PARTICIPANT INFORMED CONSENT FORM

STUDY TITLE: A Randomized, Double Blind Sham Controlled Clinical Trial to Evaluate the Efficacy of Electrical Vestibular Nerve Stimulation (VeNS), Compared to a Sham Control for Treatment of PTSD

PROTOCOL NO: MS003

STUDY INVESTIGATOR: Peter J Colvonen, PhD

STUDY SITE: University of California, Dept of Psychiatry
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SPONSOR: Neurovalens Limited

WHO IS CONDUCTING THE STUDY?

Dr. Peter Colvonen, PhD, Assistant Clinical Professor at the University of California, San Diego (UCSD) specializes in PTSD treatment and has medical responsibility for this clinical trial. Dr. Colvonen and his associates are conducting a randomized, double-blind, sham controlled clinical trial to evaluate how well electrical vestibular nerve stimulation (VeNS) works for the treatment of Post-Traumatic Stress Disorder (PTSD).

Neurovalens Ltd. is the sponsor of this clinical trial. Neurovalens is a company based in the United Kingdom that develops non-invasive neurostimulation products, to treat and help manage various medical conditions including neurological conditions such as insomnia and anxiety. Neurovalens has overall responsibility for this clinical study.

An independent clinical research organization called Clinical Trial Mentors (CTM) will conduct the study visits with you.

WHY HAVE YOU BEEN ASKED TO PARTICIPATE?

You have been invited to participate in this study because you meet the initial eligibility criteria and have expressed an interest in participating after hearing about the trial. Specifically, you have been selected because you have a diagnosis of PTSD, have sleep issues and are on a steady treatment plan. If you are deemed eligible for the trial after pre-screening, you will have a 30-minute video consultation with Dr. Colvonen or Dr. Colvonen's designee to confirm your trial eligibility.

WHAT IS THE APPROXIMATE NUMBER OF PARTICIPANTS IN THE STUDY*?*

There will be up to 200 people aged 22 to 80, inclusive, recruited remotely through UCSD.

WHY IS THIS STUDY BEING CONDUCTED?

PTSD is a disabling psychiatric disorder that results from being exposed to real or threatened injury, events, death or sexual assault. Following these traumatic events, PTSD is common and is one of the serious health concerns that is associated with comorbidity, functional impairment, and increased mortality with suicidal ideations and attempts. Many cases of PTSD include acute stress and anxiety disorders and are often associated with sleep disturbances or insomnia.

Medications are known to be effective, and currently serve as the primary treatment for insomnia but their use is limited due to the risk of adverse events. Cognitive Behavioral Therapy for Insomnia (CBT-I) has also been shown to be effective and safer in the treatment of insomnia but presents its own limitations such as the time, cost, and training required. With the knowledge that PTSD treatment options are currently limited, the Modius Spero device was designed as a non-invasive drug-free treatment for the symptoms of PTSD. The device applies a low-level electrical waveform to the vestibular system (inner ear), known as electrical vestibular nerve stimulation (VeNS).

The purpose of this study is to evaluate the effectiveness of VeNS as a method of treating the symptoms of PTSD. If vestibular stimulation is shown to be effective in the treatment of PTSD symptoms, it could serve as a safer alternative to medications. It could also require less cost, time, and training than CBT-I, providing an option that is not only safe and effective, but broadly available.

WHAT WILL HAPPEN TO YOU IN THIS STUDY AND WHICH PROCEDURES ARE STANDARD OF CARE AND WHICH ARE EXPERIMENTAL?

If you agree to participate in this study, you will be asked to complete a pre-screening questionnaire online, a screening phone call with CTM and a screening video call to assess your PTSD diagnosis with Dr. Colvonen or Dr. Colvonen's designee. Once you have completed the screening process and have signed this consent form you will be randomly (by chance, like the flip of a coin) assigned a study device. You have a 50:50 chance of receiving an active device, otherwise you will receive a sham device (a device that does not deliver active treatment). Please note that you will not be told whether you have received the active study device or the sham until all 100 participants have completed the study. This is standard procedure to ensure that any knowledge of active treatment does not affect the study outcome.

