INFORMED CONSENT FORM AND AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

For Adult Participants, Parents/Legal Guardians of Minor Participants and Minor Participants Who Reach the Age of Majority
And Assent for Minor Subjects 14 to Age of Majority

Sponsor / Study Title:	**The Division of Allergy, Immunology and Transplantation(DAIT),The National Institute of Allergy and Infectious Diseases (NIAID) / "Using the Cholinergic Anti-Inflammatory Pathway to treat Juvenile Idiopathic Arthritis"**
Protocol Number:	**AJA01**
Principal Investigator: (Study Doctor)	**«PiFullName»**
Telephone:	**«IcfPhoneNumber»**
Address:	**«PiLocations»**

The terms "you/yours" used in this form refers to you (if you are 14-18 years of age) or your child (if you are signing and dating this consent form for a child under the age of majority).

KEY INFORMATION

You are invited to take part in a research study. This research study is studying transcutaneous (tc, through the skin) vagal nerve stimulation (tcVNS) as a possible treatment for Juvenile Idiopathic Arthritis (JIA). This study is sponsored by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH). The study is being conducted through the Autoimmunity Centers of Excellence (ACE) network.

- This is a research study for people with active JIA
- Your participation is voluntary

- The study evaluates the safety and effectiveness of tcVNS on pain and inflammation (swelling) associated with JIA. tcVNS is administered with a study device that gives off mild electrical impulses through the skin to stimulate the vagus nerve (a nerve that travels underneath the skin in your neck and head). This stimulation triggers a chemical response through the nerves and has been found to be effective in reducing pain and inflammation in several diseases
- This will be a randomized (like flipping a coin), blinded (you will not know whether you are getting the actual stimulation or not), sham-controlled (sham-controlled means that the actual stimulation is not being used) study conducted for 16 weeks. The participants will be randomized to the study treatment group or sham group for the first 8 weeks followed by an open-label where all participants will receive the study treatment for the rest of the 8 weeks.
- The tcVNS technique is approved by the United States Food and Drug Administration (US FDA) for the treatment of epilepsy, chronic depression, along with use for tinnitus (ringing in the ears), chronic headaches, and pain. Positive effects in pain reduction and decreased inflammation have been reported in several autoimmune diseases, including Rheumatoid arthritis (RA), Crohn's Disease (CD), and Systemic lupus erythematosus (SLE). Decreased fatigue and measures of inflammation have been reported in a recent study for Sjogren's syndrome(SS)
- The technique or the study device has never been used and is not approved by the FDA for the treatment of JIA and its use in the study is investigational.
- Procedures, tests, and evaluations that will be done as part of this study and not as your routine clinic visit are,
    - Physical exam
    - Stimulation procedure for 5 minutes every day
    - Blood work
    - An electrocardiogram (ECG) records the electrical signals from your heart
    - Complete questionnaires and participate in assessments for JIA
    - Keep a diary about the study treatment and JIA symptoms
- The risks associated with tcVNS are experiencing a vibrating sensation during the stimulation and temporary local discomfort at the site of the stimulation. Mild skin irritation or mild redness like a sunburn in the area applied may occur. tcVNS administration should not be painful. Other possible risks are temporary lightheadedness and feeling faint and palpitations (sensation of irregular heartbeat) during tcVNS administration. Detailed information on the risks associated with the other study procedures is included under the section **Risks and Discomforts**
- You might not benefit from participating in this study. The information gathered from your participation will be helpful for the researchers to develop new treatment methods for JIA in future. See section **Benefits**
- There may be other treatments and research studies available for JIA.

Please read this form carefully. Take your time to ask the study doctor or study staff as many questions about the study as you would like. The study doctor or study staff can explain words or information that you do not understand. Reading this form and talking to the study doctor or study staff may help you decide whether to take part or not. If you decide to take part in this study, you must sign your name at the end of this form and date it. You will be given a copy of the signed form for your reference.

BACKGROUND AND PURPOSE

You are being asked to participate in this research study because you have JIA and your disease is active. JIA is a type of arthritis in children and teenagers which causes joint swelling and pain in the hands, knees, ankles, elbows, and wrists. Current treatments for JIA include steroids, pain relievers, and immunosuppressant medications. These medicines have been proven to control the disease activity and relieve symptoms, but are associated with side effects, some serious. These treatments result in effective control of the disease in only 1/3 of patients with JIA. For medications requiring intravenous infusion, in addition to the anxiety, this may cause a burden on children and parents having to miss time at school and work.

