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UF | Institutional Review Board
UNIVERSITY of FLORIDA

# *INFORMED CONSENT FORM*

***to Participate in Research, and***

# *AUTHORIZATION*

***to Collect, Use, and Disclose Protected Health Information (PHI)***

## INTRODUCTION

**Name of person seeking your consent: _____**

**Place of employment & position: _____**

## GENERAL INFORMATION ABOUT THIS STUDY

**1. Name of Participant ("Study Subject"):**

_____

**2. What is the title of this research study (this "Research Study")?**

Defining Targets for Tic Detection and Suppression in Tourette Syndrome Deep Brain Stimulation

**3. Whom do you call if you have questions about this Research Study (the "Study Team")?**

Principal Investigator: Michael S. Okun, MD (352) 273-5550

Study Coordinator: Emily Rafferty, PhD (352) 733-0082

Neurosurgeon: Kelly Foote, MD 352-273-9000 8:30 a.m. to 5:00 p.m. weekdays. Dr. Foote can be paged at 877-364-1431 at any time with questions regarding surgery.

Contact information for emergencies after hours or on weekends or holidays: (352) 265-8408, ask for the neurologist on call and reference this study and principal investigator.

**4. Who is paying for this Research Study?**

The sponsor of this study is the National Institutes of Health.

**5. In general, what do you need to know about this Research Study?**

Agreeing to be part of any research is always voluntary. By signing this form, you are not waiving any of your legal rights. If you decide not to participate in this research, you will not be punished

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in any way and you will not lose any benefits to which you are entitled. If you have questions about your rights as a research subject, please call the University of Florida Institutional Review Board (IRB) office at (352) 273-9600.

**a) In general, what is the purpose of the research? How long will you be involved?**

The purpose of this study is to learn how deep brain stimulation affects motor and vocal tics associated with severe Tourette Syndrome that is not controlled with medication. The purpose of this research study is to evaluate the effectiveness and safety of a possible new treatment for Tourette Syndrome (TS). It is a therapy called Deep Brain Stimulation (DBS). The study will also examine the brain activity associated with TS and tics and explore the possibility of setting the DBS device to provide responsive brain stimulation (RBS). RBS can be applied when the device can automatically detect a tic by recording an abnormal signal from your brain. The abnormal signal in your brain is detected and the device is set to stimulate to suppress the signal and improve or alleviate your tic(s).

You are being asked to be in this research study because you have a long-standing severe case of TS that has not responded to many standard treatments and you have been offered corrective behavior therapy that either did not work or you opted not to try it.

Your participation will last around 24 months.

**b) What is involved with your participation, and what are the procedures to be followed in the research?**

If you participate in this study, you will be screened for surgical candidacy and if eligible, you will undergo implantation of four leads (wires) deep into your brain. The neurosurgeon will put in 4 leads (wires), 2 on each side of your brain. It is also possible that the neurosurgeon may decide that the leads should be placed in your brain in 2 separate surgeries. In that case, you will have 2 leads implanted on one side of your brain and 4 weeks later come back and have 2 leads placed on the other side of your brain. The level of anesthesia could range from local anesthetic to general anesthesia and this decision will be made by the study neurosurgeon and anesthesiologist on the day of surgery. You will come back about a month after the leads implantation surgery to have two neurostimulators, which will be referred to in this form as “batteries" for simplicity, placed in your chest under general anesthesia. These neurostimulators will send electrical pulses that will control the stimulation produced by the leads implanted in your brain.

You will return to our clinic monthly for 2-3 days in a row for the first 9 months to find your optimal stimulation settings and for the research team to record your brain activity captured by the leads. After this 9-month period, you will return at months 12, 18 and 24 for similar 2-3-day visits to check and reprogram the devices as necessary. You will be asked to complete a brief survey to rate the severity of your symptoms once a day between study visits. The link for the daily survey will be sent to you via text message and you can complete it on your mobile device or computer. The purpose of this survey is for study team members to better understand your symptoms and customize your DBS programming based on them. Between

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the visits, you can reach the research team if you have any issues, contact information is in question 3 of this form.

We will collect medical, medication and family history. We will ask you questions about your mental health, your tics, whether you have thought about suicide, about whether you are depressed, demographic information such as gender, relationship status, ethnicity, education and employment status. You will be required to have a urine drug test and pregnancy test if applicable prior to the surgery.

More detail about procedures, assessments and questionnaires are discussed in further detail in this document.

**c) What are the likely risks or discomforts to you?**

This study involves 2-3 surgeries: 1-2 brain surgeries and one outpatient battery placement under general anesthesia. The most likely risks of the brain surgeries include infection, bleeding in the brain, and discomfort (headache) post-surgery. The most likely risks of the battery surgery include effects of anesthesia, infection, and soreness post-surgery. Some less likely surgical risks could potentially cause serious injury or death.

Follow up visits may be long and cause fatigue. Some questions asked about your psychiatric history or current experiences may be sensitive and make you feel uncomfortable.

A complete description of the risks is found in this consent form.

**d) What are the likely benefits to you or to others from the research?**

You may experience a decrease in severity and/or frequency of your motor and/or vocal tics.

Others may benefit from the data provided by your brain sensors, which could provide important directions for future treatment. Others may also benefit by your results by providing information about the effectiveness of deep brain stimulation for Tourette Syndrome.

**e) What are the appropriate alternative procedures or courses of treatment, if any, that might be helpful to you?**

As an alternative to participating in this study, you may opt to continue routine clinical care, including attempts to control tics with medication and/or cognitive behavioral therapy.

***Additional and more detailed information is provided within the remainder of this Informed Consent form. Please read before deciding if you wish to participate in this study.***

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.

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## WHAT CAN YOU EXPECT IF YOU PARTICIPATE IN THIS STUDY?