The Modius Spero device is an investigational medical device. Investigational means that the Modius Spero device has not been approved for use by the United States Food and Drug Administration (FDA).

In this document, the term study device will refer to both the Modius Spero device and the sham device.

In this document, you may see the terms "treatment" and "treatment period". These are terms used in research studies and these terms do not mean that you will be receiving medical treatment for any condition. These terms apply to the investigational study device and parts of the study where you will be using this study device.

The study device fits over your head like a headset with electrodes placed right behind your ears. You will be asked to use the headset for 30 minutes each day for the 12-week duration of the trial.

You will be required to complete four remote study visits conducted over a video-calling platform (for example, Zoom) over the course of 12 weeks. The study visits will be conducted at weeks 0, 4, 8 and 12. CTM will also conduct a weekly call to check in with you and you will be given the opportunity to ask questions.

During the remote screening and study visits you will be asked questions about your health status and current treatment plans. You will be asked to complete several questionnaires about your PTSD (PCL-5), sleep (ISI), general anxiety (GAD-7), general health (SF-36) and Quality of Life (EQ-5D-5L). You will also receive training on how to use the study device.

The following table summarizes these questionnaires and what they are for:

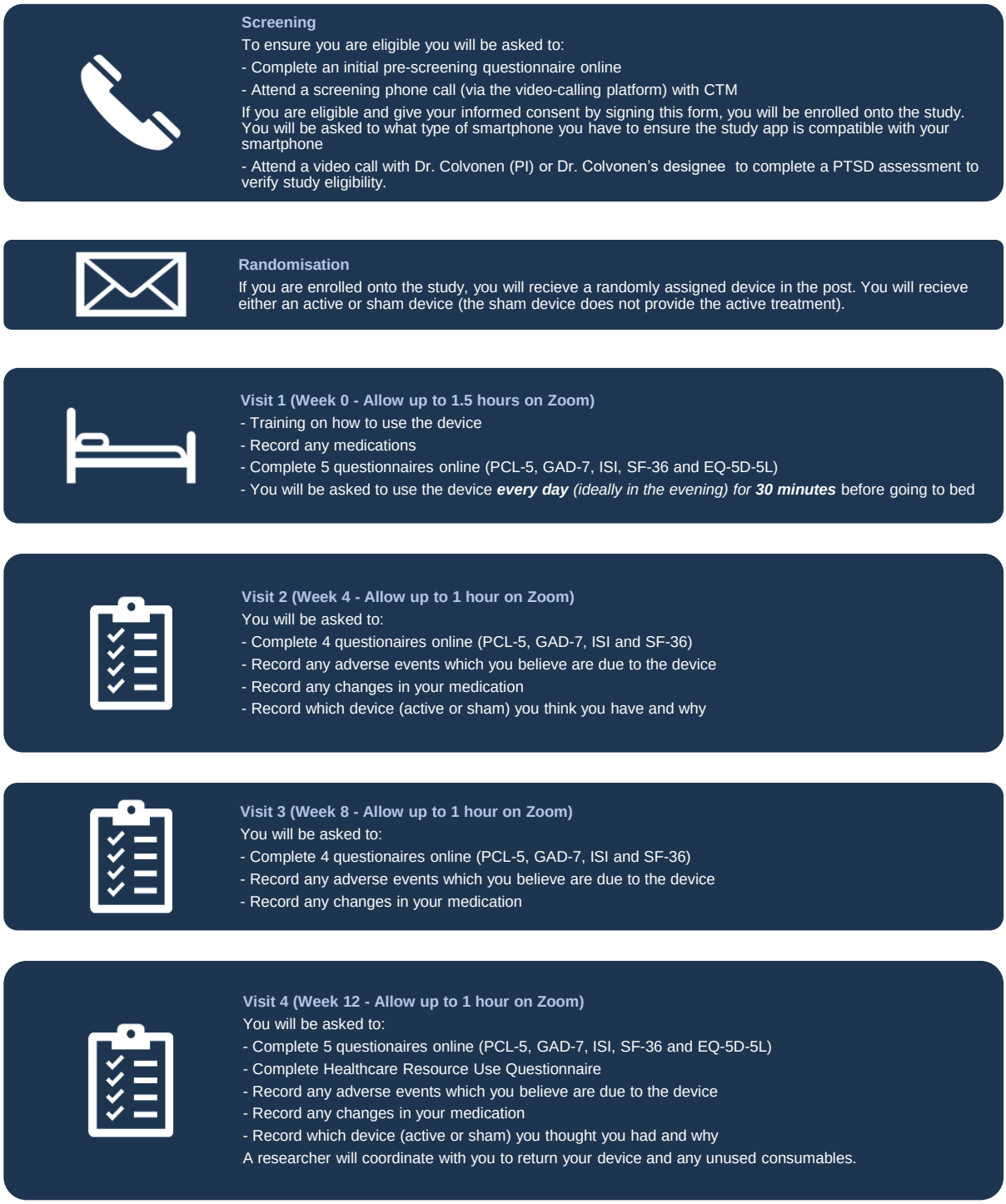
Questionnaire	**Full name of questionnaire**	**Purpose of questionnaire**
PCL-5	PTSD Checklist for the Diagnostic and Statistical Manual of Mental Disorders (Diagnostic and Statistical Manual – 5, DSM-5)	Assess the symptoms of PTSD
GAD-7	General Anxiety Disorder	Assess the symptoms of Anxiety
ISI	Insomnia Severity Index	Assess the symptoms of Insomnia
SF-36	36 Item Short Form Survey	Assess Health Status
EQ-5D-5L	EuroQol 5 Dimensions and 5 Levels	Assess health-related quality of life