Researchers are trying to find effective non-drug therapies to treat JIA. If effective, tcVNS may offer an alternative to conventional treatments that is painless with few potential negative effects, easily administered at home, and with equipment that is inexpensive.

The AJA01 study is a randomized, blinded, sham-controlled study to test the safety and effectiveness of tcVNS in JIA. This technique and study device are experimental for use in JIA. The purpose of this research study is to evaluate the safety and effectiveness of tcVNS on pain and inflammation associated with JIA. tcVNS is administered with a study device that gives off mild electrical impulses through the skin to stimulate the vagus nerve. Part of the vagus nerve and its branches are located in the head and neck. For this study, the impulses will be administered in areas overlying the vagus nerve using a small electrode. The electrode helps to conduct the stimulation through the skin.

This stimulation triggers a chemical response through the nerves and has been found to be effective in reducing pain and inflammation in several diseases. The stimulation system is assembled from components (parts) that are cleared by the US FDA for transcutaneous electrical stimulation. tcVNS is approved by the FDA for the treatment of epilepsy, and chronic depression, along with use for tinnitus (ringing in the ears), chronic headaches, and pain. Positive effects in pain reduction and decreased inflammation have been reported in several autoimmune diseases, including Rheumatoid arthritis(RA), Crohn's Disease, and Systemic lupus erythematosus (SLE). Decreased fatigue and measures of inflammation have been reported in a recent study for SS. The treatment appears to have minimal risk.

The duration of your study participation is 16 weeks, involving 8 study visits to the clinic and 2 vists that may be via telehealth or in person at the clinic depending on your preference as described later in this form. If you decide to participate and are found to be eligible you will be randomly assigned (like a flip of a coin) to receive the active or control (sham) tcVNS for 5 minutes every day for the first 8 weeks. You will have a 50% (1 in 2) chance of receiving active study treatment and a 50% (1 in 2) chance of receiving the control (sham) study treatment This is called the blinded part of the study. For the second 8 weeks, everyone will be receiving the active tcVNS study treatment. You will be sent home with the equipment and instructions to perform after performing the first 5-minute stimulation at the first study visit.

You will continue to take your regular medications in stable doses for the study while participating in this study.

About 100 participants will be in this study at about 8-10 study sites in the United States.

WHAT WILL HAPPEN DURING THE STUDY?
You will be in this study for up to 16 weeks and will include 8 visits to the study center and 2 visits that may either take place via telehealth or in person at the study center depending on your preference.

If you choose to take part in this study, you will need to sign and date this consent form before we do any study procedures. This study is divided into three stages:

- Stage 1: Screening phase to see if you qualify for the study,
- Stage 2: Blinded study treatment phase; Group Assignment and study treatment with active or sham tcVNS for 8 weeks, and
- Stage 3: Open study treatment phase where everyone receives active study treatment for the last 8 weeks.

The study is randomized which means you will be assigned randomly (like a flip of a coin) to either the tcVNS active study treatment group or the control (sham) group for the first 8 weeks. There is a 50:50 chance you will be assigned to either group. For the second 8 weeks, everyone will receive the active tcVNS. tcVNS will be administered at the study visits and at home for 5 minutes every day. You will be sent home with the equipment and instructions after having the procedure demonstrated and you performing the first stimulation at the first study visit.

This study is also blinded which means neither you nor certain study staff members will know which group you are assigned to in the first 8 weeks. Randomization and blinding are ways to avoid any factors that can negatively influence the study results. There are study staff members who will not be blinded and who will be able to discuss any concerns you have with the stimulation procedure.

It is very important that the people participating in this study (study doctors, study nurses, participants) avoid making conclusions about the results of the study until the study is over. If you participate, we request you only discuss the study with your family members and with people close to you. You also should tell any health care providers who treat you that you are participating in this study. We ask that you not discuss the study and your experience with receiving tcVNS with other participants or people outside of the study. This includes discussing the information in public places such as social media or with others with JIA in a group chat or support group. We ask this to protect the quality of the study and what we are trying to learn.

Stage 1: Screening Phase
Once you have signed and dated this consent form, the screening phase of the study is started. This visit should take about 2 hours.

Medical History and Physical Exam: During the screening visit, you will be asked about your medical history, your JIA history, and any medications you may take. You will be given a full physical exam (including vital signs) at this visit.

