UNIVERSITY OF PENNSYLVANIA
RESEARCH SUBJECT
INFORMED CONSENT AND HIPAA AUTHORIZATION FORM

Protocol Title: An prospective, randomized, dual-controlled, crossover study to evaluate the effectiveness of the Intranasal Tear Neurostimulator in acute tear production in patients with Sjögren's Syndrome and dry eye disease

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Why am I being asked to volunteer?

You are being invited to participate in a research study. You are being asked to participate in this study because you have been diagnosed with Sjögren's syndrome and dry eye disease. Your participation is voluntary which means you can choose whether or not you want to participate. If you choose not to participate, there will be no loss of benefits to which you are otherwise entitled. Before you can make your decision, you will need to know what the study is about, the possible risks and benefits of being in this study, and what you will have to do in this study. The research team is going to talk to you about the research study, and they will give you this consent form to read. You may also decide to discuss it with your family, friends, or family doctor. You may find some of the medical language difficult to understand. Please ask the study doctor and/or the research team about this form. If you decide to participate, you will be asked to sign this form.

What is the purpose of this research study?

Allergan has developed an FDA approved device for the treatment of dry eye disease. The intranasal tear neurostimulator device (ITN) is inserted into the nasal passages and provides stimulation to the mucosal nerves within the lacrimal reflex pathway, increasing acute tear production. An instructional brochure and FAQ's provided by Allergan are included at the end of this consent form for your review. This device has been shown to help with symptomatic relief and objective signs of ocular surface disease in patients with dry eye disease without Sjögren's syndrome and is FDA approved for these patients. The ITN device has not been specifically studied in patients with Sjögren's syndrome.

IRB Approval From: 11/19/2018 to 08/15/2019

Therefore, the purpose of this study is to evaluate whether the device is effective in patients with both Sjögren's syndrome and dry eye disease.

This form will provide you with more information about the study. Thank you for reading this document carefully. If you are unable to read, please have it read to you.

How long will I be in the study?

Your participation will involve 1-2 study visits. This first visit will take up to two hours to determine your eligibility to join the study. This will consist of collecting your medical history, reviewing your medications, answering questionnaires, checking your vision, examining your eyes, and undergoing a Schirmer test before and during nasal stimulation with a cotton swab. Women of childbearing potential will also need to perform a urine pregnancy test.

If you are determined to be eligible based on the results of the first visit, we will ask you to return for a second study visit that will also take up to two hours. At this visit, you will first learn how to use the device, your medications will be reviewed, your vision will be checked, and your eyes will be examined. You will then undergo two Schirmer tests, 60 minutes apart, once with the ITN applied intranasally, and once with it applied extranasally. After each test, your vision and eyes will be checked.

How many other people will be in the study?

This study will be conducted in one clinic (University of Pennsylvania/Scheie Eye Institute) and will recruit approximately 40 patients for the study.

What am I being asked to do?

Over the entire study period, you will need to come to the clinic for 2 study visits on 2 separate days.

Screening Visit (All Participants) – At the first study visit, the study team will confirm your eligibility to join the study. This will consist of:

- **Questionnaires** – complete several questionnaires that will help us determine the severity of your dry eye symptoms. These questionnaires should take approximately 5 minutes to complete.
- **Distance Visual Acuity Test** – Your vision will be checked by assessing your ability to see letters of various sizes on a chart. Checking your vision will take approximately 5 minutes to complete.
- **Eye Exam** – The study doctor will perform an examination of your eyes to note any abnormalities that may be present. This examination will take approximately 10 minutes to complete.
- **Schirmer Test with Topical Anesthesia** – This test will be performed to determine how well your eyes produce tears. It involves putting numbing drops in each eye and then placing a small strip of filter paper under your eyelid. After 5 minutes, the paper will be removed and the amount of moisture on the paper will be measured.
- **Schirmer Test with Cotton Swab Nasal Stimulation** – The Schirmer test will be repeated, but this time it will be done will cotton swabs inserted into each nostril to see how tear production changes with nasal stimulation. Again, numbing drops will be put in each eye and then a small

strip of filter paper will be placed under your eyelid. Once the strips are in place, cotton swabs will be gently inserted into each nostril and pressure will be applied to your nasal cavity during the duration of the test. After 5 minutes, the paper and cotton swabs will be removed and the amount of moisture on the paper will be measured.