You will also be asked:

- Questions about your current medication and any changes to your medication over the course of the study.
- To report any side effects that you experience (if any) from using the device
- To complete a questionnaire on your usage of Healthcare services both historic and over the course of the study
- To complete a short questionnaire (World Health Organisation-5, WHO-5) about your current well-being. This is conducted each week via the Study App
- To privately indicate what type of device you think you might have. You will be asked to choose between “Active”, “Sham” and “Don’t know” and briefly explain why. This is conducted at the week 4 visit and week 12 visit

Figure 1 below summaries the screening process, randomization, and study visits.

Overview of the study visits

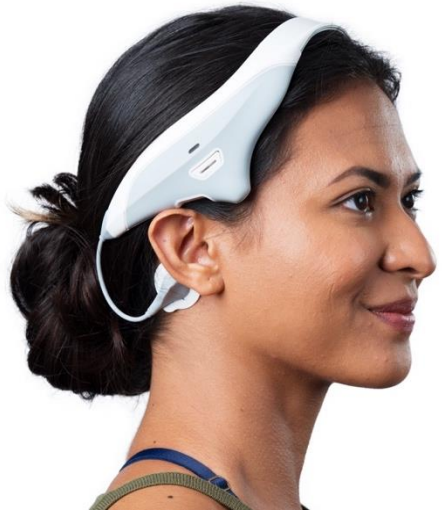


Optional survey

If you are not eligible to take part in the study following screening, you may be invited via email to complete an optional survey about the recruitment process. This survey is completely optional but if you decide to complete the survey, you will receive a $10.00 gift voucher as compensation for your time.

What is the study device?

This study uses an investigational electro-stimulation device called Modius Spero. Modius Spero consists of a battery-powered headset designed to deliver low-level energy in the form of a neurostimulation waveform that modulates the activity of the vestibular cranial nerve. The delivery of this waveform is through two self-adhesive electrode pads that are placed on the skin overlaying each mastoid process, as shown in figure 2 below. This technique is known as electrical vestibular nerve stimulation (VeNS).



Photograph of the study device, showing the headset-style design and mastoid electrode placement.

A member of CTM will show you how to use your study device during your first study visit. Briefly, you place the device on your head in the same manner as wearing headphones. The device is controlled via an app on your smartphone which you will be asked to download, or it will be pre-loaded on a provided iPod. The app allows you to turn the stimulation level of the device up and down and to pause the stimulation as required. You can also pause the stimulation by pressing the power button twice on the device. The app will record your total daily usage and display this to you.

