Title: Topiramate for Cryptogenic Sensory Peripheral Neuropathy in Metabolic Syndrome (CSPN)

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Subject Identification

Protocol Title: NN108 Topiramate as a disease modifying therapy for Cryptogenic Sensory Peripheral Neuropathy in Metabolic Syndrome (CSPN)

Protocol Principal Investigator: A. Gordon Smith, MD

Site Principal Investigator: Kelly Gwathmey, MD

NeuroNEXT Clinical Study Site: Virginia Commonwealth University

Description of Subject Population: Patients with CSPN (idiopathic neuropathy)

About this consent form

Please read this form carefully. It tells you important information about a research study. A member of our research team will also talk to you about taking part in this research study. People who agree to take part in research studies are called "subjects." This term will be used throughout this consent form.

Virginia Commonwealth University (VCU) is where all study visits will take place. We are doing this research as part of the NeuroNEXT Network for Excellence in Neuroscience Clinical Trials (NeuroNEXT), which is supported by the National Institute of Neurological Disorders and Stroke (NINDS).

If you have any questions about the research or about this form, please ask us. Taking part in this research study is up to you. If you decide to take part in this research study, you must sign this form to show that you want to take part. We will give you a signed copy of this form to keep.

Why is this research study being done?

We are doing this study to learn if the drug topiramate slows the progression of Cryptogenic Sensory Peripheral Neuropathy (CSPN) (also known as "idiopathic neuropathy"), and improves quality of life. As part of this study, we will use a number of assessments and questionnaires to determine if topiramate improves symptoms of CSPN.

Topiramate is approved by the U.S. Food and Drug Administration (FDA) for the treatment of epilepsy and migraines; however, it is not approved for the treatment of CSPN. This means that topiramate can be used in research studies such as this to help determine if it will increase your quality of life and slow the progression of your disease.

We are asking you to take part in this research study because you have Cryptogenic Sensory Peripheral Neuropathy (CSPN) and Metabolic Syndrome.

This study will compare topiramate to placebo. The placebo looks like the study drug, topiramate capsules, but contains no active study drug. You will have a 1 out of 2 chance of being assigned to topiramate. You will have a 1 out of 2 chance of being assigned to placebo. Placebos are used in research studies to see if the results are due to the study drug or due to other reasons.

The study will be conducted by the NeuroNEXT Network for Excellence in Neuroscience Clinical Trials (NeuroNEXT) at 20 sites around the United States. About 210 subjects will take part in this research study. About 125 subjects will be randomized/treated. About 10 subjects will take part in the study at VCU.

The National Institutes of Health (NIH) is paying for this study to be done.

A description of this clinical trial will be available on the website http://www.clinicaltrials.gov as required by U.S. Law. This website will not include information which can identify you. At most, the website will include a summary of the study requirements and the study results when it has ended. You can search this website at any time.

How long will I take part in this research study?

It will take about two years to complete this study. The screening period may last up to 4 weeks. We will ask you to make a number of study visits to VCU. Following the Screening Visit, we will ask you to return for a Baseline Visit and 6 Study Visits every 16 weeks: Weeks 16, 32, 48, 64, 80 and 96.

What will happen in this research study?

If you choose to take part in this research study, we will ask you to sign this consent form before we do any study procedures. If you agree to participate in this study, you should not enroll in any other research studies involving drugs or devices while you are in this study.

Study Procedures and Visits:
The first visit will be the Screening Visit and the study doctor(s) will determine if you are eligible to participate in this research study. If you don't qualify, the study doctor will tell you why.

Assignment to a Study Group and Taking the Study Drug:

We will assign you by chance (like a coin toss) to receive either topiramate or placebo. You will have a 1 in 2 chance of being assigned to the topiramate group and a 1 in 2 chance of being assigned to the placebo group.

Neither you nor the study doctor will know which group you are in, but the study doctor can find out if necessary. We will refer to both topiramate and placebo as 'study drug' from here on in the consent form.

The target dose level of topiramate for this study is 100 mg daily. Topiramate is a small pill that you should take with food and water. You will start by taking a small dose and working up to a higher dose to help reduce the risk of side effects. You will begin by taking 25 mg once daily in the evening. On the fourth day, a morning dose of 25 mg will be added. On the eighth day, an additional 25 mg will be added to the evening bringing the total to 50 mg. On the twelfth day, 25 mg will be added to the morning, bringing the total to 50 mg twice daily.