- **Pregnancy test** – Women who are able to have children will be asked to complete a urine pregnancy test at their first visit. A urine pregnancy test takes approximately 5 minutes to complete. To take part in this study, women who are able to have children and who are sexually active must use an effective means of birth control throughout the study. The study staff will discuss with you what acceptable methods of birth control can be used to prevent pregnancy while participating in this trial. If you are pregnant or planning to have a baby during the time you participate in this study, you should not participate in this study. However, if you do become pregnant during the study, notify your study eye care provider immediately.

Application Visit (Eligible Participants) – Eligible participants will be invited back for a second visit, which will consist of:

- **Distance Visual Acuity Test** – Your vision will be checked by assessing your ability to see letters of various sizes on a chart. Checking your vision will take approximately 5 minutes to complete and will be repeated after each application of the ITN device.
- **Eye Exam** – The study doctor will perform an examination of your eyes to note any abnormalities that may be present. This examination will take approximately 10 minutes to complete and will be repeated after each application of the ITN device.
- **Schirmer Test with Intranasal Tear Neurostimulation Device** – The Schirmer test will be performed twice at the Application visit, each one hour apart. During the tests, numbing drops will be put in each eye and then a small strip of filter paper will be placed under your eyelid. Once the strips are in place, the ITN device will be applied either intranasally or extranasally for the first 3 minutes of the 5-minute test. After an hour, the test will be repeated, but the ITN device will be applied the opposite of the previous test. So, if the first time it is applied extranasally, during the second test it will applied intranasally. If the first time it is applied intranasally, during the second test it will be applied extranasally. You will be trained on how to correctly apply the device before each test.

If you participate in this study, what will you be expected to do?

- Come to the clinic for all scheduled visits as requested by the study staff.
- Allow all study procedures and tests to be performed unless there is a medical reason for not doing so.
- Notify the study doctor of any illnesses or injuries, unexpected or troublesome side effects, or problems that occur during the study via the telephone immediately.
- Continue any routine medical care with the doctor(s) who look after these conditions for you, since being in the study does not take the place of regular medical care.

What are the possible risks or discomforts?

Your participation in this study involves some risks and possible discomfort:

- There have been no serious adverse events reported in connection with use of cotton swab nasal stimulation or the ITN device. Rare mild adverse events including sneezing, nasal itching and transient lightheadedness have been reported.
- Numbing drops will be put in your eye for the Schirmer test. The drops may cause redness of the eye, tearing or stinging, blurred vision, or feeling faint or dizzy.
- All examinations and procedures that you will be performing during the trial, with the exception cotton swab nasal stimulation, are routinely performed; no experimental examinations or procedures, except cotton swab nasal stimulation, are foreseen in this trial. These examinations and procedures may be performed as often if you do not participate in this study and follow the standard of care.

If new findings that would affect your safety come up while you are in the study, you will be told as soon as possible so you can decide whether to continue or leave the study.

What if new information becomes available about the study?

During the course of this study, we may find more information that could be important to you. This includes information that, once learned, might cause you to change your mind about being in the study. We will notify you as soon as possible if such information becomes available.

What are the possible benefits of the study?

You are not expected to get any benefit from being in this research study. However, others may benefit in the future from the knowledge gained by this study.

What other choices do I have if I do not participate?

There are approved medical or surgical treatments for patients with dry eye, such as Restasis (cyclosporine), a topical eye drop which has been available for several years or Lifitegrast (Xiidra), a topical eye drop which was just approved by the FDA and punctual plugs which is a small medical device that is inserted into the tear duct to prevent drainage of liquid form the eye.