You will be asked to use the device for **30 minutes every day, ideally before bed**. The device will turn off after use. You must try to use the device for the full 30 minutes every day. The app will record how often you use the device which will be monitored, and you will be contacted if your usage levels are low via email or by a member of CTM. It is a trial requirement that you use the device daily. If your usage is less than 2.5 hours a week (less than 5 sessions a week), then an

automated email will be sent to encourage you to use the device more regularly. If you do not use the device for 1 week or more (without a valid explanation), you will be considered for withdrawal from the trial.

If you are assigned to receive the active device, it will deliver a small electrical current to the skin behind the ears over the mastoid processes (the bony part that is easily felt behind the earlobe). It is normal for the sensation to be stronger when first turning on the device and then for it to quickly become less noticeable. This is because you get used to the stimulation. Not everyone is consciously aware of the stimulation taking place as everyone's response to the device is different. It is therefore possible that you may not feel any stimulation.

When using the device, you may feel a rocking sensation like being on a boat. While using the device we ask that you comply with the following:

- **Do not walk around while using the device.** We advise that you pause it or turn it off before getting up.
- **Never use the device while driving or operating machinery**.
- Please use the device while sitting upright (for example, in a chair), as opposed to lying down (for example, in a bed or recliner). We also suggest you use the device in the evening before you go to bed. This is because sometimes vestibular stimulation can make people feel slightly sleepy.
- Keep the study device out of the reach of children.

You will be given an adequate supply of disposable electrode pads and they must be changed after each use. You will also be provided with alcohol wipes, and you must clean the skin behind your ears before placing the electrode pads on the skin and using the device. A member of CTM will show you exactly where to clean and place the electrode pads during your training session.

During the course of the study, neither you nor any of the study team you meet will know what type of device you have been given to use. This is known as a double-blind study. Throughout the trial, please do not tell research team what type of device you think you have received. At the 4 week visit and at the end of the 12 weeks, you will however be asked what type of device you think you might have had and your reasoning. You will be asked to choose between "Active", "Sham" and "Don't know" and briefly explain why. You will be given a pre-paid postage label to mail back your study device and unused consumables at the end of the study.

In the case of an emergency, the study team will be able to determine which type of device you have. Otherwise, at the end of the study, the code will be broken, and it will be revealed to you and the study team if you had an active or sham device.

Once you enroll into the trial the following personal details will need to be provided to arrange the postage of your device:

- Name
- Email
- Home address
- Phone number

All the study procedure precautions will be taken to protect the confidentiality of these personal details. These details will only be shared with authorized members of the study team (the PI, CTM and unblinded staff of sponsor) to enable your device to be delivered to you.

HOW MUCH TIME WILL EACH STUDY PROCEDURE TAKE, WHAT IS YOUR TOTAL TIME COMMITMENT, AND HOW LONG WILL THE STUDY LAST?

The screening process involves three steps:

- Online initial screening questionnaire (approx. 5-10 mins)
- Screening phone call with CTM (up to approx. 30 mins)
- Video call on Zoom with Dr. Colvonen (PI)/ or designee to confirm PTSD diagnosis (approx. 30 mins)

There will be four study visits, all conducted remotely over a video-calling platform (for example, Zoom):

- Visit 1 at week 0 (approx. 1.5 hours)
- Visit 2 at week 4 (approx. 1 hour)
- Visit 3 at week 8 (approx. 1 hour)
- Visit 4 at week 12 (approx. 1 hour)

We expect that you will be enrolled in the study for a total of 12-14 weeks.

WHAT RISKS ARE ASSOCIATED WITH THIS STUDY?

It is always possible that your participation in this study may involve some level of risk. Any potential risk has been outlined below.

Risks of the study device and electrical vestibular nerve stimulation (VeNS):

Risks that may occur from participation in this study are potential side-effects from the device. Although considered a **LOW RISK** device (in the unlikely event that side effects occur they appear as temporary, mostly mild, occur only once and typically return to normal by the end of the study), the following symptoms described below have been identified as risks of vestibular stimulation from the scientific literature on VeNS (the technology used by the Modius Spero device).

Note: Not all these side effects have been seen from the use of the Modius Spero device.

