device at the beginning may be able to receive it later in the study. All of the subjects will answer questionnaires and attend study visits.

Being in this study does not replace your regular medical care. So, it is important that you understand the difference between the regular care you get from your doctor and the research study. If you are currently receiving any treatment for your chronic pain, anxiety, depression, and/or sleeplessness, you will continue to take this medication or treatment as prescribed by your doctor.

In this document, you will see the terms "medication", "treatment", and "treatment period"; these are terms used in research studies and are not meant to indicate that you will be receiving medical treatment for any condition. These terms apply to the investigational study device (Nu-V3 device) and parts of the study where you will be receiving this investigational device.

Type of Research Intervention:
This is an open-label study, which means that you will know if you are receiving active treatment. Every person taking part in the research may receive the device at some point; there are no placebos or dummy devices (which contain no active treatment).

This study involves the use of the Nu-V3 device, which clips onto the ear and has three adhesive gel pads (like small round band aids) which are placed on the external ear. The device is worn continually for two weeks with a change of the pads after the first week. The device is about 1.25 inches by 0.5 inches and weighs about .20 ounces. The total number of devices used will depend on the stage of the study. The device creates a transcutaneous electrical stimulation of the vagus and other cranial nerves. This is thought to increase your autonomic nervous system stimulation, which may have a positive effect on your symptoms.

Total Number of Participants:
About 100-200 individuals will be enrolled in the study at multiple sites. You will be randomized into one of two study regimens; 1) Nu-V3 Study Treatment or 2) Standard of Care.

If you are randomized to the Nu-V3 Study Treatment arm, you will participate in the study for about 24 weeks. You will visit the study center weekly for 12 weeks, then depending on your response to study treatment, you could be in the study for an additional 12 weeks.

If at any time after the initial 12-week treatment period, your primary symptom score is reduced for three consecutive weeks by 70% or more from baseline, then you may continue without device treatment. If your primary symptom score increases by 20% or more, you can continue device treatment until week 24. Your provider will help make these evaluations of response.

If you are randomized into the Standard of Care arm, you will be asked to complete weekly questionnaires for 12 weeks. At the end of these 12 weeks, you will be offered the opportunity to switch into the Nu-V3 Study Treatment arm as described above.

In order to be eligible to take part in this research you will need to:

- be at least 18 years of age
- have one or more of the following symptoms: chronic pain, anxiety, depression, and/ or sleeplessness
- Your primary symptom must be at least a 5/10 as scored on the Baseline Symptom Questionnaire
- The study cohort must have an available slot for you, respective of your primary symptom
- agree to voluntarily participate and sign the Informed Consent Form

You will not be able to take part in the research if you:

- have a hearing aid
- have a pacemaker
- have an irregular heart rate or a heart rate lower than 60 beats per minute (bradycardia)
- had a transplant within the last 2 years
- had a heart attack or cardiac bypass surgery within the last 12 months
- had complaints of dizziness or lightheadedness within the last 3 months
- have Diabetic Retinopathy (high blood sugar levels cause damage to blood vessels in the retina)
- have a current ear infection
- have a systolic blood pressure less than 100 and/or a diastolic blood pressure less than 60
- have a history of uncontrolled bipolar disorder within the last 12 months
- have a history of uncontrolled seizures within the last 12 months
- have a history of aneurysms (a weakness in the wall of your artery)
- have a history of syncope (fainting) within the last 12 months
- had a Transient Ischemic Attack (a mini-stroke) or stroke within the last 12 months
- have health problems that the study doctor thinks will put you at risk to take part in the research
- have had any changes to chronic pain/anxiety/depression/sleeplessness medications within the last 60 days
- are currently undergoing the process of applying for disability support from any source

If you are a woman who is pregnant, you cannot take part in this research.

Please attest to the following if you are female:

I am not pregnant, nor am I trying to become pregnant
☐ Yes ☐ No

I am actively using birth control
☐ Yes ☐ No

Procedures and Instructions:

- You will be asked to complete study questionnaires regarding all of the following symptoms: chronic pain, anxiety, depression, and/or sleeplessness, as well as your quality of life, active medications, medical history, and demographical information. Your primary symptom of concern will also be notated at this time, for later assessment of continuation after week 12.