Topiramate Blood Testing:

Blood testing will be performed to measure levels of study medication at 4 visits. You will be asked to take your morning dose of study medication AFTER your blood draw at week 32, 64, and 96. You and the study doctor will not be informed of these test results.

Screening Visit:

This visit will take about 4 hours. At this visit, we will:

- Obtain written consent from you.
- Obtain your medical, family and neurological history to make sure you can participate in this study.
- Review your medications, including all nutritional, herbal and alternative therapies.
- Perform a general medical and detailed neuromuscular physical examination.
- Evaluate the strength, sensation and reflexes in your lower legs using the Utah Early Neuropathy Scale.
- Measure your vital signs, including blood pressure, heart rate, and body temperature.
- Record your weight, height and Body Mass Index (BMI).
- Record your waist circumference.
- Perform a resting 12-Lead ECG to check your heart. To do this, we will place small stick-on pads with wires attached onto your skin. The wires are attached to a machine that will record your heart rhythm. An ECG is an electrical tracing of the heart beat and will take about 15 minutes.
- Collect a blood sample.

- Perform an Oral Glucose Tolerance Testing to measure how your body uses sugar. This test is performed by testing your blood glucose (sugar) before and 2-hours after drinking a high-sugar beverage. **You should not eat or drink anything other than water for 8 hours before this test.**
- The study team will ask you to complete some questionnaires about your health, daily life, how you are feeling, physical activity and your neuropathy symptoms.

Female subjects: If you are a woman of childbearing potential (not surgically sterile or post-menopausal defined as age > 51 years without menses for ≥ 2 years), we will perform a blood pregnancy test to ensure that you are not pregnant. If you are pregnant you will not be able to participate in this study. If you are a woman who is able to get pregnant, you must agree to use reliable birth control throughout the study. Acceptable forms of birth control include abstinence, oral contraceptives, the contraceptive patch, intra-uterine device, the contraceptive ring, and or barrier contraception such as condoms with spermicide. If you become pregnant during the study, you will stop taking the study drug.

Male subjects: Men must agree not to father a child while on the study.

If you are eligible to participate in this study, we will ask you to return to the clinic within 30 days from the last screening procedure for your Baseline Visit.

Baseline Visit (Day 0):

This visit will take about 4 hours. At this visit, we will:

- Ask you about any changes in your medical conditions, family history or medications since the last visit.
- Ask you questions about your general health and well-being.
- Measure your vital signs, including blood pressure, heart rate, and body temperature.
- Perform a short physical exam, including a visual field and fall risk assessment.
- Fall Risk and Mobility: The study team will have you perform several activities to assess your balance and ability to walk, stand, and sit. These tests will help the researchers determine how neuropathy is affecting mobility and risk of falling.
- Perform a skin biopsy above your knee. A small piece of skin about the size of a pencil eraser will be taken from a few inches above your knee. We will place a needle into your skin and inject an anesthetic (painkiller) to make the area numb. No stitches are needed. We will cover the area with a bandaid or gauze and tape. We will analyze the skin to measure how many nerves there are.
- Perform Nerve Conduction Studies. The nerve conduction studies measure how fast your nerves can respond to a small electrical stimulation, that feels like a "carpet" or "static" shock. During this test, the nerve is stimulated by a small device and the electrical activity is

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Consent Form Expiration Date: 2/26/2022 IRB Amendment Approval Date: 8/19/2021

measured on the skin on top of the nerve. This is usually performed on the leg. We will also write down your body temperature during the Nerve Conduction Studies. Your results will be shared with the central Nerve Conduction Studies laboratory at the University of Utah so that it can be reviewed.

- Collect a blood sample.
- **Female subjects**: If you are a woman of childbearing potential (not surgically sterile or post-menopausal defined as age > 51 years without menses for ≥ 2 years), we will perform a urine pregnancy test to ensure that you are not pregnant. If the urine test is positive, you will not be able to participate in this study.
- The study team will ask you to complete some questionnaires about your health, daily life, how you are feeling, and your neuropathy symptoms.
- You will receive a supply of the study drug at the end of this visit.
- You will be instructed to start taking study drug once a day (at night) beginning the evening after this visit and then increasing your dose over the next two weeks.
- Your next study visit will be in about 16 weeks. We will ask you to bring back all unused and empty study drug bottles to your next visit.