- Skin irritation behind the ear, where the electrodes are attached – as sometimes participants may have a skin sensitivity to the electrode gel
- Stimulation sites may be uncomfortable at the time of stimulation – an electrical tingling sensation may occur
- May induce the sensation of being pushed towards one side or the other
- A rocking sensation (similar to being on a boat), that some people find uncomfortable may occur. A small chance of vertigo/dizziness or nausea/vomiting could result.
- Dizziness

- Nausea
- Blurred vision
- Fatigue/tiredness
- Headache – Please note that headaches are commonly reported in the literature relating to use of this device (about 15% of users), and if you suffer from migraine then use of the device could trigger further headaches and/or migraines. For this reason, we have decided to screen out individuals with active migraines.
- A small theoretical risk of developing tinnitus (ringing in the ears)
- Seizures (which may have legal implications on driving). Note – this is very rare in the literature and has never been associated with Neurovalens VeNS devices.

You are encouraged to reach out to CTM immediately if you experience any symptoms or side effects while using the study device. We will help to assess and provide information for follow up.

Risks of loss of confidentiality:

Even with all the study procedure precautions that will be taken to protect confidentiality, there is always still a risk of loss of confidentiality associated with clinical trial research. Research records will be kept confidential to the extent provided by law. The study personnel are well trained in securing and safely storing all your data.

Pregnancy

You cannot participate in this study if you are pregnant or breast-feeding a child. If you get pregnant during the study, you will not be able to participate further in the study but instead will be asked to see your regular healthcare provider for further assessment. We ask that you refrain from becoming pregnant for the duration of your participation in the study.

Unknown risks:

Because this is a research study, there may be some unknown risks that are currently unforeseeable. You will be informed of any significant new findings.

WHAT ARE THE ALTERNATIVES TO PARTICIPATING IN THIS STUDY?

The alternatives to participation in this study are not to participate in the study. You may continue your current PTSD treatment or talk to your personal doctor about other alternatives to your current treatment.

WHAT BENEFITS CAN BE REASONABLY EXPECTED?

You may or may not benefit directly from participation in this study. Your health may benefit if you see improvements in your PTSD symptoms.

Other patients with PTSD may benefit in the future from the findings of this research study.

CAN YOU CHOOSE TO NOT PARTICIPATE OR WITHDRAW FROM THE STUDY WITHOUT PENALTY OR LOSS OF BENEFITS?

Participation in research is entirely voluntary. You may refuse to participate or withdraw at any time without penalty or loss of benefits to which you are entitled. If you decide that you no longer wish to continue in this study, you will be requested to contact CTM, and they will inform Dr. Colvonen. You will be told if any important new information is found during the course of this study that may affect your decision to continue.

CAN YOU BE WITHDRAWN FROM THE STUDY WITHOUT YOUR CONSENT?

You may be withdrawn from the study for the following reasons:

- You become ill
- You become injured and cannot get around without assistance

You may also be withdrawn from the study if you do not follow the instructions given to you by the study personnel, including low usage issues (missing a total of 7 days usage over the course of the research study). You may also be withdrawn from the study by the study staff if it is believed to be in your best medical interest.

HOW DO I WITHDRAW FROM THE STUDY IF I NO LONGER WISH TO PARTICIPATE?

Participation in this research is entirely voluntary. If you decide not to participate in this study, there will be no negative consequence for you and your medical treatment will not be affected in any way.

You may refuse to participate or withdraw at any time. If you decide that you no longer wish to continue in this study, you are requested to tell CTM, and they will request that you return the study device and any unused consumables.

WILL YOU BE COMPENSATED FOR PARTICIPATING IN THIS STUDY?

In compensation for your time, you will receive payment, totaling $100.00 for completing the study and return of the study device. Payment will be made in the form of direct bank transfer / gift cards. You will not be entitled to a share of any profits that may arise from the future use of your study data or products derived from it

ARE THERE ANY COSTS ASSOCIATED WITH PARTICIPATING IN THIS STUDY?

There will be no cost to you for participating in this study.

WHAT IF YOU ARE INJURED AS A DIRECT RESULT OF BEING IN THIS STUDY?

