Sterling Achieve More. IRB

office 770.690.9491 **toll free** 1.888.636.1062 **fax** 770.690.9492
6300 Powers Ferry Road Suite 600-351 Atlanta, Georgia 30339
www.sterlingirb.com **e-mail** info@sterlingirb.com

PRINCIPAL INVESTIGATOR – APPROVAL NOTIFICATION

Date Issued:	September 25, 2019
Issued To:	Jeffrey A Craven, MD
Protocol Title:	BRIDGE Device for Symptoms of Opioid Withdrawal: A Randomized, Double-Blind, Placebo-Controlled Study
IRB ID#:	**7454-JACraven**
	Please include the IRB ID# listed above on all correspondence pertaining to this study.
Sponsor:	Innovative Health Solutions

Review Type:	Full Board
Review Determination:	Approved with Contingencies
Approval Date:	**September 24, 2019**
Contingency Verification Date (*if applicable*):	September 25, 2019
Study/Site Expiration Date:	**September 23, 2020**
Study Status Report Due:	**30 Days Prior to Expiration Date**

Approved Principal Investigator: Jeffrey A Craven, MD

Approved Site Locations:
Brightview Morgan Center
446 Morgan St.
Cincinnati, OH 45206

Please see Section A for approved study items.

Please see Section B for additional study information.

Please see Section C for Principal Investigator/Site Responsibilities.

The current Sterling IRB Membership List is available on our website, www.sterlingirb.com.

The Principal Investigator's qualifications to conduct the above referenced study were reviewed and **approved** as indicated above. If applicable, satisfaction of the Board-determined contingencies was verified by the Chairman or his/her designee on the date listed above.

Sterling IRB has approved this Principal Investigator to conduct this study at the above-listed site(s). Approval will expire on the Study Expiration Date listed above, and if the study is to continue the Principal Investigator must receive Sterling IRB approval for study continuation prior to the expiration date. The Principal Investigator should submit the **Study Status Report** not less than one month prior to the last Sterling IRB meeting preceding the expiration date (form available in Sterling IRB's web portal, SilverLink). If approval for study continuation is not obtained prior to the expiration date, the study will be considered to be in noncompliance with Federal Regulations and IRB requirements, may be suspended, and may be subject to termination.

A **final Study Status Report** will be due at the conclusion of the study (form available in SilverLink).

The Sponsor/CRO may receive a copy of all documentation issued to your site.

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SECTION A: APPROVED STUDY ITEMS

- Protocol
- * Participant Informed Consent Form and Authorization to Use and Disclose Medical Information (Version Date: September 5, 2019)
- Instructions For Use NSS-2® BRIDGE® (Part No.: 01-1017-NSS-2 / BRIDGE, Rev. No.: 003)
- Investigator's Qualifications

Study Materials:

- * Pain and Craving Symptom Survey
- * CNSVS SUBTESTS
- * Clinical Opiate Withdrawal Scale (COWS) (5M 11/11)

For approved recruitment/study materials, you may insert or change site-specific information without resubmitting to the IRB. This is not applicable to the Informed Consent Form(s).

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* For any approved items which are labeled with the **asterisk (*)** symbol, copies of these items can be found in SilverLink in the Attachments page for this submission's Event. Items not labeled with the asterisk (*) symbol will be provided by the Sponsor/CRO.

You must use the most current Informed Consent Form(s) approved by Sterling IRB for consenting participants.

End of Section A

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SECTION B: STUDY INFORMATION

Sterling IRB has determined that the research involves minimal risk.

End of Section B

Sterling Achieve More. IRB

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SECTION C: PRINICIPAL INVESTIGATOR / SITE RESPONSIBILITIES

The Principal Investigator is responsible for following all policies of Sterling IRB as described in the Investigator's Compliance Agreement which was attested to on the submission application. It is the Principal Investigator's responsibility to ensure this research is conducted in accordance with applicable regulations (local, state/provincial and federal) as well as any requirements established by the IRB at the time of the approval. Refer to the Investigator Handbook at www.sterlingirb.com for details of these responsibilities.