Weeks 16, 32, 48, 64 and 80 Follow-Up Visits:

The safety monitoring visits will take place at Weeks 16, 48 and 80. Each of these visits will take about 3 hours. The evaluation visits will take place at Weeks 32 and 64. Each of these visits will take about 4 hours. At these visits, we will:

- Ask you about any changes in your medical conditions or medications since the last visit.
- Ask you questions about your general health and well-being.
- Measure your vital signs, including blood pressure, heart rate, and body temperature.
- Record your weight and BMI.
- Record your waist circumference.
- Perform a short physical exam, including a visual field and fall risk assessment.
- Perform Functional and mobility testing [Weeks 32 and 64 ONLY]
- The study doctor will evaluate the strength, sensation and reflexes in your lower legs using the Utah Early Neuropathy Scale.
- Complete a 6-minute walk test and test your balance [Weeks 32 and 64 ONLY].
- Perform the Nerve Conduction Studies [Weeks 32 and 64 ONLY].
- Perform a skin biopsy on your thigh using the same procedures as described above [Weeks 32 and 64 ONLY].
- Collect a blood sample.
- Perform an Oral Glucose Tolerance Testing to measure how your body uses sugar. This test is performed by testing your blood glucose (sugar) before and 2-hours after drinking a high-

sugar beverage. **You should not eat or drink anything other than water for 8 hours before this test.** [Weeks 32 and 64 ONLY]

- **Female subjects**: If you are a woman of childbearing potential (not surgically sterile or post-menopausal defined as age > 51 years without menses for ≥ 2 years), we will perform a blood pregnancy test to ensure that you are not pregnant. If the blood test is positive, you will be required to stop taking the study drug.
- The study team will ask you to complete some questionnaires about your health, daily life, how you are feeling, and your neuropathy symptoms.
- The study team will ask you to complete some questionnaires about your physical activity [Weeks 32 and 64 ONLY].
- You will receive a supply of the study drug (topiramate or placebo) at the end of this visit.
- We will collect your study drug bottle(s) (empty and unused) and make sure that you have been taking the study drug properly.
- We will give you more bottle(s) of study drug to take, and remind you how to take the study drug twice per day (morning and evening).
- Remind you to bring unused and empty study drug bottle(s) to each study visit, and to immediately report any symptoms that concern you to the study doctor.
- Your next study visit will be in about 16 weeks.

Week 96 Termination Visit/Early Termination Visit:

The final termination visit will take place at Week 96. If you decide to stop the study early, we will ask you to complete an Early Termination Visit. The procedures for these visits are the same. This visit will take about 5 hours. At this visit, we will:

- Ask you about any changes in your medical conditions or medications since the last visit.
- Ask you questions about your general health and well-being.
- Measure your vital signs, including blood pressure, heart rate, and body temperature.
- Record your weight and BMI.
- Record your waist circumference.
- Perform a physical and neurological exam, including a visual field and fall risk assessment.
- The study doctor will evaluate the strength, sensation and reflexes in your lower legs using the Utah Early Neuropathy Scale.
- Fall Risk and Mobility: The study team will have you perform several activities to assess your balance and ability to walk, stand, and sit. These tests will help the researchers determine how neuropathy is affecting mobility and risk of falling.
- Perform the Nerve Conduction Studies.
- Perform a skin biopsy on your thigh using the same procedures as described above.
- Collect a blood sample for laboratory analysis.

- Perform an Oral Glucose Tolerance Testing to measure how your body uses sugar. This test is performed by testing your blood glucose (sugar) before and 2-hours after drinking a high-sugar beverage. **You should not eat or drink anything other than water for 8 hours before this test.**
- The study team will ask you to complete some questionnaires about your health, daily life, how you are feeling, physical activity and your neuropathy symptoms
- Collect your unused and empty study drug bottle(s) and make sure that you have been taking the study drug properly.