If you are injured as a result of being in this study, UCSD will provide necessary medical treatment. The costs of the treatment may be covered by the University of California or the study sponsor, Neurovalens, Ltd. or billed to you or your insurer just like other medical costs, depending on a

number of factors. The University and the sponsor do not normally provide any other form of compensation for injury. For more information about this, you may contact the UC San Diego Office of IRB Administration. You may also contact the UC San Diego Office of IRB Administration at 858-246-4777 or irb@ucsd.edu to inquire about your rights as a research subject or to report research-related problems.

WHAT ABOUT YOUR CONFIDENTIALITY?

Research records will be kept confidential to the extent provided by law. To guard your confidentiality, you will be assigned a unique identifying number to label all your data collection sheets. All personal information will be kept strictly confidential by the study investigators. All study forms, and data collected will be kept locked in a secure location. All your data forms will only list your unique study ID number. All members of the research team are trained in the protection of subject privacy and confidentiality. Research records may be reviewed by the UCSD Institutional Review Board, Sterling Institutional Review Board or the study Sponsor, Neurovalens. Members of the research team and other staff or representatives of UCSD whose work is related to the research or to protecting your rights and safety will have access to your health information.

Because of the need to release information to these parties, absolute confidentiality cannot be guaranteed. The results of this research study may be presented at meetings or in publications; however, your identity will not be disclosed in those presentations.

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.

A federal regulation known as the Health Insurance Portability and Accountability Act of 1996 (HIPAA) gives you certain rights concerning the privacy of your health information. Researchers covered by this regulation are required to get your authorization (permission) to use and disclose (share with others) any health information that could identify you.

You will be asked to sign and date a separate form authorizing access, use, creation, or disclosure of health information about you.

You have the right to cancel your consent at any time by giving written notice, calling or telling a member of the study team including the study investigator. If you cancel your consent, then the study staff will no longer use or disclose your medical information, unless it is necessary to do so to preserve the scientific integrity of the study. However, cancelling your consent will not affect previous uses and disclosures and your medical information will not be removed from the study records unless you request for it to be withdrawn. If you fail to give your consent by signing this document, you will not be able to participate in this study. If you cancel your consent later, you will be removed from the study. Unless and until you do cancel your consent, it will remain valid and effective.

WHO CAN YOU CALL IF YOU HAVE QUESTIONS?

CTM will explain this study to you and answer your questions before you sign this consent form. If you have other questions or research-related problems or injury, you may reach CTM at team@ctmentors.com or via phone +1 (442) 369-7964.

You contact the UC San Diego Office of IRB Administration at 858-246-4777 or irb@ucsd.edu to inquire about your rights as a research subject or to report research-related problems.

If you have questions regarding your rights as a research participant, or if you have questions, concerns, complaints about the research, would like information, or would like to offer input, you may contact the Sterling Institutional Review Board Regulatory Department, 6300 Powers Ferry Road, Suite 600-351, Atlanta, Georgia 30339 (mailing address) at telephone number 1-888-636-1062 (toll free) or info@sterlingirb.com.

YOUR SIGNATURE AND CONSENT

I have read the Participant Informed Consent Form and I agree to participate voluntarily in this study. I give my permission to the study doctor to use and disclose my protected health information as described in this consent form.

I will receive a signed copy of this consent form.

I agree that I have been given a chance to ask questions about this research study. These questions have been answered to my satisfaction.

I have not waived any of my legal rights by signing this document.

I have received a copy of the “Experimental Subject's Bill of Rights” (if based in California) to keep.

_____ _____

Subject’s Name **Date**

_____

Subject's Signature

_____ _____

Name of Person Obtaining Consent **Date**

_____

Signature of Personnel Obtaining Consent Date

IRB# 801272

University of California, San Diego

[1] Permission to Use Personal Health Information for Research

Study Title (or IRB Approval Number if study title may breach subject's privacy):

Principal Investigator Name: Peter Colvonen, Ph.D.

Sponsor/Funding Agency (if funded): Neurovalens, Ltd.

A. What is the purpose of this form?

State and federal privacy laws protect the use and release of your health information. Under these laws, the University of California or your health care provider cannot release your health information for research purposes unless you give your permission. Your information will be released to the research team which includes the researchers, people hired by the University or the sponsor to do the research and people with authority to oversee the research. If you decide to give your permission and to participate in the study, you must sign this form as well as the Consent Form. This form describes the different ways that the UC SAN DIEGO HEALTH[2] can share your information with the researcher, research team, sponsor and people with oversight responsibility. The research team will use and protect your information as described in the attached Consent Form. However, once your health information is released by UC SAN DIEGO HEALTH[3] it may not be protected by the privacy laws and might be shared with others. If you have questions, ask a member of the research team.