You do not have to participate in this study to receive treatment for your condition. If you do not participate in this study, you may still receive other types of treatment including other experimental or surgical options that your personal physician feels are appropriate.

Your personal physician or the study doctor can discuss other potential options with you and answer any questions you have about other treatments.

You should also contact your personal physician to inquire about other research currently being conducted for the treatment of dry eye.

Will I be paid for being in this study?

If you agree to take part in this research study, we will pay you $50 in appreciation of you making the effort to complete the visit. You will also receive a free parking voucher for the parking lot at Scheie Eye Institute for each of your study visits.

In order to be compensated for your participation in this study, you must provide your Social Security Number. Additionally, please note that the University of Pennsylvania is required to report to the Internal Revenue Service (IRS) any cumulative payments for participation in research studies that exceed a total of $600 in a calendar year.

Will I have to pay for anything?

The study device and disposable intranasal tips are provided at no cost to you, and you will not be charged for any doctor's visits or procedures that are needed for the study.

You are still responsible for any deductibles or applicable co-pays for routine office visits. Please talk to your doctor and study team about putting you in touch with a financial counselor to determine exactly what the deductible and co-pay will be for you; this is highly variable depending on your type of insurance.

What happens if I am injured from being in the study?

If you think you have been injured as a result of taking part in this research study, tell the person in charge of the research study as soon as possible. The researcher's name and phone number are listed in the consent form.

We will offer you the care needed to treat injuries directly resulting from taking part in this research. We may bill your insurance company or other third parties, if appropriate, for the costs of the care you get for the injury, but you may also be responsible for some of them.

There are no plans for the University of Pennsylvania to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this form.

If you have an illness or injury during this research trial that is not directly related to your participation in this study, you and/or your insurance will be responsible for the cost of the medical care of that illness or injury.

Neither financial compensation nor reimbursement for such things as pre-existing conditions, illnesses or diseases totally unrelated to the study, lost wages, property damage, disability, or discomfort is available. It is your obligation, if you feel impaired in any way (or if you feel your vision is impaired in any way), to stop activity that may cause injury to yourself, to any other person, or to property as a result of participating in this study (e.g., driving a vehicle, operating machinery, climbing a ladder).

You or insurance company will be responsible for payment for any tests or care done outside of the scope of the study.

When is the Study over? Can I leave the Study before it ends?

This study is expected to end after all participants have completed all visits, and all information has been collected. This study may also be stopped at any time by your physician, the study Sponsor, or the Food and Drug Administration (FDA) without your consent because:

- The Principal Investigator feels it is necessary for your health or safety. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.
- You have not followed study instructions.
- The Sponsor, the study Principal Investigator, or the Food and Drug Administration (FDA) has decided to stop the study.

If you decide to participate, you are free to leave the study at any time. Withdrawal will not interfere with your future care.

Who can see or use my information? How will my personal information be protected?

We will do our best to make sure that the personal information obtained during the course of this research study will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used. If this study is being overseen by the Food and Drug Administration (FDA), they may review your research records.

If you join the study, some parts of your medical records, consent form and the data collected for the study will be looked at by authorized persons from the company sponsoring and/or the company organizing the research. They may also be looked at by representatives of Regulatory Authorities and by authorized representatives from the Clinic, and/or the FDA (The Food and Drug Administration) to check that the study is being carried out correctly. All will have a duty of confidentiality to you as a research participant and we will do our best to meet this duty.

All information which is collected about you during the course of the research will be kept strictly confidential, and any information about you which leaves the hospital/surgery will have your name and address removed so that you cannot be recognized. The published trial results will not include information that can identify you.

Information from this study will be submitted to Allergan and to the FDA.
Your GP may be informed of your participation in this study.

A brief description of this clinical study 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 of this study. You can search this web site at any time.

Electronic Medical Records and Research Results

What is an Electronic Medical Record?

An Electronic Medical Record (EMR) is an electronic version of the record of your care within a health system. An EMR is simply a computerized version of a paper medical record.