Please note that as a result of the 2020 COVID-19 outbreak and the related guidelines put in place at Virginia Commonwealth University there may be changes to the events that happen at each of the above visits. These changes may include:

- Visits being performed remotely (by telephone or video conferencing) instead of in-person at Virginia Commonwealth University.
- Certain tests and collections happening at different visits than scheduled above.
- An additional visit after the one at week 96, if the visit at week 96 is performed remotely. If this additional visit is needed, another supply of study drug will be provided to you.

We will inform you in advance of any of these changes, should they be needed.

Remote Visits Performed with Video

Study staff will provide you information on how to access the video conferencing platform. We will launch the video conferencing in a private and secure area. To protect your privacy we ask that you do not take screenshots, photographs, or recordings of any kind with any electronic equipment

We would like to remind you that a video meeting is similar to us visiting you at home. We may learn more about your home and the people living with you than we would during a visit at the hospital. For example, we may learn information from you that must be reported to public health or public safety authorities. We are required by law to report known or suspected child or elder abuse. If we make such a report, the public health and safety authorities can use the information as they see fit and may end up sharing it with other government agencies. Please ask the research staff if you have any questions about this prior to your video visit.

Optional Notification of Primary Care Provider in the Event of Diabetes Diagnosis:

Throughout the course of the study, we will monitor your blood sugar levels. If during the study you test positive for diabetes, your study doctor may contact your primary care provider to notify him or her of this diagnosis.

OPTION TO CHOOSE:

In the event that you are diagnosed with diabetes during the course of the study, do you approve the study doctor to notify your primary care provider?

☐ YES ☐ NO Initials_____

You can still take part in this study, even if you decline to give consent for your primary care provider to be notified if you test positive for diabetes.

Blood Sample Use and Storage:
We will only use your blood samples for this research study and for lab test development related to this study. We will store your blood samples until lab testing is completed, unless you agree to long-term DNA banking.

Study Phone Calls:
We may call you up to 5 times between study visits to see how you are doing, discuss your study medication, and remind you of upcoming visits. Each of these phone calls will take about 10 minutes.

Early Withdrawal
The study doctor may have to take you out of the study. This may happen because:

- Staying in the study would be harmful.
- You need treatment not allowed in the study.
- You fail to follow instructions.
- You experience side effects from the study drug.
- The study is cancelled.
- There may be other reasons to take you out of the study that we do not know at this time.

If you decide to stop taking part in the study, we will ask you to complete one or more visits.

Information in Your Medical Record
We will try to keep sensitive information related to the study out of your hospital electronic health record. However, information about serious side effects, serious allergic reactions, or important, unexpected results in imaging studies might become part of your records at **VCU**. The pharmacy keeps copies of all drug dispensing information as required by law.

What are the risks and possible discomforts from being in this research study?

Your symptoms may get better, worse or stay the same during this study. You may have side effects from taking the study drug. The study drug may cause all, some or none of the following side effects.

Minor side effects that could be caused by topiramate include:

- anorexia - a lack or loss of appetite for food
- fatigue – extreme tiredness
- memory problems
- nausea
- skin tingling
- feeling of pins and needles in your hands and feet

Potentially serious side effects include:

- glaucoma – an eye condition that can result in vision loss and pain
- kidney stones
- metabolic acidosis - increased acidity in the body
- decreased sweating
- increased pressure within the eyes

Allergic Reaction
As with any drug, an allergic reaction can occur. Allergic reactions can be mild or serious, and can even result in death in some cases. Common symptoms of an allergic reaction are rash, itching, skin problems, swelling of the face and throat or trouble breathing. If you think you are having an allergic reaction call the study doctor right away.

Blood Draws:
You may have a bruise (black-and-blue mark) or pain where we take the blood samples. There is also a small risk of feeling lightheaded, fainting or infection.

Oral Glucose Tolerance Testing (OGTT):
Some people do not like the taste of the glucose beverage and it can make some people feel nauseated. You will have a second blood draw at the end of this test that has the same risks as described above.

Nerve Conduction Studies:
The nerve conduction study involves administering a very small electrical shock, about as strong as a "carpet shock" or "static shock" over the nerves. Some people find this mildly

uncomfortable but there is no risk of injury or damage. You will undergo up to four nerve conduction studies over the course of the study.

Fall Risk and Mobility Testing

These tests involve walking, standing, and balance testing movements that may make some people tired or short of breath. Because your balance is being tested there is a small risk of falling. The study staff will be with you to protect against falls.