Electrocardiogram (ECG): An ECG will be performed as part of the screening visit. An ECG test measures the rate and regularity of your heartbeat. Electrodes (sticky sensors attached to wires) are attached to your arms, legs, and chest to record the electrical activity of your heart.

Participant Reported Questionnaires: You will be asked to complete questionnaires about how you are feeling and how your JIA is affecting your life. These questionnaires should take approximately 15 to 20 minutes to complete.

Laboratory Tests: These lab tests will help us learn more about you overall health. About 1 tablespoon of blood will be needed for the tests. If you are able to have children (a female who has reached puberty), a urine pregnancy test will be done.

After all screening tests are complete and you qualify for the study, you will move to Stage 2 of the study. Unless necessary for your health we ask that you not change your JIA medications while participating in this study. Please talk with your study doctor before making any changes to medications.

Stage 2: Randomization to active or sham tcVNS
If you qualify for Stage 2, you will be assigned randomly (like flipping a coin, 50/50 chance) to receive either active or sham tcVNS. Below is a description of the stimulation study treatment and what to expect during the study visits and what you will do at home.

- The electrodes will be applied to your skin over an area where the vagus nerve travels in the head and neck. You will likely feel a sensation with the stimulation though you should not feel pain. The study staff will help you find the right dose for you. Please let the study staff know if it is uncomfortable or painful for you
- Heart rate and blood pressure will be repeated
- You will be given a chance to ask any questions related to the stimulation and show the study staff that you can operate the device correctly at home.
- You will take the study device home for the nerve stimulation, along with instructions and a diary

- You should not attempt to use the study device if you do not feel comfortable to operate the study device. Please consult the study staff
- You will be doing the stimulations for 5 minutes each day until the next visit and record the time and any problems you felt in the diary provided
- You are asked to not discuss the stimulation with any study staff or other participants other than the study staff who provide you instructions on performing the stimulation. You will be given head and neck coverings provided by the study staff which everyone will be asked to wear to all study visits. This is to keep the study doctor who is evaluating your JIA disease from knowing the location of the electrodes. There could be signs of tape or mild skin irritation from the electrodes. There will be a second study staff to talk freely with about any study treatment concerns or problems.

At each study visit you will also have the following:

- Physical exam: including exam of joints for active swelling, pain, redness, stiffness and vital signs
- Medical history and health status: including questions about all your medications, other medical problems, symptoms related to arthritis (such as morning stiffness and pain)
- Questionnaires: You will be asked to complete questionnaires about pain, well-being, fatigue and how arthritis affects your quality of life

At some of the study visits:

- Laboratory tests:
    - to check your general health and JIA disease status
    - For research to study your disease and the effects of tcVNS
    - If you are female and able to have a child then a urine pregnancy test will be performed

You will bring the study device and diary with you when you come to the clinic. You will perform the 5- minute stimulation at the study visit on the days you visit the study site. Please make sure you put on the head and neck coverings before you enter the clinic for the study visits. You will be requested at the end of stage 2 to complete a survey about the type of stimulation you thought you received.

These visits will take approximately 2 hours.

Stage 3: Open Study Treatment Phase

Everyone who completes stage 2 will move to stage 3 where everyone receives an active stimulation. The unblinded site coordinator will provide instructions on where to apply the electrodes on the site of stimulation and you will perform the stimulation similar to stage 2. All the other procedures remain the same as stage 2. The duration of these visits will be approximately 2 hours.

At the end of stage 3, you will return the study device and diary to the unblinded site staff.

In addition to these visits, you are asked to contact the study staff right away if you have health concerns or problems with the stimulation procedure. You may be asked to come in for an unscheduled study visit if thought necessary for your well-being.

Below is a schedule of the visits and procedures that you will have for all of the study visits:

	Screen	Blinded Study Treatment					Open Study Treatment				
Time Point	**Screening**	**Baseline**	**Day 2**	**Week 1**	**Week 4**	**Week 8**	**Day 57**	**Week 9**	**Week 12**	**Week 16**	**End of Study/ unscheduled Safety Visit**
Visit Number	**1**	**2**	**3***	**4**	**5**	**6**	**7***	**8**	**9**	**10**	
Physical Exam	X	X		X	X	X		X	X	X	X
Vital Signs	X	X		X	X	X		X	X	X	X
JIA Assessment	X	X		X	X	X		X	X	X	X
Participant Reported Questionnaires		X		X	X	X		X	X	X	X
ECG	X										
Clinical Labs	X	X			X				X	X	X
Research Labs		X				X				X	X
Diary				X	X	X		X	X	X	X
tcVNS daily for 5 minutes		X	X	X	X	X	X	X	X	X	
Survey						X					

*maybe performed as televisits

Collection and Storage of Samples/Information

For this research study, we collect, store, and use blood samples and study information (data).