**6. What will be done as part of your normal clinical care (even if you did not participate in this Research Study)?**

Even if you are not enrolled in this study, you will continue to receive standard medical care for your Tourette diagnosis.

**7. What will be done only because you are in this Research Study?**

If you decide to participate, a member of the research team will review the consent with you and you will be asked to read, sign and date this form before any study-related procedures are performed. You will also have the opportunity to confirm whether you would like us to inform your primary care physician (PCP) of your participation in this study. Notification of your PCP is not required for enrollment in this study.

**Screening Visit, 2-3 days:**

You will be asked to read, sign, and date this informed consent before any study-related procedures are performed. In order to find out if you meet the requirements to participate in the study, you will be evaluated by study doctors and members of the research staff and have an MRI of your brain with contrast (contrast helps to see better inside your brain). Magnetic resonance imaging (MRI) is a procedure that allows doctors to look inside the body by using a scanner that sends out a strong magnetic field and radio waves. This procedure is used routinely for medical care and is very safe for most people, but you will be monitored during the entire MRI scan in case any problems occur. You may be sedated or placed under general anesthesia during the MRI to prevent you from moving during the scan.

During this screening visit, you will be asked a series of questions by interview, questionnaires, and checklists about your symptoms. If you become uncomfortable, overly anxious or sad as a result of being asked any items on the questionnaires, at any of the visits, you can choose to stop. If the assessor feels you have feelings of self-harm or depression, study staff may refer you to mental health services available at UF Health Shands.

The screening evaluation will include meeting with a team including neurology, neuropsychology, psychiatry and neurosurgery. The evaluation will also involve collecting basic information (such as age, sex, race, drug use) and psychiatric, medical, and family history. The questionnaires and checklists are listed below. You will also have a physical and neurological exam that will include measuring vital signs (heart rate and blood pressure) and a urine drug test to screen for illegal drug use. In addition, females of childbearing potential will be screened for pregnancy (urine test).

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**The following assessments will be administered**:

- Yale Global Tic Rating Scale (YGTSS) and Modified Rush Tic Rating Scale (MRTRS) - this evaluates your current level of tics.
- The SF-36® Health Survey and Quality of Life Assessment Schedule (QOLAS) are forms that measure quality of life and will be completed by you.
- Hamilton Rating Scale for Depression (HAM-D) and Beck Depression Inventory II (BDI) –evaluates your current level of depression.
- Beck Anxiety Inventory (BAI) – evaluates your current level of anxiety.
- Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) –evaluates your level of obsessions and compulsions.
- Young Mania Rating Scale (YMRS) - evaluates the presence and level of mania.
- Columbia Suicide Severity Rating Scale (CSSRS)- evaluates the presence of suicidal ideas or behavior.
- The Conner's Attention Deficit Questionnaire (CAARS) – asks questions about your social life, schoolwork, your job, home life and relationships.
- Premonitory Urge for Tics Scale (PUTS)- assesses intensity of urge to tic.
- You will be interviewed and other information about your medical condition will be documented.

You will be asked to complete these questionnaires and checklists at this screening visit and throughout this study. You and the study doctor or study coordinator will be videotaped (including sound) while you are completing some of these questionnaires throughout the study (particularly the YGTSS and MRTRS, which evaluate current tics). These sessions are videotaped so they can be reviewed and/or scored by a doctor who is not involved in your treatment. The videotapes will be used for study purposes and will be destroyed after the study has closed. If you decline to be videotaped, you will not be able to participate in the study. You will also have weekly UF telemedicine calls to complete YGTSS assessments with the study coordinator during months 4-9 of the study. These calls are used to score the real time effects of different DBS programs and are expected to take less than 30 minutes.

You will also have detailed neuropsychological testing, including tests of perception, learning, and memory. For those tests you will use paper and pencil or a computer. These evaluations include: the Weschler abbreviated scale of intelligence (WASI-II), digit span and spatial span, California Verbal Learning Subtest, Story ("Logical Memory") and Face ("Visual Reproductions") Memory Subtests of Wechsler Memory Scale-WMS-III, Judgment of Line Orientation, Stroop Test, Trailmaking Test, Word Fluency Test, Grooved Pegboard, and mood measures to evaluate how your mood is being affected by the DBS treatment (Beck Depression Inventory-2 and State Trait Anxiety Inventory). You can choose to discontinue taking any of these assessments or tests at any time.

You will also meet with the neurosurgeon. This visit will give you a chance to ask any questions you may have about the surgery. The neurosurgeon will take a medical history and perform a physical exam. The doctor will also review any brain imaging you have in your medical record, and will tell you about the surgical procedure. The neurosurgeon will

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then discuss the risks and benefits of surgery and answer any additional questions you may have.

Any other procedures you had done previously, along with the results of our screening will be reviewed by a DBS panel (neurologist, neurosurgeon, neuropsychologist, psychiatrist). They will make sure that all other options for treatment have been explored. They will also make sure you have an accurate diagnosis of severe TS with no other treatment options. All panel members must agree that you meet all inclusion/exclusion criteria and are a suitable candidate for surgery.

**Baseline Visit, 2 hours:**

This visit will occur only if the surgery is scheduled to be more than 6 weeks after the Screening Visit. This visit will take up to 2 hours and review your medical history for any changes and some of the same questionnaires that were completed at the Screening Visit.

**Description of Surgery**

DBS is a surgical procedure that involves putting a wire (lead) with tiny stimulating electrodes into each side of your brain. An electrode is a small piece of metal used to take an electric current to or from a power source. These electrodes are connected under the skin to a small electrical unit called a neurostimulator that includes a battery, you may sometimes hear this device called a pulse generator or implantable pulse generator (IPG), a pacemaker, or simply a battery. For the remainder of this document and for simplicity this device will be referred to as a battery. This device sends out electrical signals that interrupt this flow of electricity and will be located in your chest under the collarbone. A wire is placed under the skin to connect the battery in the chest to the DBS leads in the brain.