- Check all addresses (sites) and phone numbers for accuracy in the Approval Document and Informed Consent Form(s). **Let our office know ASAP if there are any inaccuracies.**
- Please note the due date listed on the Approval Document for the Study Status Report. A final Study Status Report should also be submitted once the study at your site is completed. **These reports are required by the Board and by Federal Regulations.**
- Sterling IRB forms (including English and Spanish versions of the California Experimental Subject's Bill of Rights) for use by the Principal Investigator/Site are available on our website, www.sterlingirb.com.
- Sterling IRB has developed an Investigator Handbook that outlines the responsibilities of the Principal Investigator. **The Investigator Handbook should be read by all key personnel on the research team.** It can be located on the Sterling website, www.sterlingirb.com.
- Sterling IRB requires Principal Investigators to **promptly** report all events that may constitute unanticipated problems involving risk to subjects or others and new or updated safety information relating to the study or study product. Please refer to Chapters 7 ('Reportable Events') and 10 ('Research Conflicts') of the Investigator Handbook (located on our website at www.sterlingirb.com) for additional information regarding reporting guidelines.
- Any changes to the research must be submitted in writing to Sterling IRB for review and approval prior to implementation.
- Sterling IRB should be informed immediately of any serious adverse reaction or should any unanticipated problems involving risks to the subject or others occur or should the Sponsor provide safety information.
- Local prejudices or negative attitudes in the community toward the conduct of research projects must be reported immediately.
- State/provincial or local laws (including tribal law passed by the official governing body of an American Indian or Alaska Native tribe) pertaining to Patient/Volunteer Bill of Rights and specific state/provincial or local laws (including tribal law passed by the official governing body of an American Indian or Alaska Native tribe) laws concerning research which affect the conduct of clinical research must be enforced.
- Non-English speaking subjects enrolled in this study must be provided with an informed consent written in their fluent language, which must be approved by Sterling IRB before use.

If you have any questions please call our office at 888-636-1062.

End of Section C / End of Document

PARTICIPANT INFORMED CONSENT FORM AND AUTHORIZATION TO USE AND DISCLOSE MEDICAL INFORMATION

STUDY TITLE: BRIDGE Device for Symptoms of Opioid Withdrawal: A Randomized, Double-Blind, Placebo-Controlled Study

STUDY DOCTOR: Jeffrey A Craven, MD

STUDY SITE: Brightview Morgan Center
446 Morgan St.
Cincinnati, OH 45206

TELEPHONE: 1-833-510-HELP (24 hours)

SPONSOR: Innovative Health Solutions

You are invited to participate in a medical research study. You are being asked to take part in this research study to learn more about the treatment of people like you who suffer from opioid withdrawal symptoms. Currently, there is very little known about how to effectively treat symptoms of opioid withdrawal without medications.

Your participation in this research study is strictly voluntary, meaning that you may or may not choose to take part. Please read this document carefully and ask any questions you may have before agreeing to be in the study. After reading the consent form, if you would like to participate, you will be asked to sign this form. You will be given a signed copy of your consent form to take home and keep for your records.

STUDY PURPOSE

The BRIDGE device (Innovative Health Solutions, Versailles, IN) is a new device that is approved by the United States Food and Drug Administration (FDA) for the symptoms of opioid withdrawal. It is considered a minimally invasive auricular (relating to the ear) device that is thought to significantly reduce pain and affect the autonomic nervous system. This device uses electrical stimulation of the external ear to allow access into central brain regions involved in fear and pain. In this study, the BRIDGE device will be compared to a “sham” device. The sham device will be identical in appearance to the active device but will have no electrical current. Neither you nor the study doctor/study staff will know whether you receive the BRIDGE or sham device during the study.

The purpose of the study is to determine if this new, FDA-cleared device is effective in reducing signs and symptoms of opioid withdrawal. This will be done by:

- Determining the severity of opioid withdrawal symptoms
- Assessing improvements in pain, craving and cognition

NUMBER OF PEOPLE TAKING PART IN THE STUDY AND DURATION

If you agree to participate, you will be one of 50 men and women age 18 to 60 years old, inclusive, who will be participating in this research study at Brightview treatment center. Your participation in this study will last approximately 5 days.