The samples and data are used for research now and in the future. Information about you, including your biospecimens, collected for this study may be shared with other researchers. It may also be used for other research studies. We will make sure that your identity cannot be linked to the information we share. Results from the study and related health information are stored in a secure database. Details of how we plan to store and share the samples and data as well as how your identity is protected will be described later in this form. Also, at the end of this form, you are asked to consider allowing the storage of unused samples for future use which may not be directly related to this study.

The amount of blood and how often it is collected will meet safety guidelines for children and young adults as outlined by the NIH. This is based on your weight. You will not have more than about 1 teaspoon of blood for every 2 pounds of weight drawn in a single day, or more than about 1 teaspoon of blood for every pound of weight drawn over any eight-week period.

EXPECTATIONS

If you participate in this study, you will be expected to:

- Attend each visit
- Perform nerve stimulation as instructed
- Complete study diaries
- Contact study staff if you have new symptoms or worsening of your JIA symptoms

RISKS, SIDE EFFECTS, AND/OR DISCOMFORTS

The risks associated with tcVNS and the study procedures are described below.

tcVNS

The risks associated with tcVNS are experiencing a vibrating sensation at the area of the stimulation with possible local discomfort. Mild skin irritation or mild redness like a sunburn in the area applied may occur. tcVNS administration should not be painful. Other possible risks are temporary lightheadedness and feeling faint and palpitations (sensation of irregular hearbeat) during tcVNS administration. You should be sitting during the study treatment sessions to reduce the risk of feeling lightheaded or faint. You should report any concerns or any new problems to the study staff immediately.

There is a 50:50 chance you will be assigned to the group where the participants do not receive active study treatment for the first 8 weeks. There is a risk that the tcVNS may have no effect or even worsen your disease. If your JIA symptoms worsen, it is very important for you to let the study staff know of any problems.

RISKS OF STUDY PROCEDURES

Blood-Draw

It can be uncomfortable and can sometimes cause a bruise, bleeding, redness or swelling at the site. There is also a slight chance of infection. In rare cases, some people may faint during blood draw. Only trained study staff will draw your blood. Please let the study staff know if you develop any problems.

ECG

The sticky pads attached to your skin may cause mild irritation. You may be uncomfortable lying down during the test. The test itself is painless. If there are any irregular heartbeats, you will not be able to continue in the study.

Blinding and Randomization

There is a 50:50 chance you will be assigned to the group where the participants do not receive active study treatment for the first 8 weeks. There is a risk that the tcVNS may have no effect or even worsen your disease. If your JIA symptoms worsen, it is very important for you to let the study staff know of any problems.

Medication Management

We ask that you not change medications for your JIA unless necessary for your health if your disease worsens. Please discuss any potential changes to these medications with your study doctor beforehand if possible. Please inform the study staff right away for any concerns or any worsening in your JIA symptoms.

Urine collection for pregnancy testing

If you are a female and have reached puberty we will collect a urine sample for a pregnancy test at some of the visits as a precaution. There are no anticipated risks from urine collection.

Questionnaires

Some of the questionnaires could be lengthy and time-consuming. The questions about your health and health conditions could make you feel worried or anxious. You do not have to answer any questions that make you feel uncomfortable.

Loss of Confidentiality

The study staff will take every precaution to protect your identity. There are chances that people who are not authorized to have access may obtain your records. It is also possible there could be violations to the security of the computer systems used to store the codes linking your genetic and medical information to you. There may also be other privacy risks that we have not foreseen. We will make every effort to protect your confidential and potentially identifiable health information to the extent possible by law.