The use of DBS in the treatment of TS is investigational, which means it has not been approved by the Food and Drug Administration (FDA).

For this study, we will be using the Medtronic Percept device. It is an implantable, battery powered device that can be programmed to deliver stimulation through the leads in your brain. Providing stimulation to these areas of your brain may relieve symptoms of TS. The battery also records brain electrical activity. Study doctors will use a tablet to communicate with the battery after it is implanted.

It is extremely important that your head does not move during the surgery. To accomplish this, the morning of your surgery a metal frame called a stereotactic head-ring will be attached to your head under local anesthesia. It will be attached to your skull using plastic and aluminum set pins. You will feel a lot of pressure as the head-ring is attached. The head-ring is a special instrument that allows the neurosurgeon to find the correct path to where he needs to place the DBS leads in your brain. Next, a CT (computerized tomography) scan of your brain will be performed. The images of the MRI and CT scans are then fused together so we can determine the exact areas in your brain where the leads will be placed.

After you have been prepared for the surgical portion of the procedure, a member of the surgical team will inject local anesthetic in your scalp and begin the procedure. An opening

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will be made in your scalp on each side of your skull for placing the deep DBS leads; two leads will be placed on each side of your brain over 1 or 2 surgeries. The exact shape of the opening will be made to fit the DBS lead. Each lead will be placed deep within your brain tissue. If all 4 leads are placed in one surgery you will be under general anesthesia. If the neurosurgeon decides that two surgeries would provide a better outcome, the level of anesthesia will be decided on the day of surgery by the neurosurgeon and anesthesiologist. The level of anesthesia for lead implantation surgery could range from local anesthetic to general anesthesia. The neurosurgeon will implant 2 leads on one side of your brain and 2 leads on the other side of your brain. During surgery you will have an X-ray of your skull to allow your doctor to place leads correctly. After brain surgery you will spend 1-2 days in the hospital, to make sure all went well. For your safety, the neurosurgeon recommends that you do not fly for 2 weeks following brain surgery.

One month after the leads implantation surgery, two batteries will be implanted in your chest under general anesthesia. With general anesthesia, you will be given one or more drugs that make you sleep and not feel pain during the surgery. During the battery implantation surgery, a second CT scan will be performed to check that the leads in your brain are in the correct place.

In case your batteries are depleted, the surgery necessary to replace a battery is not as major as the original surgery to implant the DBS System. A small opening is made in the chest over the battery so that it can be disconnected from the leads and be removed. Once the new battery is put in place, the leads are then connected and the opening in the chest is closed.

We will explain to you the battery life expected for the device used in this study so that you can understand and anticipate what is required for battery replacement. The battery is labeled to last about 5 years after implant, depending on use. However, frequent and/or high current stimulation may shorten the "life" of the battery. When the battery runs out, an additional surgery for replacement will be required if you or your study doctor still want the device to work. The risks for this procedure are expected to be lower than those of the first implant since the replacement surgery does not involve cutting into bone or placement of leads in the brain. A new Medtronic Corporation product called the Percept RC rechargeable DBS battery has been FDA approved for use. All battery replacements will be with the Percept RC battery as it has a 15-year life. The cost of battery replacements following the study will be the responsibility of either your insurance plan, out of pocket expense or you may apply for a device donation (from the hospital and/or Medtronic Corporation). In some cases, a battery replacement may be required within the study window, in those cases the study will cover the charges of the battery replacement, and a Percept RC will be used.

**Postoperative Procedures/Evaluations:**

One month after battery implant surgery you will come in for your first office visit. You will come to the clinic once a month for the first 9 months. During each visit starting with Months 1-3 (+/- 14 days) the study team will collect your brain signal data which will take about 2 days. For this portion of the study, you will be asked to put on several body sensors, which will capture muscle activity. The signals from your deep brain stimulation

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device will also be collected. You may be asked to collect physiology at home using your Percept device, the study team will explain how to collect this data. This information will be used to inform programming settings for future visits that are tailored to your individual case. Also, at every visit the study coordinator will conduct surveys and assessments, take your vital signs, ask you about changes in your medications, or if you have noticed any health problems post-surgery. You will also be asked to fill out a short survey about your current symptoms on your mobile device or computer no more than once a day between study visits. The survey link will be sent via text message and should be completed daily. You will receive reminder text messages if you do not complete the daily survey. The purpose of this survey is for study team members to get a better understanding of your symptoms to personalize your DBS programming.

At the Month 4 visit you will have an initial programming appointment where your battery will be turned on for the first time. You will return to the clinic for routine programming visits once a month (+/- 14 days) until month 8 post-surgery. You will also be given a remote control that can be used to turn off the battery at any time in case you feel discomfort from the stimulation. You also will be given a remote-control user guide and explained how to use it. You will have weekly UF telemedicine calls to complete YGTSS assessments with the study coordinator during months 4-9 of the study. These calls are used to score the real time effects of different DBS programs and are expected to take less than 30 minutes.

After your Month 9 appointment you will come in at 12 Months, 18 Months, and 24 Months for follow up and assessment. During these check-up visits the effectiveness and functioning of your batteries will be checked. You will also receive a Neuropsychology assessment at Month 18 and a physical exam by the study neurologist at Month 12 and 24.

At the end of the 24-month study period, you will have the choice of 1) continuing active stimulation at current settings, 2) discontinuing stimulation, and 3) discontinuing stimulation and removing the device.

We will then evaluate you every year for as long as you wish to remain implanted. We will monitor for battery depletion and monitor if the battery needs replacement. We will at the completion of the study encourage you to seek a general neurologist and a primary care doctor for care of your tics, medications and device.

If any identifiable information was collected as part of this research, it is possible that your research information, with all personally identifiable information removed, could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you or your legally authorized representative.