B. What Personal Health Information will be released?

If you give your permission and sign this form, you are allowing: UC SAN DIEGO HEALTH to release the following medical records containing your Personal Health Information. Your Personal Health Information includes health information in your medical records, financial records and other information that can identify you.

☒Entire Medical Record	☐Lab & Pathology	☐Emergency Department
☐Ambulatory Clinic	☐Dental Records	☐Financial records
☐Progress Notes	☐Operative Reports	☐Imaging Reports
☐Other Test Reports	☐Discharge Summary	☐History & Physical Exams
☐Other (describe)	☐Consultations	☐Psychological Tests

[1] Each UC Health System or business unit may elect to leave this as UC or add the name of their specific

[2] The name here should match how the organization is identified in the Notice of Privacy Practices.

[3] The name here should match how the organization is identified in the Notice of Privacy Practices.

C. Do I have to give my permission for certain specific uses?

Yes. The following information will only be released if you give your specific permission by putting your initials on the line(s).

___I agree to the release of information pertaining to drug and alcohol abuse, diagnosis or treatment.
___I agree to the release of HIV/AIDS testing information.
___I agree to the release of genetic testing information.
___I agree to the release of information pertaining to mental health diagnosis or treatment.

D. Who will disclose and/or receive my Personal Health Information??

Your Personal Health Information may be shared with these people for the following purposes:

1. To the research team for the research described in the attached Consent Form;
2. To others at UC with authority to oversee the research
3. To others who are required by law to review the quality and safety of the research, including: U.S. government agencies, such as the Food and Drug Administration or the Office of Human Research Protections, the research sponsor (insert the name of the sponsor) or the sponsor's representatives including but not limited to (insert the name of the CRO), or government agencies in other countries.

E. How will my Personal Health Information be shared for the research?

If you agree to be in this study, the research team may share your Personal Health Information in the following ways:

1. To perform the research
2. Share it with researchers in the U.S. or other countries;
3. Use it to improve the design of future studies;
4. Share it with business partners of the sponsor; or
5. File applications with U.S. or foreign government agencies to get approval for new drugs or health care products.

F. Am I required to sign this document?

No, you are not required to sign this document. You will receive the same clinical care if you do not sign this document. However, if you do not sign the document, you will not be able to participate in this research study.

G. Optional research activity

If the research I am agreeing to participate in has additional optional research activity such as the creation of a database, a tissue repository or other activities, as explained to me in the informed consent process, I understand I can choose to agree to have my information shared for those activities or not.

☐ I agree to allow my information to be disclosed for the additional optional research activities explained in the informed consent process.

H. Does my permission expire?

This permission to release your Personal Health Information expires when the research ends and all required study monitoring is over.

I. Can I cancel my permission?

You can cancel your permission at any time. You can do this in two ways. You can write to the researcher or you can ask someone on the research team to give you a form to fill out to cancel your permission. If you cancel your permission, you may no longer be in the research study. You may want to ask someone on the research team if canceling will affect your medical treatment. If you cancel, information that was already collected and disclosed about you may continue to be used for limited purposes. Also, if the law requires it, the sponsor and government agencies may continue to look at your medical records to review the quality or safety of the study.

J. Signature

Subject

If you agree to the use and release of your Personal Health Information, please print your name and sign below. You will be given a signed copy of this form.

_____

Subject's Name (print)--*required*

_____ _____

Subject's Signature Date

Parent or Legally Authorized Representative

If you agree to the use and release of the above named subject's Personal Health Information, please print your name and sign below.

_____

Parent or Legally Authorized Representative's Name (print) Relationship to the Subject

_____

Parent or Legally Authorized Representative's Signature Date

Witness

If this form is being read to the subject because s/he cannot read the form, a witness must be present and is required to print his/her name and sign here:

Witness' Name (print)

Witness' Signature

Date