Genetic Testing

This research may include genetic tests. Genetic tests are laboratory tests that study your inherited (present from birth) characteristics which are present in each of your cells. Genetic tests study an individual's inherited characteristics, found in DNA, which is present in each of the cells of your body. DNA contains information needed to construct and operate the human body. Genetic tests can also study RNA. RNA is genetic material that reflects the genes that are being used by cells of your body. This research study will only look at your RNA, not whole chunks of DNA. Genetic testing may help researchers learn more about your disease or help to find treatments for your disease. As with all research tests, these results will not be shared with you. Please see section **future research studies** for additional information.

Genetic tests may reveal some future health conditions you and your family may develop. The information gained might be of interest to your employers or insurers. A federal law, the Genetic Information Nondiscrimination Act (GINA) prohibits health insurers from requesting or using genetic information and employment discrimination based on your health information. However, GINA does not address the denial of life insurance, disability insurance, or long-term care insurance for genetic conditions or diseases. GINA also does not protect you against discrimination based on an already diagnosed genetic condition or disease.

You will be informed of any new risks/side effects that may be identified during the study. Please ask your study doctor or the study staff to explain any procedures or risks that you do not understand.

UNFORESEEN RISKS
As with any research study, there might be side effects that are unknown at this time. You should report any concerns to the study staff.

BIRTH CONTROL RESTRICTIONS
The risks to a developing fetus or breastfeeding infant related to the study device is unknown at this time.

You cannot participate in this study if:

- You are currently pregnant or breast feeding.
- You plan to get pregnant in the next 18 weeks.

If you can get pregnant, a urine pregnancy test will be done several times during this study. If at any time you become pregnant, the tcVNS must be discontinued and it is important that you notify the study staff right away. The study doctor will explain that you and your partner must agree to use birth control throughout the course of the study if you are sexually active. You and your study doctor will discuss acceptable methods of birth control such as birth control pills, patch, intrauterine device (IUD), condom, sponge, diaphragm or avoiding sexual activity. If you become pregnant while participating in the study or if you have unprotected sex, it is very important to notify the study doctor immediately. If you become pregnant, the study staff will collect information about the pregnancy, its outcome, and the health of the child after birth.

ALTERNATIVES TO PARTICIPATION
The study doctor and/or study staff will talk with you about this study and other options available to you. You may choose not to be in this research study.

NEW FINDINGS
Any new important information that is discovered during the study and which may influence your willingness to continue participation in the study will be provided to you.

BENEFITS
If you agree to take part in this study, there may be no direct medical benefit to you. Information learned from this study may someday benefit people in the future.

COMPENSATION FOR PARTICIPATION
«Compensation»

You will be paid $ 25 for each study visit. If you do not complete the study, for any reason, you will be paid for each study visit you do complete.

If you have any questions regarding your compensation for participation, please contact the study staff.

CONFIDENTIALITY

Your medical and research records will be confidential to the extent permitted by law. Efforts will be made to keep your personal information private. However, we cannot guarantee complete confidentiality.

You will be identified by a code, and personal information from your records will not be released without your written permission. You will not be identified in any publication or in the sharing of your data about this study. After the study is completed, the data may be placed in a central storage location. These data will not include your name or other information that can identify you. The purpose is to make study data available to other researchers. Information from this study may be put into databases along with information from other studies. There are different kinds of databases; some are publicly accessible, and some are restricted. Anyone on the internet can access publicly accessible databases. Only researchers who apply and are approved can access restricted databases. Traditionally used identifying information about you (such as name, phone number, address) will NOT be included or shared with others.

Your privacy is important to us, and we will use safety measures to protect your privacy. Despite all the safety measures that we use, we cannot guarantee that your identity will never become known. Although your genetic information is unique to you, you share some genetic information with your children, parents, brothers, sisters, and other blood relatives. Consequently, it may be possible that genetic information from them could be used to help identify you. Similarly, it may be possible that genetic information from you could be used to help identify them.

While we will not use information that is traditionally used to identify you, people may develop ways in the future that would allow someone to link your genetic or medical information in our databases back to you. For example, someone could compare information in our databases with information from you (or a blood relative) in another database and be able to identify you (or your blood relative). It is also possible there could be violations to the security of the computer systems used to store the codes linking your genetic and medical information to you. There may also be other privacy risks that we have not foreseen.

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.