Skin Biopsies:

The skin biopsy has a very low risk. You will undergo five skin biopsies over the course of the study. There can be some bleeding at the biopsy site although this is very rarely a problem. There is a very small risk of infection, about 1 in 2000 biopsies. In order to minimize this risk, you will be given bandages with instructions on how to care for the wound. If an infection does occur, it can usually be easily treated with antibiotics taken by mouth. There is also a small risk of an allergy to lidocaine. If you have an allergy to lidocaine, please inform the nurse or doctor performing your biopsy and an alternative agent will be used. Any scarring is typically small and fades over time. Infrequently, a skin biopsy may need to be repeated due to a technical or laboratory error.

Pregnancy and Fertility Risks:

Topiramate, particularly when given at higher doses, may cause fetal problems such as a defect in the formation of the mouth, a cleft lip and or cleft palate, which is an opening in the lip and/or roof of the mouth.

Because of these risks, if you are capable of giving birth to or fathering a child, you and your sexual partner should use adequate birth control measures while you are in this study.

Women cannot take part in this study if they are:

- Pregnant
- Trying to become pregnant
- Breastfeeding

If you are a menopausal woman and have not had a period for the past 48 weeks or more, you will not need to have a pregnancy test. Also, if you have had any well-documented method of surgical sterilization, you will not need to have a pregnancy test. The documented methods of sterilization include having had a hysterectomy (removal of the uterus), bilateral oophorectomy (removal of both ovaries), tubal ligation (having your tubes tied), and transvaginal occlusion (blocking the tubes with a coil). All other female subjects will need to have a negative pregnancy test before starting the study drug.

If you are a female who is sexually active with a male partner and able to become pregnant, or a man with a sexual partner who is able to become pregnant, you must agree to use one of the birth control methods listed below. You must use birth control for the entire study (96 weeks).

Acceptable birth control methods for use in this study are:

- Abstinence (no sex)
- Birth control pills
- IUD (a small T-shaped device containing either copper or a hormone inserted into the womb for birth control)
- Contraceptive Patch
- Contraceptive Ring
- Approved hormone injections
- Diaphragm with spermicide (a foam, cream or gel that kills sperm)
- Condoms with spermicide

If during the study you think you are pregnant, you must tell your study doctor immediately. Your study doctor will ask you about the outcome of your pregnancy.

Men cannot take part in this study if they are actively trying to get their sexual partner pregnant. If your female partner becomes pregnant, the sponsor would like to follow the outcome of the pregnancy. You should notify us immediately if your partner becomes pregnant. We will work with you and your female partner to provide contact information to the sponsor. She may be asked to sign a release of medical information form that gives her doctors permission to provide information to the sponsor.

What are the possible benefits from being in this research study?

You may or may not benefit from taking part in this research study. If you receive topiramate, it is possible that the symptoms of your neuropathy will improve more than if you had not received topiramate. It is also possible that your symptoms will not improve or could worsen. Others who have CSPN may benefit in the future from what we learn in this study.

What other treatments or procedures are available for my condition?

You may already be taking other drugs to help you control your CSPN symptoms. You should talk to your physician about these if you are unhappy with their usefulness.

In order to participate in this study, you may or may not have to stop taking these medications. No drugs have been proven to improve the nerve damage caused by CSPN. Several studies suggest that diet and exercise may be helpful.

Many patients with Metabolic Syndrome are overweight, which is defined as a body mass index (BMI) of ≥ 25 kg/m^2. People who are very overweight (BMI ≥ 40 kg/m^2) may benefit from weight loss surgery if they cannot lose weight after a period of diet and exercise. It is not known whether weight loss surgery improves neuropathy. If you have a BMI ≥ 40 kg/m^2 it is possible you are a candidate for weight loss surgery. Because it is not known if weight loss surgery can improve neuropathy, if you decide to take part in this study you must agree not to have weight loss surgery during the time you are participating.

You do not have to take part in this study. If you do not want to join this study you will receive the standard treatment that your doctor prescribes for patients like you.

Can I still get medical care within Virginia Commonwealth University if I don't take part in this research study, or if I stop taking part?

Yes. Your decision won't change the medical care you get from us now or in the future. There will be no penalty, and you won't lose any benefits you receive now or have a right to receive. Taking part in this research study is up to you. You can decide not to take part. If you decide to take part now, you can change your mind and drop out later. We will tell you if we learn new information that could make you change your mind about taking part in this research study.