PROCEDURES FOR THE STUDY

The initial visit will involve procedures to determine if you are eligible for the study. If you are eligible and agree to participate, baseline assessments will be measured. The study doctor or study staff will explain the details and purpose of the study prior to you agreeing to participate during what is called informed consent. Once you have had enough time to consider participation, understand the risks and benefits and agree to participate, you will be asked to sign this Participant Informed Consent Form. Once you have signed the consent form, the following procedures will take place at this visit:

- You will be asked about your symptoms, current medications, surgeries, other medical issues and will review your past medical records. You will also be asked about the duration of opioid misuse and the types of medications or illicit drugs used.
- General information such as your age, race and sex will be collected.
- Medical information will be collected including height, weight, and vital signs (temperature, heart rate and blood pressure)
- The study doctor will perform a physical exam. The physical exam will not include a pelvic, rectal, or breast exam.
- The study doctor will conduct an assessment of the severity of opioid withdrawal symptoms as measured by the Clinical Opioid Withdrawal Scale (COWS).
- You will fill out questionnaires that include the visual analog scale (VAS) for pain (rating your pain questions on a 0-10 pain scale) and the opioid craving scale (rating your craving for opioids with 3 questions on a 0-10 scale). You will also do computer test known as cognitive function test called the CNS Vital Signs (The Stroop test). This test measures reaction time, attention and ability to think. The test takes approximately 5 minutes to complete. All the information collected will be kept in a secure database. The information you provide on the questionnaires will be kept strictly confidential, meaning nobody will know what you answered, except for the study team. There are no right or wrong answers to these questions. Being in this study is strictly your choice. You can choose not to answer questions that you don't feel comfortable answering. All the questionnaires should take a total of about 20-30 minutes total to complete. If you like, you can ask to have the questions read out loud to you and the questions filled out for you.

If you are eligible to participate and agree to continue, the study device (BRIDGE or sham) will be placed on you. You will be assigned by chance, like the flip of a coin, to receive wither the BRIDGE or the Sham device. You have an equal chance (50%) of receiving either the BRIDGE or the Sham. The study device contains a battery powered generator and four wire leads.

Neither you nor the study doctor will know whether you are receiving the BRIDGE or Sham device. However, the study doctor can find out in the case of a medical emergency.

The following procedures will take place during the study device placement:

- Your vital signs (temperature, heart rate and blood pressure) will be collected
- Your ear and the skin behind your ear will be cleaned with alcohol.
- The device stimulator will be attached behind your ear with a sticky adhesive strip.
- The device wires contain small needles that will be placed under the skin positioned on and near your ear. A round adhesive bandage will be placed over each electrode needle.
- A sticky adhesive strip will be placed over the device stimulator to help keep it in place.

After successful placement of the study device you will remain at the study clinic for at least two hours to receive your first dose of buprenorphine. The following procedures will take place one hour after placement of the study device:

- The study doctor will conduct an assessment of the severity of opioid withdrawal symptoms as measured by the Clinical Opioid Withdrawal Scale (COWS).
- You will be asked to fill out the visual analogue pain and craving scale
- You will complete an assessment of cognitive function (your ability to think) on the computer
- You will be given the first dose of buprenorphine with a starting dose of 2, 4 or 8 mg depending on what that study doctor thinks you need. This will be based on your needs for comfort and other factors such as your body mass index (BMI), your previous experience with the medication or level of anxiety about the process. No adjustments to this dose will be made for at least an hour after receiving the first dose, but the study doctor may order additional buprenorphine as indicated by the initial response, previous experience, the clinical opioid withdrawal scale (COWS) and BMI. Adjustments of the medication will be made based on the study doctor's discretion and your needs and comfort as per clinic standard. You will not receive ancillary (supportive) medications to help manage signs and symptoms of opioid withdrawal for one hour after the first dose of buprenorphine.

One hour after your first dose of buprenorphine, the following will be done:

- The study doctor will conduct an assessment of the severity of opioid withdrawal symptoms as measured by the Clinical Opioid Withdrawal Scale (COWS).
- You will be asked to fill out the visual analogue pain and craving scale
- You will complete an assessment of cognitive function (your ability to think) on the computer
- Symptom control medications including ibuprofen, clonidine, ondansetron, loperamide, and acetaminophen may be given depending on symptoms. A medication log will be provided to track medications usage.

You will need to keep the device on for 5 days regardless of whether you think it is an active or sham device. You will be asked to return to clinic for additional visits based on the clinic standard of care which will be Day 2 and in some cases Days 3 & 4

You will be sent home and monitored as outpatients and asked to return to clinic within 2-5 days. In order to monitor whether the BRIDGE device has any added benefit, you will be asked to fill out the same questionnaires and be assessed for the severity of opioid withdrawal symptoms as measured by the Clinical Opioid Withdrawal Scale (COWS) at each clinic visit during the 5-day study.