If you have any questions now or at any time during this Research Study, please contact one of the Research Team members listed in question 3 of this form.

**8. What identifiable health information will be collected about you and how will it be used?**

The Research Team will collect:

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- Complete past medical and psychiatric history to determine eligibility criteria
- Demographics
- Records of past physical exams, treatments, evaluations, and any other procedures you may have done in terms of Tourette only
- Physical exam, laboratory results, MRI and CT imaging results, and other test results
- Psychiatric and neurological assessments, in the form of interviews, questionnaires and video
- Information related to diagnosis and treatment of a mental health condition
- Urine pregnancy test for females of childbearing potential
- Urine drug test to test for illicit drugs other than marijuana
- Information about any health issues that you might have during your participation in this study (to insure your safety and wellbeing)
- Records about study devices
- Social security number for purposes of compensation
- Telephone number
- E-mail address

The Research Team may collect this information from other healthcare providers, such as laboratories, which are a part of this research, as well as healthcare providers that are not part of this research (other doctors, hospitals or clinics). Other professionals at the University of Florida or Shands Hospital who provide study-related care, and the University of Florida Institutional Review Board (IRB), may also collect your health information.

The Research Team listed in question 3 above will use or share your health information as described below to carry out this research study.

**9. With whom will this health information be shared?**

This health information may be shared with:

- The study sponsor (listed in Question 4 of this form);
- United States Governmental agencies which are responsible for overseeing research, such as the Food and Drug Administration, the Department of Health and Human Services, and the Office of Human Research Protections;
- United States Government agencies which are responsible for overseeing public health concerns, such as the Centers for Disease Control and federal, state and local health departments,
- The University of Florida Review Board that reviewed this Research Study and ensures your rights as a Study Subject are protected.

Otherwise, your identifiable health information will not be shared without your permission unless required by law or a court order. Once your health information is shared with those listed above, it is possible that they could share it without your permission because it would no longer be protected by the federal privacy law.

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**10. How long will you be in this Research Study?**

We expect your participation will last at least 24 months. At the end of this initial 24-month study period you will have the choice of continuing or discontinuing stimulation.

This Authorization to use and share your health information expires at the end of the study, unless you take it back sooner.

**11. How many people are expected to take part in this Research Study?**

We expect to screen 34 individuals in order to enroll 8 in the study.

## WHAT ARE THE RISKS AND BENEFITS OF THIS STUDY AND WHAT ARE YOUR OPTIONS?

**12. What are the possible discomforts and risks from taking part in this Research Study?**

The implantation of a battery requires major surgery and you will experience pain and discomfort during the post-surgical recovery period. The possible risks to you as a participant include, but are not limited to, the potential risks outlined below. You will also be given the Medtronic Patient Manual. It is important that you read it and discuss any questions and concerns with your study doctor and/or staff. In particular, you should be aware that you might experience a worsening of symptoms.

Subjects will be monitored throughout the study for the presence of suicidal ideas or behavior using the Columbia Suicide Severity Rating scale (C-SSRS) at each visit.

If any side effects or any other signs or symptoms develop after the surgery you should report them to Kelly Foote, M.D. Dr. Foote is the neurosurgeon involved in implanting the wires and batteries and can be reached at 352-273-9000 from 8:30 a.m. to 5:00 p.m. weekdays. Dr. Foote can be paged at 877-364-1431 at any time if you have questions related to surgeries

<u>Possible risks of surgical implantation of the device:</u>

*Possible risks associated with your DBS surgery:*

1. Bleeding or fluid inside of the brain, on the surface of the brain, or in the space between the skull and brain during your surgery that could result in change in consciousness, paralysis (not being able to move), stroke, or death.
2. Cerebrospinal Fluid (CSF) leakage during your surgery could result in a dull or throbbing headache or need for additional surgery.

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3. There is the possibility of complications, injury and even death from all forms of surgical anesthesia.
4. Meningitis, encephalitis, or brain abscess resulting from infection involving the brain and/or central nervous system.
5. Swelling of a small part of the brain around the DBS lead.
6. Bleeding into the brain or stroke-like conditions resulting in temporary or permanent injury to the nervous system, or death; these could occur at any time after the DBS leads are placed.
7. Non-infected cyst of the brain around the end of the DBS lead.
8. There is a risk of seizure post-operatively.

*Possible risks immediately after your DBS surgery:*

1. CSF leakage after your surgery could occur and might result in a dull or throbbing headache or need for additional surgery.
2. Short-term pain in the head and neck might occur.
3. Infection could occur after surgery, including meningitis (an infection that causes swelling of the lining around the brain and the spinal cord) which has the potential to cause brain damage or hearing loss.
4. Allergic reaction to the implanted parts is possible but rare.
5. Discomfort or lack of healing of the skin area could occur at or around the site of the implanted parts.
6. Surgery could cause swelling under the skin of the scalp or a mass of clotted blood inside or on the surface of the brain or in the space between the skull and brain that may apply pressure to the brain.

*Possible risks with the DBS system*:

1. Although pain and negative changes in mood during stimulation could occur, test stimulation is performed to determine stimulation settings that do not cause pain, discomfort, or negative changes in mood.
2. Pain or discomfort that lasts a long time and/or additional sensitivity may occur where the implanted parts were placed.
3. Movement of the lead from where it should be in the brain or loose electrical connections could cause therapy to stop working, could cause pain, or possibly cause a sensation of pricking, tingling, or creeping on the skin.
4. Stimulation has the potential to cause a seizure and there is a possibility that this could bring about a seizure disorder.
5. Certain therapy settings may cause involuntary movements (i.e., eyelid blinking, twitching). These movements usually go away after the therapy settings have been adjusted.
6. Changes in your brain cells or reduced sensitivity of your brain to stimulation could cause therapy to stop working.
7. The effects of long-term brain stimulation are not completely known and there could be some risk of brain tissue damage.