To make sure that the health information collected in this study is accurate, it will need to be checked from time to time against your medical records. Some persons may need to see these records in order to monitor the research and verify the accuracy of the study data, including:

- The National Institute of Allergy and Infectious Diseases, (NIAID), the sponsor of the research.
- NIAID representatives, agents, employees, contractors, and other persons assisting in conducting, monitoring, or analyzing the study.
- The research ethics review board – Advarra Institutional Review Board (IRB) (an independent ethics committee that reviewed the ethical aspects of this study to help protect the rights and welfare of study participants),

- Government regulatory authorities, such as the United States Food and Drug Administration (FDA)
- Other state and local health authorities

Certificate of Confidentiality
This research is covered by a Certificate of Confidentiality from the NIH. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research participants.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the study that is needed for auditing or program evaluation by the agency which is funding this study or for information that must be disclosed in order to meet the requirements of the US FDA. You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law of, for instance, child abuse or neglect, harm to self or others, and communicable diseases.

The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document.

Your study records including confidential information about you collected during the study will be kept at a secure location.

While every effort will be made to protect the privacy of your information, absolute confidentiality cannot be guaranteed. This does not limit the duty of the researchers and others to protect your privacy.

By signing and dating this information and consent form, you consent to the collection, access, use and disclosure of your information as described above.

COMPENSATION FOR INJURY
If you are injured or get sick while in this study, it is important to tell your study doctor listed on page one of this consent form. The study doctor may arrange to see you at the study site or may direct you to an emergency care center.

Emergency medical treatment will be available to you. The provider or hospital will bill you or your insurance company in the normal way for the cost of such care. No payment or additional compensation is available to you for such injuries. There is no provision for medical care or monetary compensation from the study sponsor, the NIAID/NIH. You do not lose any legal rights by signing and dating this form.

COSTS

Costs related to usual clinical care of your JIA or other medical problems will be billed to you and/or your insurance provider(s). The study device and all supplies needed to administer the tcVNS is being provided by the chair site, the Feinstein Institute for Medical Research (FIMR). Other clinical and professional services including diagnostic and laboratory tests that are a part of this study and not part of your regular care will be covered by the study.

FUTURE RESEARCH STUDIES

Information about you, including your biospecimens, collected for this study may be shared with other researchers. It may also be used for other research studies. We will make sure that your identity cannot be linked to the information we share. We will not ask you for additional permission before sharing the information.

We are asking your permission to store samples of blood collected during the study to be used in the future for tests that are not yet planned.

Your stored samples may be used to obtain knowledge about genetic information in relation to the immune system. Genetic tests study an individual's inherited characteristics, found in DNA, which is present in each of the cells of your body. DNA contains information needed to construct and operate the human body. Whole genome sequencing may be performed even though it is not planned for this study.

The results of tests performed on stored samples or reports resulting from the analysis of your samples will not be given to you or your doctor and they will not be put in your medical record. They will not identify you and will not affect your routine medical care.

There is no benefit to you from the storage of samples and information. However, the use of your samples and information may help researchers learn more about your disease or the genetics related to a specific condition. The purpose of storage and sharing data is to make information available for use in health research and to share what is stored with other researchers. Collecting, storing, sharing information, and making it available for other studies may help people in the future. Coded information put into databases together with other stored information from many studies conducted in different places allows researchers to study the combined information and learn even more about health and many different diseases.

Samples will be stored at Boaz Biorepository at the Feinstein Institutes, New York if you decide to allow storage, your samples and information may be stored for an unknown length of time.

There may be unknown risks associated with the storage of samples and information. For example, if future research involves genetic testing it is possible that it could be traced back to you because your genes are specific to you. We will make every attempt to protect your confidentiality and to make sure that your personal identity does not become known.

You can change your mind at any time and ask to have your samples destroyed. This request should be made in writing to the study doctor. If you make this request, all remaining stored samples will be destroyed. However, the results of any previous tests using your stored samples will be used. Your decision regarding the storage of samples or the information resulting from the analysis of your samples will not affect your ability to participate in this study. The future use of your samples and information may contribute to learning more about disease or help to study the genetics related to a specific condition.

COMMERCIAL PROFIT

Although your stored research samples will not be sold, the information obtained from the research performed on your samples may in the future lead to the development of commercial products. You will not receive any money from research using your stored samples and information.

CLINICALLY RELEVANT RESULTS

During the study testing, unexpected (not study-related) information is learned that would be important for your wellbeing, you will be informed. Counseling will be provided on next steps to take. The study will not cover the costs for related follow-up outside of this study.