If you are receiving care or have received care within the University of Pennsylvania Health System (UPHS) (outpatient or inpatient) and are participating in a University of Pennsylvania research study, results of research-related procedures (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your existing EMR maintained by UPHS.

If you have never received care within UPHS and are participating in a University of Pennsylvania research study that uses UPHS services, an EMR will be created for you for the purpose of maintaining any results of procedures performed as part of this research study. The creation of this EMR is required for your participation in this study. In order to create your EMR, the study team will need to obtain basic information about you that would be similar to the information you would provide the first time you visit a hospital or medical facility (i.e. your name, the name of your primary doctor, the type of insurance you have). Results of research procedures performed as part of your participation in the study (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in this EMR. Once placed in your EMR, these results are accessible to appropriate UPHS workforce members that are not part of the research team. Information within your EMR may also be shared with others who are determined by UPHS to be appropriate to have access to your EMR (e.g. Health Insurance Company, disability provider, etc).

What information about me may be collected, used or shared with others?

Information from this study may be used or shared with others. This may include, for example, information in the medical record, results of physical examinations, medical history, lab tests, or protected health information such as name, address or social security number, e.g.,

- Name, address, telephone number, date of birth
- Social Security number
- Personal and family medical history
- Results from a physical examinations tests or procedures
- Medical record number
- Email address

Why is my information being used?

Your information is used by the research team to contact you during the study. Your information and results of tests and procedures are used to:

- do the research
- oversee the research
- to see if the research was done right
- to evaluate and manage research functions.

Who may use and share information about me?

The following individuals may use or share your information for this research study:

- The Investigator for the study and the study team
- Other authorized personnel at Penn

Who, outside of the School of Medicine, might receive my information?

- Those working under the direction of Dr. Massaro for the study,

- All research centers participating in the study, even if they are not part of the School of Medicine
- Oversight organizations
- The Food and Drug Administration
- The Office of Human Research Protections

Once your personal health information is disclosed to others outside the School of Medicine, it may no longer be covered by federal privacy protection regulations.

The Principal Investigator or study staff will inform you if there are any additions to the list above during your active participation in the trial. Any additions will be subject to University of Pennsylvania procedures developed to protect your privacy.

How long may the School of Medicine use or disclose my personal health information?

Your authorization for use of your personal health information for this specific study does not expire. Your information may be held in a research database. However, the School of Medicine may not re-use or re-disclose information collected in this study for a purpose other than this study unless:

- You have given written authorization
- The University of Pennsylvania's Institutional Review Board grants permission
- As permitted by law

Can I change my mind about giving permission for use of my information?

Yes. You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the Investigator for the study. If you withdraw your permission, you will not be able to stay in this study.

What if I decide not to give permission to use and give out my health information?

Then you will not be able to be in this research study. You will be given a copy of this Research Subject HIPAA Authorization describing your confidentiality and privacy rights for this study. By signing this document, you are permitting the School of Medicine to use and disclose personal health information collected about you for research purposes as described above.

Who can I call with questions, complaints or if I'm concerned about my rights as a research subject?

If you have questions, concerns or complaints regarding your participation in this research study or if you have any questions about your rights as a research subject, you should speak with the Principal Investigator listed on page one of this form. If a member of the research team cannot be reached or you want to talk to someone other than those working on the study, you may contact the Office of Regulatory Affairs with any question, concerns or complaints at the University of Pennsylvania by calling (215) 898-2614.

When you sign this form, you are agreeing to take part in this research study. This means that you have read the consent form, your questions have been answered, and you have decided to volunteer. Your signature also means that you are permitting the University of Pennsylvania to use your personal health information collected about you for research purposes within our institution. You are also allowing the University of Pennsylvania to disclose that personal health information to outside organizations or people involved with the operations of this study.

A copy of this consent form will be given to you.

_____	_____	
Name of Subject (Please Print)	Signature of Subject	Date

_____	_____	
Name of Person Obtaining Consent (Please Print)	Signature	Date