The study device will be removed at the clinic visit on Day 5 and disposed of in a sharp's container. If you cannot come back on day 5, you will be instructed to remove the device at home and bring it back at the next clinic appointment for proper disposal. In addition to study device removal, the following procedures will be done at this visit:

- The study doctor will conduct an assessment of the severity of opioid withdrawal symptoms as measured by the Clinical Opioid Withdrawal Scale (COWS).
- You will be asked about any symptoms and side effects you have experienced and about any changes to your medications.
- You will be asked to fill out the visual analogue pain and craving scale
- You will complete an assessment of cognitive function (your ability to think) on the computer

Overall, the study will not change the treatment that would normally be given to you to treat substance use disorder (SUD), with the exception of: 1) use of the Bridge device or sham for 5 days, 2) no buprenorphine during the first hour after device placement, and 3) no supportive medication the first hour after receiving buprenorphine.

POTENTIAL RISKS, SIDE EFFECTS, DISCOMFORTS, INCONVENIENCES

Some discomfort from the application of the study device is normal at first but should be reported if the discomfort persists or gets worse after a few minutes. You may feel a slight pulsing sensation or no sensation at all after electrodes are affixed. The pulsing sensation, if present, may disappear after approximately 5 minutes. If the discomfort level increases the needles can be slightly repositioned until your discomfort level decreases to an acceptable level.

You should not immerse the device in water as the device is water resistant but not water proof. If showering or washing your hair, place a dry wash cloth over the area to help protect the device.

It is possible that your withdrawal symptoms will not get better with the study device, especially since you could get one that is inactive. You will still get treatment with medications as needed.

The known risks/discomforts of the study device are listed below. There may be risks or discomforts to you, or if applicable your unborn or breastfeeding child, that are not known at this time.

Overall the risks/ discomforts involved are very minimal and have occurred rarely (in 1% to < 5% of participants).

Possible risks/discomforts may involve:

- Discomfort upon insertion of the electrodes for less than 5 minutes
- Discomfort at the lead placement site greater than 5 minutes
- Bleeding at the electrode site
- Localized discomfort if the electrodes should become dislodged during the wearing of the device
- Localized dermatitis (itchy inflammation of the skin)

- Drop in blood pressure
- Syncope (fainting)

In a recently completed research study using neurostimulation for functional abdominal pain disorders in adolescents, there were no serious adverse events. The rate of reported side effects was no different between the study device and placebo groups.

RISKS AND THE PRECAUTIONS WHICH WILL BE TAKEN TO MINIMIZE RISK EXPOSURE

All procedures will be performed by trained professionals within the standard of care under continuous medical supervision while in the outpatient clinic. COWS score ratings will be filled out by study staff as per standard of care. All participants will be carefully monitored. If any serious harm or discomfort is identified by the participant or the study personnel, the study device will be removed. Any patient with worsening or no improvement in symptoms who has a device placed during the study will be able to drop out at any time and receive standard of care medical therapy. The skin of the external ear will be carefully monitored for signs of irritation or infection.

POTENTIAL BENEFITS

There are possible immediate medical benefits to you if you decide to participate in this study. It is possible that the Bridge device may improve your symptoms of withdrawal. Currently, only medication therapies are available to treat acute opioid withdrawal. These medications are not always effective and often have side effects. If effective, this alternative approach using a device may provide an alternative treatment for opioid withdrawal and have a substantial impact on the wellbeing of patients, health care costs, morbidity and mortality.

NEW INFORMATION

You will be informed in a timely manner if new information that may influence your willingness to continue participation in the study becomes available.

ALTERNATIVES TO PARTICIPATING IN THE STUDY

You do not have to participate in this study to receive treatment for opioid withdrawal symptoms. You can choose not to participate in this study and receive standard of care medications or other alternative therapies.

COMPENSATION TO YOU

Patients will receive a $100.00 gift card to a local store as compensation for the time spent participating in the study. This will be given at the end of the study.

COSTS TO YOU

You will not be billed for the nerve stimulator device or placement. Your standard care, including buprenorphine and visit procedures, will be charged to your insurance company in the usual manner.