GENOME SEQUENCING

Researchers can look closely at large amounts of your genetic information by sequencing, or "reading," every letter in your DNA (your genome). Reading a person's entire genetic code is called whole genome sequencing. The research may include whole genome sequencing (for example, sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen) in the future. Samples are being collected and may be used in the future to look at variations in your genes that may influence the response to the vagus nerve stimulation. This study looks at the RNA transcribed from the DNA to look at whether gene expression changes with the vagus nerve stimulation.

Please indicate your response below:

I agree to the storage and sharing of samples (urine, blood) for genetic tests not currently planned.

☐ **Yes** ☐ **No**

_____

Initials of Adult Research Participant

☐ **Yes** ☐ **No** _____

Initials of Parent/Legal Gurdian of Minor Participant

I agree to the storage and sharing of samples (urine, blood) and information resulting from the analysis of my samples for other tests not currently planned.

☐ **Yes** ☐ **No**

_____

Initials of Adult Research Participant

☐ **Yes** ☐ **No** _____

Initials of Parent/Legal Gurdian of Minor Participant

WHOM TO CONTACT ABOUT THIS STUDY

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study such as:

- Whom to contact in the case of a research-related injury or illness;
- Payment or compensation for being in the study, if any;
- Your responsibilities as a research participant;
- Eligibility to participate in the study;
- The study doctor's or study site's decision to exclude you from participation;
- Results of tests and/or procedures;

Please contact the study doctor at the telephone number listed on the first page of this consent document.

If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research participants. If you have any questions about your rights as a research participant, contact:

- By **mail**:
  Study Subject Adviser
  [redacted]
- or call **toll free**: [redacted]
- or by **email**: [redacted]

Please reference the following number when contacting the Study Subject Adviser: [redacted]

VOLUNTARY PARTICIPATION / WITHDRAWAL

Your decision to participate in this study is voluntary. You may choose to not participate, or you may withdraw from the study for any reason without penalty or loss of benefits to which you are otherwise entitled and without any effect on your future medical care. However, please note that the FDA requires that any information collected up to the point of your withdrawal cannot be removed from the study.

If you are willing, the study staff would like for you to return to the study site for a final visit for a safety evaluation and to collect the study equipment.

You should talk to your study doctor who will discuss future treatment and procedures for your continued care.

The study doctor or the sponsor can stop your participation at any time without your consent for the following reasons:

- If it appears to be medically harmful to you;
- If you fail to follow directions for participating in the study;
- If it is discovered that you do not meet the study requirements;
- If the study is canceled; or
- For administrative reasons.

If you are removed from the study, your study doctor will contact you to discuss stopping the tcVNS and the plan for your return to the study site for follow-up procedures required for your safety and to evaluate the effects of the tcVNS.

PRIMARY HEALTH CARE PROVIDER NOTIFICATION OPTION

I consent to having my family doctor or primary health care provider notified by the study site of my participation in this study and/or any significant findings related to my health (please check yes or no).

❒**YES** (If yes, please complete the information below)
❒**NO**

Name and address of family doctor or primary health care provider:	Name: Address:
Telephone and Fax Number:	Tel: Fax:

FUTURE CONTACT

May we contact you by phone to find out if you are interested in hearing about new research studies or to ask you about how your current health is? Contact would be made by the lead study doctor's staff. If you decide at any time that you no longer want to be contacted, please tell us, and we will stop calling you.

Would you like us to contact you about future research studies or to ask you about how your current health is?

☐ **Yes** ☐ **No** _____

Initials of Adult Research Participant

☐ **Yes** ☐ **No** _____

Initials of Parent/Legal Gurdian of Minor Participant

If you say "no" to this question, this will not affect your participation in this study.

CONSENT

I have read and understand the information in this informed consent document. I have had an opportunity to ask questions and all of my questions have been answered to my satisfaction. I voluntarily agree to participate in this study until I decide otherwise. I do not give up any of my legal rights by signing and dating this consent document. I will receive a copy of this signed and dated consent document.

For Minor Participants Ages 14 to the age of majority:

_____	_____	_____
Printed Name of Participant (Typed or Printed)	**Participant's Signature**	**Date**

For Parent/Legal Guardian of Minor Participants:

_____	_____	_____
Parent Name (If applicable; typed or printed)	**Participant Parent's Signature**	**Date**

_____	_____	_____
Research Participant's Name (Typed or printed)	**Research Participant's Signature**	**Date**

Signature of person explaining and obtaining the consent:

_____	_____	_____
Name and Title (Typed or printed)	**Signature**	**Date**

WITNESS SIGNATURE FOR PARTICIPANTS WHO CANNOT READ

The study participant has indicated that he/she is unable to read. The consent document has been read to the participant by a member of the study staff, discussed with the participant by a member of the study staff, and the participant has been given an opportunity to ask questions of the study staff.