- At each subsequent visit, you will be asked to complete study questionnaires regarding all the following symptoms: chronic pain, anxiety, depression, and/or sleeplessness, as well as your quality of life.
- If you are in the group that receives the Nu-V3 device, each session will begin with the Nu-V3 device being clipped on your ear and three small pads (non-invasive) adhered to the surface of the ear. Each Nu-V3 device you receive stays on your ear for approximately 28 days, with a change of pads after approximately 7 days.
    - Each session takes approximately 15 – 20 minutes. The placement of the device takes approximately 5 minutes, while the remaining time is spent verifying mobile questionnaire completion and checking for any immediate effects from the device.
    - After the initial week-1 device placement, you will be asked to wait 15 minutes for observation, as some participants can experience a brief period of dizziness.
    - The Nu-V3 device is mobile, fits comfortably behind your ear and is worn for 24 hours a day during treatment. An electrical signal is sent to your external ear through coated wire leads attached to the device and adhesive pads which attach to three sites on your ear.
    - You should be able to perform your typical day-to-day activities while wearing the device. You may shower while wearing the Nu-V3 device, provided that you do not get the device wet and use the small disposable ear covers that are provided for you.
    - In the event the Nu-V3 gel pads are inadvertently removed or the device comes off, you must contact the site coordinator. Participants are encouraged to adjust the device placement as needed for comfort.
- You should not make changes to your existing treatment or medications without discussion with your medical provider.
- If you are in the standard care control group, at completion of 12 weeks of standard of care treatment, you will be offered a crossover into the treatment arm of the study for an additional 24 weeks.

Do you know why we are asking you to take part in this study?
☐ Yes ☐ No

Do you know what the study is about?
☐ Yes ☐ No

Alternative Procedures or Treatment:
Your alternative to study participation is to continue standard of care treatment and NOT participate. Your doctor will continue to monitor your medical care according to the current clinical standards of care.

Will I be compensated for participating in this study?
You will not be compensated for participation in this study.

What are the costs to me for participating in this study?
There will be no direct study costs for your participation in this study. All study visits, tests and procedures will be billed to you per a typical standard of care maintenance visit.

Financial Disclosure:
The Investigator has received consulting fees from the sponsor in the past 12 months. Please feel free to ask any further questions you might have about this matter.

Voluntary Participation:
Your participation in this research is entirely voluntary. It is your choice whether to participate or not.

Side Effects:
Dizziness: When the Nu-V3 device is first placed on your ear, you may experience a slight dizziness – caused by the stimulation of the ear nerves - and/or a mild headache. For this reason, you will be asked to wait for 10-15 minutes following the placement of the Nu-V3 device to check for any side effects and ensure they are resolved before you leave the clinic.

Discomfort: If the device becomes uncomfortable, you may move the device (not the gel pads) along the ear, following discussion with the Investigator. If any severe side effects occur, such as a rash or a sore, you may simply remove it and report this event to your study doctor.

Risks:
There is a risk that you may not receive any benefit from the Nu-V3 device, or it may take a number of weeks to see any benefit. There is a risk that benefits received from the Nu-V3 device may not be long lasting. By stimulating the cranial nerves and the autonomic nervous system, there may be side effects that you are not expecting.

There is a risk that you may develop an allergic reaction to the pads. If you develop a rash, skin irritation or swelling, please remove the pads and contact your study doctor. There may be risks for participating in this research that are currently unknown.

There is a risk of loss of confidentiality.

Benefits:
If you participate in this research study and receive the study device, you may or may not experience an improvement in your symptoms. Your participation will help advance the technology of the Nu-V3 device for others who are suffering. Your participation is likely to help the Sponsor refine the device so it may help others in the future.

Notification of Significant New Findings:
During the course of the study, we may learn new information which could be important to you. This includes information that might cause you to withdraw from the study. You will be notified as soon as possible if such information becomes available.

In the event of a Nu-V3 device related injury:
In the event that the Nu-V3 device causes an injury, even though all instructions have been followed and cautions considered, your insurance will be billed for the medical treatment and the study Sponsor will pay for the costs not covered by your insurance. The sponsor will only pay for reasonable costs and only if the Nu-V3 device has been used in accordance with the study protocol and any other instructions provided by the Sponsor. If you are injured as a result of this study, you do not give up your right to pursue a claim through the legal system.