FINANCIAL INTEREST DISCLOSURE

This is an investigator-initiated study. The study doctor and Brightview will use funding from the sponsor for purposes of the study for which it was provided. At the completion of the study, the study doctor will confirm in writing that the support has been used only to support the activities of the study. The sponsor has agreed to pay Brightview $150,000 for fulfilling its duties related to this study. This includes a facility fee, participant stipends, and salary support for study staff. The study sponsor will provide Brightview with enough devices to complete the study at no charge with a minimum of 25 active and 25 sham devices.

VOLUNTARY PARTICIPATION/WITHDRAWAL

Your decision to participate is entirely voluntary. You may refuse to participate or withdraw from the study, at any time, without penalty or loss of benefits to which you are otherwise entitled. Your ongoing medical care will not be affected by your decision and your current and future relations with BrightView.

CONFIDENTIALITY AND AUTHORIZATION TO COLLECT, USE AND DISCLOSE YOUR MEDICAL INFORMATION

You will be assigned a unique identifying number which will be the only identifier listed on the questionnaires, device kits and data collection forms. Your identifying number and related electronic data will be kept on a secured, password-protected database that provides access only to the study doctor and study staff. Only authorized study staff will have access to the database. A separate secure database will have the subject identification number linked to your name. The BRIDGE devices will be shipped directly from the manufacturer to the study clinic. The devices will be stored in a locked room in the offices. The study staff will record that device was disposed of properly.

The health information being collected for this study is called “Protected Health Information” (PHI). It is protected by a federal law called the Privacy Rule of the Health Insurance Portability and Accountability Act (HIPAA). We cannot use your health information for research without your permission. If you do not give permission, you cannot be in this study. We will only use your information needed for this study. The only people allowed to see your information will be the people who work on the study and people who make sure the study is done the right way. Efforts will be made to keep your personal information confidential. Your personal information may be disclosed if required by law. Your identity will be kept confidential in reports in which the study may be published or presented at meetings.

A copy of this consent form will be stored in your medical record. We may also record your research information in your medical record. The information put in your medical record by the

study team may be seen by people allowed to see your medical records for healthcare, people that run the hospital or clinic, those you give written permission to see your medical records, and by others when required by law. Organizations that may inspect/or copy your research records for quality assurance and data analysis include groups such as the study doctor and staff at Brightview, the study sponsor, the U.S. Food and Drug Administration (FDA), and Sterling Institutional Review Board (IRB), who may need to access your medical and/or research records.

Your study information may be released to the groups listed above. If your study information is reviewed by these people, they may need to see your entire medical record; it is possible that your Social Security number may be included in the records reviewed. Because of this, it cannot be assured that your confidentiality will always be protected. It is possible that your information will be shared (re-disclosed) in a way that it would no longer be protected. However, this access to your records will be granted without violating your confidentiality to the extent permitted by applicable laws and regulations. By signing this form, you are authorizing this access to your records.

The results of the study, including your information, may also be presented at meetings or in articles written about the study (publications). If the results of the study (including your research or health information) are published, your identity will remain confidential.

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.

QUESTIONS

If you have questions, concerns or complaints about the research study, please contact Dr. Jeffrey Alan Craven (MD ABIM, ABAM DABPM) at (513) 403-4032 or (Dr. Samin Rezania (PhD) at 317-200-2805).

This research study has been reviewed by Sterling Institutional Review Board, whose purpose is to make sure the rights and welfare of participants are protected, and that risks are balanced by potential benefits. A member of this committee is available to speak to you if you have any questions, concerns, complaints about the research, would like information, or would like to offer input. They can be reached at, Sterling Institutional Review Board Regulatory Department, 6300 Powers Ferry Road, Suite 600-351, Atlanta, Georgia 30339 (mailing address), telephone number 1-888-636-1062 (toll free).

PARTICIPANT STATEMENT AND AUTHORIZATION

I have read or have had read to me the Participant Informed Consent Form and Authorization to Use and Disclose Medical Information and I give my consent to participate in this study. I will receive a signed copy of this form to keep for my records and all my questions have been answered. I have not waived any of my legal rights by signing this document.

_____
Printed Name of Participant

_____ _____
Signature of Participant Date

_____
Printed Name of Person Explaining Consent

_____ _____
Signature of Person Explaining Consent Date