_____

Printed Name of Impartial Witness

_____ _____

Signature of Impartial Witness **Date**

FOR CHILDREN WHO BECOME ADULTS

I have been told that my parents/legal guardian agreed for me to participate in this research study as a minor. I have read and understand the information in this informed consent document. I have had an opportunity to ask questions and all of my questions have been answered to my satisfaction. I voluntarily agree to continue to participate in this study until I decide otherwise. I do not give up any of my legal rights by signing and dating this consent document. I will receive a copy of this signed and dated consent document.

_____

Participant's Printed Name

_____ _____

Participant's Signature **Date**

AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

If you decide to be in this study, the study doctor and study staff will use and share health data about you to conduct the study. Health data may include:

- Your name.
- Address.
- Phone number.
- Date of birth.
- Medical history.
- Information from your study visits, including all test results.

Health data may come from your study records or from existing records kept by your doctor or other health care workers.

For this study, the study staff may share health data about you with authorized users. Authorized users may include:

- Representatives of the National Institute of Allergy and Infectious Diseases (NIAID).
- Representatives of Advarra IRB (an Institutional Review Board that reviews this study).
- The Food and Drug Administration (FDA) and other US federal and state agencies.
- Government agencies to whom certain diseases (like HIV, hepatitis, and STDs) must be reported.
- Outside individuals and companies, such as laboratories and data storage companies, that work with the researchers and sponsor and need to access your information to conduct this study.
- Other research doctors and medical centers participating in this study, if applicable.
- A data safety monitoring board which oversees this study, if applicable.

Your health data will be used to conduct and oversee the research, including for instance:

- To see if the study device works and is safe.
- For other research activities related to the study device.

Once your health data has been shared with authorized users, it may no longer be protected by federal privacy law (Health Insurance Portability and Accountability Act [HIPAA]) and could possibly be used or disclosed in ways other than those listed here.

Your permission to use and share health data about you will end in 50 years unless you revoke it (take it back) sooner.

You may revoke (take back) your permission to use and share health data about you at any time by writing to the study doctor at the address listed on the first page of this form. If you do this, you will not be able to stay in this study. No new health data that identifies you will be gathered after your written request is received. However, health data about you that has already been gathered may still be used and given to others as described in this form.

Your right to access your health data in the study records will be suspended during the study to keep from changing the study results. When the study is over, you can access your study health data.

If you decide not to sign and date this form, you will not be able to take part in the study.

STATEMENT OF AUTHORIZATION

I have read this form and its contents were explained. My questions have been answered. I voluntarily agree to allow study staff to collect, use and share my health data as specified in this form. I will receive a signed and dated copy of this form for my records. I am not giving up any of my legal rights by signing and dating this form.

For Parent/Legal Guardian of Minor Participants:

_____	_____	_____
Parent Name (If applicable; typed or printed)	**Participant Parent's Signature**	**Date**

For participants the age of majority and above:

_____	_____	_____
Research Participant's Name (Typed or printed)	**Research Participant's Signature**	**Date**

Signature of person explaining and obtaining the consent:

_____	_____	_____
Name and Title (Typed or printed)	**Signature**	**Date**

WITNESS SIGNATURE FOR PARTICIPANTS WHO CANNOT READ

The study participant has indicated that he/she is unable to read. This Authorization document has been read to the participant by a member of the study staff, discussed with the participant by a member of the study staff, and the participant has been given an opportunity to ask questions of the study staff.

_____

Printed Name of Impartial Witness

_____	_____
Signature of Impartial Witness	**Date**

FOR CHILDREN WHO BECOME ADULTS

I have been told that my parents/legal guardian agreed to the use and disclosure of my Protected Health Information as outlined in this document. I have read and understand the information in this authorization. I have had an opportunity to ask questions and all of my questions have been answered to my satisfaction. I continue to authorize the use and disclosure of my Protected Health Information. I will receive a copy of this signed and dated authorization.

_____

Participant's Printed Name

_____ _____

Participant's Signature **Date**