What should I do if I want to stop taking part in the study?

If you take part in this research study, and want to drop out, you should tell us. We will make sure that you stop the study safely. We will also talk to you about follow-up care, if needed. It is possible that we will have to ask you to drop out before you finish the study. If this happens, we will tell you why. We will also help arrange other care for you, if needed. You may choose to complete some study visits even if you discontinue study medication.

Will I be paid to take part in this research study?

We understand that you may have to pay for travel, parking, and meals in order to come to your clinic visits and that this can be burdensome. To help offset some of these costs, we will pay you $50 for the screening visit and $100 every time you have a clinic follow-up visit after that. (Baseline, Weeks 16, 32, 48, 64, 80 and 96). The maximum amount we will pay for taking part in this study is $750.

We may use your samples and information to develop a new product or medical test to be sold. The Sponsor, hospital, and researchers may benefit if this happens. There are no plans to pay you if your samples/information are used for this purpose.

What will I have to pay for if I take part in this research study?

Clinical services provided during a clinical trial are either research-related or related to usual medical care. All research related services and study drug (topiramate/placebo) will be provided at no cost to you.

Study funds will pay for certain study-related items and services. However, we may bill your health insurer for, among other things, routine items and services you would have received even if you did not take part in the research. You will be responsible for payment of any deductibles and co-payments required by your insurer for this routine care or other billed care. If you have any questions about costs to you that may result from taking part in the research, please speak with the study doctor(s) and study staff. If necessary, we will arrange for you to speak with someone in Virginia Commonwealth University Patient Financial Services about these costs.

What happens if I am injured as a result of taking part in this research study?

If you are injured by, or become ill, from participating in this study, please contact your study doctor immediately. The researcher's name and phone number are listed in the next section of this consent form. Medical treatment is available at the Virginia Commonwealth University Health System (VCU Health System). Your study doctor will arrange for short-term emergency care at the VCU Health System or for a referral if it is needed.

Fees for such treatment may be billed to you or to appropriate third party insurance. Your health insurance company may or may not pay for treatment of injuries or illness as a result of your participation in this study. To help avoid research-related injury or illness, it is very important to follow all study directions.

Injuries sometimes happen in research even when no one is at fault. There are no plans to pay you or give you other compensation for an injury, should one occur. However, you are not giving up any of your legal rights by signing this form.

If you think you have been injured or have experienced a medical problem as a result of taking part in this research study, tell the person in charge of this study as soon as possible.

If I have questions, concerns or complaints about this research study, whom can I call?

You can call us with your questions, concerns or complaints. Our telephone numbers are listed below. Ask questions as often as you want.

Dr. Kelly Gwathmey is the person in charge of this research study. You can call her at 804-628-6480 Monday – Friday during normal business hours. You can also call Virginia Commonwealth University Institutional Review Board at 804-828-0868 Monday-Friday during normal business hours**.** with questions, concerns or complaints about this research study.

If you have questions about the scheduling of appointments or study visits, call the Clinical Research Coordinator at 804-628-6480.

If you want to speak with someone **not** directly involved in this research study, please contact the NeuroNEXT Central IRB (the Partners HealthCare System Human Research office) in Boston, Massachusetts. The Central IRB is the ethics board that oversees the research conducted by NeuroNEXT. You can call them at 857-282-1900.

You can talk to them about:

- Your rights as a research subject
- Your concerns about the research
- A complaint about the research

Also, if you feel pressured to take part in this research study, or to continue with it, they want to know and can help.

If I take part in this research study, how will you protect my privacy?

The sponsor and researchers may use health information that identifies you to do the research described in this form, and to do related research. This means research related to a drug or device being studied alone or in combination with other drugs or devices, the medical condition being studied, or general medical field being studied; for example, neurological diseases or muscle

disorders. The sponsor and researchers may also use health information that no longer identifies you to do any type of research.

During this research, identifiable information about your health will be collected. In the rest of this section, we refer to this information simply as "health information." In general, under federal law, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use, and share your health information for research and why they may need to do so.