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8. The battery is labeled to last about 5 years after implant, depending on use. However, frequent and/or high current stimulation may shorten the "life" of the battery. When the battery runs out, an additional surgery for replacement will be required if you or your study doctor still want the device to work. The risks for this procedure are expected to be lower than those of the first implant since the replacement surgery does not involve cutting into bone or placement of leads in the brain.
9. As with any electronic device, the DBS System may not work. A system malfunction may be because the battery is running low or is out of energy. It could also be because of an electrical short, open circuits, lead fractures, or lead insulation failures, or damage as a result of head trauma. These malfunctions are unpredictable, and may result in too little stimulation. A malfunctioning battery may require minor surgery to replace. Although the battery is designed to turn off if over stimulation or excess current occurs there is a possibility that product failure could result in brain tissue damage.

*Other Possible Risks Associated with this Study:*

1. The device can be removed or left implanted until the battery runs out. Device removal will be paid for by your private insurance and/or Medicare or CMS. Device removal may involve the removal of the battery in your chest, while your DBS electrodes could be left in place. You may also choose to have the DBS electrodes removed as well. One publication by Liu and colleagues published in the Journal of Neurosurgery in 2012 reported 12.8% chance of bleeding within the skull when DBS electrodes were removed. These bleeds were detected by postoperative CT scans. However, they were reported to be asymptomatic.
2. Worsening of TS and other psychiatric symptoms, such as those associated with mania, could possibly occur and might require medical treatment.
3. You might experience, or have a worsening of, suicidal thoughts or impulses.
4. Replacing or permanently removing any or all implantable parts may be medically necessary. The implanted parts may cause fibrosis (a "build-up" of scar tissue) that could get in the way or stop their removal. With any surgery involving removal of such parts, there is a risk of bleeding inside the brain.
5. The following risks have been reported with the use of systems that provide constant stimulation to deep brain structures. These reported risks may be related to areas of your brain that will be stimulated.
    a. In a study of 160 people treated for Parkinson's disease with another deep brain stimulator (DBS), serious side effects included bleeding in the brain (7.5%), infection related to the deep brain stimulator (10.6%), weakness or loss of energy (10%), and weakness or paralysis affecting one side of the body (8.1%). There were ongoing serious side effects related to the stimulation in 3.1% of the patients, including pain, problems with speech, and worsening of the Parkinson's disease symptoms. Serious on-going side effects related to the device occurred in 6.3% of the patients and included problems with the DBS system, infection, skin breakdown in the area where the device was implanted, and worsening of Parkinson's disease symptoms.
    b. In another study of 424 patients with tremor who were implanted with the same deep brain stimulator used for the patients with Parkinson's Disease, side effects

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related to the surgery to implant the device included pain (6.6%), bleeding in the brain (3.1 %), infection (2.6%), skin breakdown in the area of the device (1 .9%) and a change in skin sensation (1.4%). Side effects related to brain stimulation included a change in skin sensation (33%), difficulty saying words (9%), difficulty with balance (5%), and weakness (5%). Most of these side effects were tolerable and did not require any change in the treatment.

6. While the following potential risks have not been reported with the use of the DBS System, they have been reported with systems that provide chronic (constant) stimulation to deep brain structures. These reported risks may be related to the area being stimulated, and include:

   Abnormal dreams, thinking and vision; amnesia (not being able to remember); apathy (disinterest in others and events); chest pain; delusions (thinking things that are not true or real); encephalopathy (slowing of thoughts); deep thrombophlebitis (deep blood clots); difficulty breathing, swallowing and walking; dizziness; drowsiness; dysesthesia (pain or uncomfortable sensations after being touched by ordinary things); fainting; hallucination (seeing or hearing things that are not real); hostility; increased salivation (increased amount of saliva); paresthesia (abnormal burning or prickling sensation); paresis/paralysis (not being able to move part or all of your body); pneumonia; postural hypotension (dizziness upon standing); rapid heart rate; speech disorders/difficulty speaking; vomiting/nausea.

7. While the following potential risks have not been reported with the use of the DBS System, they have been reported with systems that provide stimulation to deep brain structures in a short-term environment, like in the doctor's office. These reported risks include all those risks listed above as well as:

   Changes in cognitive function (the way you think); changes in movement, standing or walking; changes in smell/taste; encephalopathy (brain disease); gastrointestinal symptoms (upset stomach); increased depression or worsening of depressive symptoms; memory experiences.

*Possible risks associated with other medical procedures and devices:*

1. We obtain an **MRI** pre-operatively so as part of the protocol you do not require an MRI post-operatively. If you do require one for another reason here is the information you will need. Percept devices are Magnetic Resonance Conditional which means they are safe for MRI scans only under certain conditions. If the conditions are not met, the MRI could cause tissue heating especially at the implanted lead(s) in the brain which may result in serious and permanent injury or death. Before having an MRI, always talk with the doctor who manages your DBS Therapy to determine your eligibility and discuss potential benefits and risks of MRI. **Please note that if an MRI is needed post-operatively it is not FDA approved when 4 DBS leads are in place as in this protocol**. For further information, please call Medtronic at 800-328-0810. You will be provided with a device info card to show other providers/doctors/clinical staff.

2. **Electromagnetic Interference** (EMI) is electrical or magnetic energy that battery strong enough to interfere with the function of your device. This may cause the battery to not deliver stimulation for minutes to hours. Experience with the DBS System to date suggests that EMI has not compromised device performance or safety. While it is extremely unlikely to happen, there is a possibility that the DBS settings could change because of EMI.

