

Approval Date: November 21, 2017

RESEARCH PARTICIPANT CONSENT AND PRIVACY AUTHORIZATION FORM

Study Title: A Phase I Prospective, Single-arm, Open-Label, Multi-Center Study Using the Nu-V3 Cranial Nerve Stimulation Treatment Device in Patients with Pain, Anxiety, Depression, and/or Sleeplessness

Study Number: Nu-V3

Sponsor: Nu-Life Solutions

Protocol Number: Nu-V3 PROTOCOL NO. 1

Principal Investigator:

24-Hour Telephone Number:

This Informed Consent Form is for adults 18 years and older who suffer from the symptoms of 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 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 Informed Consent Form.

Approval Date: November 21, 2017

Name and Clinic Number
 Patient ID Sticker Here

CONTACT INFORMATION

You can contact...	At...	If you have questions about...
Principal Investigator: 	Phone: Address: 	<ul style="list-style-type: none"> • Study tests and procedures • Research-related injuries or emergencies • Any research-related concerns or complaints • Withdrawing from the research study • Materials you receive • Research-related appointments
Institutional Review Board (IRB): Aspire IRB	Phone: (619) 469-0108 Address: 11491 Woodside Ave, Santee, CA 92071	<ul style="list-style-type: none"> • Rights of a research participant
Clinical Trial Manager Eric Siebeneck, MS	Phone (7a-7p MST): 317-941-6709	<ul style="list-style-type: none"> • Issues with accessing your mobile questionnaires

Approval Date: November 21, 2017

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: 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 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.

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 pain, anxiety, depression, and/or sleeplessness, you will continue to take this medication 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 that you are receiving active treatment. Every person taking part in the research will receive the device, 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 50-100 individuals will be enrolled in the study at multiple sites. You will be in the study for about 12 weeks. You will visit the study center weekly for 8 weeks, then you will have a follow up phone call weekly for another 3 weeks. At the 12th week, you will visit the study center for an evaluation, and will be offered the opportunity to continue treatment with an

Approval Date: November 21, 2017

optional maintenance period. This optional maintenance period will last another 12 weeks and will consist of a 2-weeks on, 2-weeks off treatment, followed by an 8 week observation period.

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: pain, anxiety, depression, and/ or sleeplessness
- be capable of understanding the use and maintenance of the device
- be capable of and agree to participate in the ongoing assessment
- agree to voluntarily participate and sign the Informed Consent Form
- be willing to commit to follow all protocol study timepoints and instructions

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

- 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
- have a history of substance abuse, including prescription drugs 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 pain/anxiety/depression/sleeplessness medications within the last 60 days
- are currently undergoing the process of applying for disability support from any source

Approval Date: November 21, 2017

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:

- Prior to the study, you will be asked to complete study questionnaires regarding all of the following symptoms: pain, anxiety, depression, and/or sleeplessness, as well as your quality of life, active medications, medical history, and demographical information.
- At each subsequent visit, you will be asked to complete study questionnaires regarding all the following symptoms: pain, anxiety, depression, and/or sleeplessness, as well as your quality of life.
- Each session will begin with the Nu-V3 device being placed on your left ear and three small pads (non-invasive) being placed on three areas of the ear. Each Nu-V3 device you receive stays on your ear for approximately 14 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.
- The Nu-V3 device is mobile, fits comfortably behind your left 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.
- You should not make changes to your existing treatment or medications without discussion with your medical provider.
- Nu-Life reserves the right to capture video, photographs and written testimonials from you with written permission. It may be possible to tell your identity from the videos, photography and testimonials. It is optional for you to take part in these activities. In the event that you elect to participate in any or all of these activities, you will be asked to sign a waiver (a separate permission form) giving exclusive rights to Nu-Life for the materials gathered from you, such as video, photographs and written testimonials. Your participation in this study is not dependent upon your willingness to provide these testimonial materials. Please ask your study doctor or study staff to explain the use of

Approval Date: November 21, 2017

these photographs, videos or testimonials before you make a decision whether to agree to take part in this optional part of the research.

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. This research study does not offer alternative procedures or treatment. 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.

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, 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

Approval Date: November 21, 2017

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.

Benefits:

If you participate in this research study, 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.

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)
- Aspire Independent Review Board (IRB)/ Western IRB

Approval Date: November 21, 2017

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 Web site 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 for your safety.

In addition, the Principal Investigator, the study sponsor, or the facility listed on page 2 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 2 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 2 of this document.

For questions about your rights as a study participant, please contact the Institutional Review Board (IRB) at the number listed on page 2 of this document.

For issues, questions, or concerns related to your mobile study questionnaires, please contact the Clinical Trial Manager at the number listed on page 2 of this document.

Approval Date: November 21, 2017

**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 2 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.

Approval Date: November 21, 2017

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

[Optional] Consent to Continued Maintenance and Observation Beyond Initial 12 Weeks:

If you have completed the initial 12-Week treatment period, and would like to continue receiving therapy, you are eligible to continue treatment with the Nu-V3 device. We will provide you with any new information including risks, discomforts, or new alternative treatments that might affect whether you wish to continue to be in the study.

I freely accept to continue my participation in this study:

Signature of Participant _____ Date: _____

Signature of person obtaining re-consent _____ Date: _____

Signature of Investigator/Physician _____ Date: _____