In this study, we may collect health information about you from:

- Past, present, and future medical records
- Research procedures, including research office visits, tests, interviews, and questionnaires

Who may see, use, and share your identifiable health information and why they may need to do so:

- Research staff involved in this study
- Non-research staff within the institution who need this information to do their jobs (such as for treatment, payment (billing), or health care operations)
- The sponsor(s) of this study, and the people or groups it hires to help perform this research
- Other researchers and medical centers that are part of this NeuroNEXT clinical study (NeuroNEXT Clinical Study Sites) and their ethics boards
- Other researchers and medical centers that are not part of this NeuroNEXT clinical study (NeuroNEXT Clinical Study Sites) but are part of the NeuroNEXT Network
- Partners HealthCare System, Inc. ("Partners"), Brigham and Women's Hospital and Massachusetts General Hospital ("MGH") and their ethics boards (the NeuroNEXT Central IRB)
- MGH (the NeuroNEXT Clinical Coordinating Center)
- University of Iowa (the NeuroNEXT Data Coordinating Center)
- A group that oversees the data (study information) and safety of this research
- People from organizations that provide independent accreditation and oversight of hospitals and research
- People or groups that we hire to do work for us, such as data storage companies, insurers, and lawyers
- Federal and state agencies (such as the Food and Drug Administration, the Department of Health and Human Services, the National Institutes of Health, and other US or foreign government bodies that oversee or review research)

Public health and safety authorities (for example, if we learn information that could mean harm to you or others, we may need to report this, as required by law)
Some people or groups who get your health information might not have to follow the same privacy rules that we follow. We share your health information only when we must, and we ask anyone who receives it from us to protect your privacy. However, once your information is shared outside our institution, we cannot promise that it will remain private.

Because research is an ongoing process, we cannot give you an exact date when we will either destroy or stop using or sharing your health information.

The results of this research study may be published in a medical book or journal, or used to teach others. However, your name or other identifying information **will not** be used for these purposes without your specific permission.

Certificate of Confidentiality

A federal Certificate of Confidentiality (Certificate) has been issued for this research to add special protection for information and specimens that may identify you. With a Certificate, unless you give permission (such as in this form) and except as described above, the researchers are not allowed to share your identifiable information or identifiable specimens, including for a court order or subpoena.

Certain information from the research will be put into your medical record and will not be covered by the Certificate. This includes records of medical tests or procedures done at the hospitals and clinics, and information that treating health care providers may need to care for you. Please ask your study doctor if you have any questions about what information will be included in your medical record. Other researchers receiving your identifiable information or specimens are expected to comply with the privacy protections of the Certificate. The Certificate does not stop you from voluntarily releasing information about yourself or your participation in this study.

Even with these measures to protect your privacy, once your identifiable information is shared outside Partners, we cannot control all the ways that others use or share it and cannot promise that it will remain completely private.

Because research is an ongoing process, we cannot give you an exact date when we will either destroy or stop using or sharing your identifiable information. Your permission to use and share your information does not expire.

The results of this research may be published in a medical book or journal, or used to teach others. However, your name or other identifiable information will not be used for these purposes without your specific permission.

Your Privacy Rights

You have the right **not** to sign this form that allows us to use and share your health information for research; however, if you don't sign it, you can't take part in this research study.

You have the right to withdraw your permission for us to use or share your health information for this research study. If you want to withdraw your permission, you must notify the person in charge of this research study in writing. Once permission is withdrawn, you cannot continue to take part in the study.

If you withdraw your permission, we will not be able to take back information that has already been used or shared with others.

You have the right to see and get a copy of your health information that is used or shared for treatment or for payment. To ask for this information, please contact the person in charge of this research study. You may only get such information after the research is finished.

OPTIONAL BLOOD BANKING

Some of your blood collected during this study will also be used to study your DNA (deoxyribonucleic acid). DNA is the building block of an individual's genetic make-up. We would like to store some of your blood and DNA samples for future research in CSPN. One way we may use this DNA is to try to understand why some people get CSPN and others don't, and why some people have severe pain and others don't. The results of these studies will not be made available to you.

Staff where the samples are stored will assign a code number to your samples and health information. Your name, medical record number, or other information that easily identifies you will not be stored with your samples or health information. The key to the code that connects your name to your samples and information will be stored securely in a separate file.

We will store your samples and information indefinitely.