3. **Diathermy**, a treatment that uses high-frequency electromagnetic radiation, electric currents, or ultrasonic waves to produce heat in body tissues, should not be applied anywhere on the body even if your battery is turned OFF. Energy from shortwave or microwave treatments can be sent through the implanted brain stimulation system and can cause permanent brain damage which may cause severe injury, coma, or death. This is not caused by a device malfunction. Rather, it is caused by the interaction of two devices (neurostimulation system and diathermy machine) when they are working properly. This warning does not apply to microwave ovens. Microwave ovens are safe to use and will not interfere with the battery.

   **You absolutely CANNOT be treated with any type of short wave or microwave diathermy device whether or not it is used to produce heat.**
   Both heat producing and non-heat producing treatments and diagnostic tests involving the use of sound, vibration, or electromagnetic (such as shortwave or microwave) energy are used by a variety of health care professionals, such as physical therapists, occupational therapists, chiropractors, physicians, dentists, sports therapists, ophthalmologists (eye doctors) and others. Because some of these treatments and diagnostic tests could interfere with or damage the DBS or battery, **please advise all of your health care professionals that you should not be exposed to diathermy treatment.**

4. **You CANNOT receive therapeutic ultrasound treatment to your head or neck.** Energy like this may be sent through your implanted brain leads resulting in brain damage. You should avoid therapeutic ultrasound treatment below the head or neck unless the risks of not using the treatment outweigh the risks of using it. The effects on the DBS System of the energy made from therapeutic ultrasound treatments below the head or neck are not known. Diagnostic ultrasound to any part of the body is safe and will not interfere with the DBS System.

5. **Lithotripsy** (the crushing of stones, usually in the gallbladder or urinary tract, using shock waves) should be avoided unless the risks of not using the treatment outweigh the risks of using it. If lithotripsy therapy is required, avoid directing the lithotripter (the device used to crush the stones) at the head. Energy delivered to the head may damage the DBS System. This could result in loss of therapy, and additional surgery to remove or replace parts of the DBS System.

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6. **Radiation therapy** (usually for cancer) anywhere on the body should be avoided unless the risks of not using the treatment outweigh the risks of using it.

7. **Electrocautery** (using electrical current to stop bleeding during surgery) applied near the battery may cause it to turn off and temporarily stop delivering therapy until it is reprogrammed by your doctor. Electrocautery applied directly to the battery or leads may send energy through your implanted brain Leads resulting in brain tissue damage. If electrocautery is required, keep the electrical current as far away from the battery and leads as possible. Use of bipolar electrocautery is recommended.

8. Other medical procedures such as dental work, electrolysis, or the implant of another medical device in the body may be performed with caution. Talk to the study doctor before such procedures.

9. Your battery may interact with other active medical devices (such as cardiac pacemakers and defibrillators) implanted in you. Talk to the study doctor about any such medical devices you may have currently implanted.

*Possible risks associated with other equipment:*

1. Magnets that are contained in such products as stereo speakers and power tools, as well as those used as a remedy for other ailments, should be kept at least 4 inches away from the battery. The battery may not deliver stimulation while these magnets are closer than 4 inches from the battery or for minutes to hours after removing the magnets. Most headsets and earphones available in stores will not interfere with the battery, but not all have been tested.

2. It is possible that security screening devices (such as theft detectors, airport security systems, etc.) may stop stimulation by the battery for minutes to hours. You should present the letter from the study doctor and/or the Medtronic device card, that will be provided to you, to the staff performing security screening.

*Other possible risks:*

1. You may feel minor discomfort during a complete neurological and psychiatric evaluation. Sometimes people may feel uncomfortable talking about sensitive topics. The research team will take every precaution to make sure you are comfortable talking about these kinds of subjects.

2. You may experience mild discomfort resulting from answering the questionnaires and checklists and discussing potentially difficult topics. However, most people welcome the opportunity to discuss their experiences with a trained clinician.

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3. The psychological tests that will be administered at different times during this study are either computer or paper and pencil tests. None of the tests poses any significant risk, although some people may find the testing tedious or even frustrating. The testing can last up to 8 hours, spread over two days. Breaks are included during the testing to make it easier to complete.

4. The risks of CT and MRI scans are relatively minor.

   The MRI scanner contains a very strong magnet. Therefore, you may not be able to have the MRI if you have any type of metal implanted in your body, for example, any pacing device (such as a heart pacer), any metal in your eyes, or certain types of heart valves or brain aneurysm clips. Someone will ask you questions about this before you have the MRI.

   There is not much room inside the MRI scanner. You may be uncomfortable if you do not like to be in close spaces ("claustrophobia"). During the procedure, you will be able to talk with the MRI staff through a speaker system, and, in the event of an emergency, you can tell them to stop the scan. You may be sedated or placed under general anesthesia during the MRI to prevent you from moving during the scan.

   The MRI scanner produces a loud hammering noise, which has produced hearing loss in a very small number of patients. You will be given earplugs to reduce this risk.

   If you are a woman of childbearing potential, there may be unknown risks to the fetus. Therefore, before you can have the MRI, you must have a pregnancy test.

   This research study involves exposure to radiation from brain CT scan. The total amount of radiation that you will receive from one of these studies is about 210 millirems and is approximately equivalent to a whole body exposure of 8 months of natural background radiation.

   The radiation exposure in this study is thought to be minor. However, the effects of radiation exposure add up over your lifetime. Repeated exposures may increase your risk of injury or disease. When deciding to enter this study you should consider previous and future potential exposures. The investigator can provide you with a contact person if you would like more information about radiation exposure.

5. DBS Stimulation

   Although this procedure is designed to control your TS symptoms, it is an unproven therapy and experience with it is limited. Therefore, the possibility exists that stimulation could have no effect on your symptoms or even make them worse. It is possible that you may have side effects when the stimulation comes on, including tingling or uncomfortable sensations on the face or body, perceiving unusual tastes or smells, or experiencing weakness, unsteadiness, dizziness, fainting, or possibly seizures. Other possible side effects of stimulation are trouble speaking, or changes in mood, memory (including a memory flashback to past events), thinking process and

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energy level. It is also possible that the combination of the stimulation and your medication might result in more side effects than you would have from either treatment alone. Medication treatment will continue during the study, since we believe that the chance of your TS symptoms improving is better if stimulation is added to your ongoing medication and behavior therapies.