Confidentiality:
Your personal information collected from this study will be kept confidential to the extent permitted by law. Your personal identity will be protected by assigning an identification number to you. We cannot guarantee absolute confidentiality. By signing this document, you give permission to access your medical records, including after withdrawal from the study, for data verification purposes.

Information about you collected during the research will be available to:

- the researchers and study staff involved in the study
- Nu-Life Solutions, the sponsor of this study or those who work for or represent the sponsor
- the clinicians treating you
- The U.S. Food and Drug Administration (FDA)
- WCG IRB

The results from the study, including laboratory tests, may be published for scientific purposes, but your identity will be kept confidential.

In the rare event that your information is required to be disclosed by law to another entity, privacy laws may not apply, and neither the Sponsor nor Aspire/ Western IRB can protect your information.

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

Do you understand the procedures that will be used to ensure your information remains confidential?
☐ Yes ☐ No

Right to Refuse or Withdraw:
You do not have to sign this form, but if you do not, you cannot take part in this research study. You do not have to take part in this research study. You may decide to stop at any time. You should tell the Principal Investigator if you decide to stop, and you will be advised whether any additional assessments may need to be done to check your health.

In addition, the Principal Investigator, the study sponsor, or the facility listed on page 1 of this document may stop you from taking part in this study at any time: if it is in your best interest, if you don't follow the study procedures, or if the study is stopped.

If you cancel your permission to use or share your health information, your participation in this study will end and no more information about you will be collected; however, information already collected about you during your study involvement may continue to be used.

If you choose not to take part or if you withdraw from this study, it will not harm your relationship with your doctors or with the facility listed on page 1 of this document.

Whom to Contact:
For questions, concerns or complaints or information about the study or a research-related injury, contact the Principal Investigator at the number listed on page 1 of this document.

This research is being overseen by WCG IRB. An IRB is a group of people who perform independent review of research studies. You may talk to them at 855-818-2289 or researchquestions@wcgirb.com if:

- You have questions, concerns, or complaints that are not being answered by the research team.
- You are not getting answers from the research team.
- You cannot reach the research team.
- You want to talk to someone else about the research.
- You have questions about your rights as a research subject.

What if I experience an Adverse (Bad) Event related to my study participation?
If you need emergency care:

- Go to your nearest hospital or emergency room right away or call 911 for help. It is important you tell the doctors at the hospital or emergency room that you are participating in a research study. If possible, take a copy of this Informed Consent Form with you. Neither Nu-Life, nor the study site, have an emergency room or provide emergency care.
- Call the study doctor as soon as you can. They will need to know that you are hurt or ill. Call the Principal Investigator using the contact information provided to you on page 1 of this document (Contact hours 24 hours a day, 7 days a week).

If you do not need emergency care:

- Contact the Principal Investigator and your Primary Care Physician or go to an urgent care facility. It is important that you tell your Primary Care Physician or the urgent care Facility that you are participating in a research study. If possible, take a copy of this Informed Consent Form with you.

The sponsor and Principal Investigator will determine whether the adverse event is related to your study participation.

What if the device inadvertently comes off during my treatment?
In the event the Nu-V3 device is inadvertently removed or comes off, the participant should contact the Principal Investigator. The Principal Investigator will determine the appropriate course of action to be taken.

Enrollment and Permission Signatures

I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it, and any questions I have asked have been answered to my satisfaction.

I consent voluntarily to participate as a participant in this research. I have been told that I can change my mind later if I want to. I will be given a signed and dated copy of this agreement. By signing this consent form, I am not giving up any of my legal rights.

_____	___/___/_____	_____:_____AM/PM
Printed Name of Subject	Date	Time

_____
Signature of Subject

If this consent form is read to the subject because the subject is unable to read the form, or unable to physically sign the form, an impartial witness not affiliated with the research or investigator must be present for the consent and sign the following statement on behalf of the subject:

I confirm that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the subject. The subject freely consented to be in the research study.

_____ / / _____ : _____ AM/PM
Printed Name of Impartial Witness Date Time

_____
Signature of Impartial Witness

Statement by the researcher/person taking consent:
I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this ICF has been provided to the participant

_____ / / _____ : _____ AM/PM
Printed Name of Person Obtaining Consent Date Time

_____
Signature of Person Obtaining Consent