The Genetic Information Nondiscrimination Act (GINA) of 2008 is a federal law that prohibits health insurance companies, group health plans, and most employers from discriminating against you based on your genetic information. This Federal law does **not** protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care

insurance. GINA also does not protect you against discrimination if you have already been diagnosed with the genetic disease being tested.

OPTION TO CHOOSE:
Do you approve the collection and storage of your DNA for future uses as described above?

☐ YES ☐ NO Initials_____

You can still take part in this study, even if you decline to provide consent for the storage and analysis of your DNA samples and information.

OPTIONAL TISSUE BANKING

As part of this study, we would like to put some of your tissue from the skin biopsy in a tissue bank. This will allow us to test future methods for diagnosing neuropathy and determining potential causes for nerve damage. The tissues will be kept in the laboratory of J. Robinson Singleton, MD, at the University of Utah. **It is not mandatory that you consent to banking your tissue in order to participate in the study.**

Personally identifiable information including name, date of birth, and medical history will be collected with each sample, but not stored with the sample. Your sample will be coded so that your name is not on the sample. Only your Study Doctor will have access to the identifiable information so that we can link your sample back to your study information later if needed. The banked samples may be shared with researchers at other institutions, although they will not be provided your name, but only information like your diagnosis and age. The information about the uses and disclosures of your health information for the main study also applies to this future research.

Please read each sentence below, think about your choice, and initial "YES" or "NO". No matter what you decide to do, your decision will not affect your medical care.

May the University of Utah or its research partners retain your tissue after the end of this research project for use in future research?

_____YES, my sample(s) may be saved for future diabetes and neuropathy research.
(Initial)

_____NO, my sample(s) must be destroyed at the end of this research project.
(Initial)

Can I stop allowing my samples and information to be stored and used for research?

If you give permission for your blood and tissue sample(s) to be saved for future research by the University of Utah or its research partners, the Institutional Review Board may review and approve each new project. The Institutional Review Board may require that you be contacted for your permission prior to the use of the sample(s) in a new project if it determines new consent is required for your protection.

You have the right to withdraw your consent in the future; however, you would need to notify J. Robinson Singleton, MD of this decision in writing:

J. Robinson Singleton, MD
Professor of Neurology
University of Utah School of Medicine
30 North 1900 East, SOM 3R228
Salt Lake City, UT 84132

Tissue or blood samples obtained from you in this research may help in the development of a commercial product by the University of Utah or its research partners. There are no plans to provide financial compensation to you should this occur.

Future results from banked tissue will not be shared with you or your doctors because the results will not directly affect your health care. Results of genetic testing will only be available to Dr. Singleton and his colleagues for research purposes. They will not be provided to employers, insurance companies etc. and they will not be included in your medical record.

The choice to share your samples and information is completely voluntary. You can decide not to have your samples used and still participate in the main study. If you do choose to participate, you can withdraw your permission at any time. If you do, your samples and your information will be destroyed. However, it will not be possible to destroy samples and information that have already been given to researchers. If you have any questions you can talk to the study doctor or the study team.

Subject Identification

Informed Consent and Authorization

Statement of Study Doctor Obtaining Consent

- I have explained the research to the study subject.
- I have answered all questions about this research study to the best of my ability.

Study Doctor Obtaining Consent	Date	Time

Statement of Person Giving Informed Consent and Authorization

- I have read this consent form.
- This research study has been explained to me, including risks and possible benefits (if any), other possible treatments or procedures, and other important things about the study.
- I have had the opportunity to ask questions.
- I understand the information given to me.

Signature of Subject:

I give my consent to take part in this research study and agree to allow my health information to be used and shared as described above.

Subject	Date	Time

Subject Identification

Consent of Non-English Speaking Subjects Using the "Short Form" in the Subject's Spoken Language

Statement of Hospital Medical Interpreter

As someone who understands both English and the language spoken by the subject, I interpreted, in the subject's language, the researcher's presentation of the English consent form. The subject was given the opportunity to ask questions.

Hospital Medical Interpreter	Date	Time

OR

Statement of Other Individual (Non-Interpreter)

As someone who understands both English and the language spoken by the subject, I represent that the English version of the consent form was presented orally to the subject in the subject's own language, and that the subject was given the opportunity to ask questions.

Name	Date	Time

Consent Form Version: 4.0