As discussed above, if stimulation improves your TS symptoms, mood or anxiety during this trial, it is possible that these symptoms may worsen if the stimulation stops, especially if the stimulation stops suddenly. That could happen when the battery becomes depleted, or if the battery is inadvertently shut off, as discussed in the section right below. This worsening might take the form of worsened TS, anxiety or symptoms of depression including low energy, motivation, sadness and even suicidal thinking. If any such symptom worsening occurs during this study, whether or not you believe that the stimulation has changed, you should immediately notify your study doctor.

We cannot predict whether brain electrical stimulation for TS that has not responded to other available treatments will be effective for you as an individual. We cannot guarantee you will receive any benefits from this study. As noted above, there is the possibility that your symptoms might worsen as a result of stimulation.

The safety and effectiveness of the DBS System has not been studied in pregnant women. Therefore, women of childbearing potential must use an acceptable method of birth control while in this study. This includes women in perimenopause/early menopause, but who have not achieved two years without a period. Birth control for the purposes of this study is: hormonal contraceptives ("the pill", Depo-Provera injections); intrauterine devices (IUDs); double barrier method of contraception (condom plus spermicide, condom plus diaphragm, etc.). If you become or suspect that you are pregnant during the study, you must notify the study doctor immediately. You and your doctor will discuss the risks versus benefits of continued stimulation. If you become pregnant after you have enrolled in this study but before your implant surgery, you must withdraw from the study due to the risks of general anesthesia to a developing fetus.

6. Collected Information

The Study Team will take appropriate steps to protect any information they collect about you. However, there is a slight risk that information about you could be revealed inappropriately or accidentally. Depending on the nature of the information, such a release could upset or embarrass you, or possibly affect your insurability or employability. Questions 18-22 in this form discuss what information about you will be collected, used, protected, and shared.

This Research Study may also include risks that are unknown at this time.

UF IRB-01 Approved

Please note, participating in more than one research study or project may further increase the risks to you. If you are already enrolled in a research study, please inform one of the Research Team members listed in question 3 of this form or the person reviewing this consent with you before enrolling in this or any other research study or project.

During the study, the Research Team will notify you of new information that may become available and might affect your decision to remain in the study.

The University of Florida is required by law to protect your health information. Your health information will be stored in locked filing cabinets or on computer servers with secure passwords, or encrypted electronic storage devices, as required by University policy. However, there is a slight risk that information about you could be released inappropriately or accidentally. Depending on the type of information, a release could upset or embarrass you, or possibly affect your ability to get insurance or a job.

If you wish to discuss the information above or any discomforts you may experience, please ask questions now or call one of the Research Team members listed in question 3 in this form.

**13a. What are the potential benefits to you for taking part in this Research Study?**

You may or may not personally benefit from participating in this study. There is a possibility that you will have improvement in your TS symptoms. You may experience a reduction in severity and/or frequency of your motor and/or vocal tics.

**13b. How could others possibly benefit from this Research Study?**

The information obtained from this study may help improve the treatment of severe TS in the future.

**13c. How could the Research Team members benefit from this Research Study?**

In general, presenting research results helps the career of a researcher. Therefore, the Research Team listed in question 3 of this form may benefit if the results of this Research Study are presented at scientific meetings or in scientific journals.

**13d. Will you be allowed to see the research information collected about you for this Research Study?**

You may not be allowed to see the research information collected about you for this Research Study, including the research information in your medical record, until after the study is completed. When this Research Study is over, you will be allowed to see any research information collected and placed in your medical record.

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**14. What other choices do you have if you do not want to be in this study?**

Although you meet criteria for brain surgery such as DBS, it does not mean brain surgery is the only option remaining for you. You may elect to seek current treatments for your Tourette syndrome and associated medical conditions, including both pharmacological and psychological interventions. Sometimes people with TS who have had severe illness for many years will show improvement with a particular combination of medications. Dr. Okun will be glad to discuss these with you.

When considering participating in this study, you will need to carefully weigh the pros and cons, the potential benefits and the potential risks. Remember that there may be other options.

You may also refuse to authorize the use of your health information, but if you refuse, you may not be allowed to be in this research study or receive any research-related treatment that is only available in this research study. However, your decision not to sign this Authorization will not affect any other treatment you may be eligible to receive.

**15a. Can you withdraw from this study?**

You may withdraw your consent and stop participating in this Research Study at any time. If you do withdraw your consent, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled. If you decide to withdraw your consent to participate in this Research Study for any reason, please contact the Research Team listed in question 3 of this form. They will tell you how to safely stop your participation. If you would like to stop your participation in the study, we will ask you to sign a withdrawal letter for our records.

You can also change your mind and take back this Authorization at any time by sending a written notice to the Research Team listed in question 3 of this form to let them know your decision. If you take back this Authorization, the Research Team may only use and disclose your health information already collected for this research study. No additional health information about you will be collected or disclosed to the Research Team. However, if you take back this Authorization, you may not be able to continue in this study. Please discuss this with a member of the Research Team listed in question #3.

**15b. Can the Principal Investigator withdraw you from this Research Study?**

You may be withdrawn from this Research Study without your consent for the following reasons:

- The sensing function of your device fails but you are still receiving symptom benefit. In this case, you would be withdrawn from the study and be followed in clinic for standard device programming.
- You do not qualify to be in the study because you do not meet all the study requirements. Ask the Principal Investigator if you would like more information about this.
- You need a medical treatment not allowed in this study.

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- You do not follow instructions of the Study Team members and it affects your safety and well-being.
- The investigator decides that continuing in the study would be harmful to you.
- Study treatments adversely affect your quality of life by making your symptoms worse.
- If you are a female and you become pregnant, and the study treatment could be harmful to the baby.
- The study is cancelled by the Food and Drug Administration (FDA), the National Institutes of Health (NIH), and/or other administrative reasons.

## WHAT ARE THE FINANCIAL ISSUES IF YOU PARTICIPATE?

**16. If you choose to take part in this Research Study, will it cost you anything?**

**Study Devices**

The Percept devices will be provided at no cost to you while you are participating in this study. However, the cost of the battery replacements will be billed to you or your insurance company. You will be responsible for paying any deductible, co-insurance, or co-payments for these services, and for any non-covered or out-of-network services. In some cases, a battery replacement may be required within the study window, in those cases the study will cover the costs of battery replacement.

**Study Services**

The sponsor will pay for all health care costs related to your participation, including all required study items, services and procedures described in this consent form. However, if you feel you have received a bill related to this study, please contact the Study Coordinator.

**Items/Services Not Paid for by the Sponsor**

If you receive any healthcare at UF Health that is not related to this study, this care will be billed as usual. After the study ends, you will be responsible for any cost incurred due to the need for a device or battery replacement, device explantation or any medical services needed as a result of participating in the study. You may be able to apply for a device donation from the hospital and/or Medtronic Corporation. You should discuss this with your insurance plan provider prior to enrolling in the study.

**Replacement Procedures**

Battery replacement and replacement procedure(s) will be billed to you or your insurance company. You will be responsible for paying any deductible, co-insurance, or co-payments for the replacement procedures, and for any non-covered or out of network services. In some cases, a battery replacement may be required within the study window, in those cases the study will cover the costs of battery replacement.

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**Device Removal**

If your study doctor determines it is necessary to remove the device, the cost of removal will be covered by the sponsor. If you request that the device be removed, the cost of removal will be billed to you or your insurance company.
You will be responsible for paying any deductible, co-insurance, or co-payments for these explant services, and for any non-covered or out-of-network services.

Some insurance companies may not cover costs associated with studies. Please contact your insurance company for additional information.

**17. Will you be paid for taking part in this Research Study?**

You will receive a $200 stipend for each completed study visit to help compensate you for your time and travel. This will be payable on a prepaid Visa card at the conclusion of each study visit, except the post implant visit (as it does not require a separate trip to the study site). If you complete all required research visits, you could receive up to $3,200.00. One unscheduled visit will be compensated ($200) per calendar year, though you may request as many as needed. Any unscheduled visits requested by the study team will be compensated ($200).

If you are paid more than $199 for taking part in this study, your name and social security number will be reported to the appropriate University of Florida employees for purposes of making and recording the payment as required by law. You are responsible for paying income taxes on any payments provided by the study. Payments to nonresident aliens must be processed through the University of Florida Payroll and Tax Services department. If the payments total $600 or more in a calendar year, the University must report the amount you received to the Internal Revenue Service (IRS). The IRS is not provided with the study name or its purpose. If you have questions about the collection and use of your Social Security Number, please visit: http://privacy.ufl.edu/SSNPrivacy.html.

Your payment for participation in this research study is handled through the University of Florida's Research Participant Payments (RPP) Program. Your information which will include your name, address, date of birth, and SSN (depending on amount of money you are paid) is protected. Access to the (RPP) Program site is limited to certain staff with the assigned security role. You will be randomly assigned a specific identification (ID) number to protect your identity.

If you have any problems regarding your payments contact the study coordinator.

**18. What if you are injured while in this Research Study?**

If you are injured as a direct result of your participation in this study, only the professional services that you receive from any University of Florida Health Science Center healthcare provider will be provided without charge. These healthcare providers include physicians, physician assistants, nurse practitioners, dentists or psychologists. Any other expenses, including Shands hospital expenses, will be billed to you or your insurance provider.

You will be responsible for any deductible, co-insurance, or co-payments. Some insurance

companies may not cover costs associated with research studies or research-related injuries. Please contact your insurance company for additional information.

The Principal Investigator will determine whether your injury is related to your participation in this study.

No additional compensation is routinely offered. The Principal Investigator and others involved in this study may be University of Florida employees. As employees of the University, they are protected under state law, which limits financial recovery for negligence.

Please contact one of the research team members listed in question 3 of this form if you experience an injury or have questions about any discomforts that you experience while participating in this study.

## SIGNATURES

As an investigator or the investigator's representative, I have explained to the participant the purpose, the procedures, the possible benefits, and the risks of this Research Study; the alternative to being in the study; and how the participant's protected health information will be collected, used, and shared with others:

_____ _____

Signature of Person Obtaining Consent and Authorization Date

You have been informed about this study's purpose, procedures, possible benefits, and risks; the alternatives to being in the study; and how your protected health information will be collected, used and shared with others. You have received a copy of this form. You have been given the opportunity to ask questions before you sign, and you have been told that you can ask questions at any time.

You voluntarily agree to participate in this study. You hereby authorize the collection, use and sharing of your protected health information as described above. By signing this form, you are not waiving any of your legal rights.

_____ _____

Signature of Person Consenting and Authorizing Date

# Consent to be Photographed, Video and/or Audio Recorded

With your permission, you will have the following done during this research (check all that apply):

☐ photographed ☐ video recorded ☐ audio recorded

Your name or personal information will not be identified on the photograph(s), video or audio recordings, and confidentiality will be strictly maintained. However, when these photograph(s), video and/ or audio recordings are shown or heard, others may be able to identify you.

The Principal Investigator (PI) of this study, Dr Michael S. Okun, or his successor, will keep the photograph(s), video and/or audio recordings in a locked cabinet, in a folder on a password protected computer server drive, or as an encrypted electronic file. These photograph(s), video and/or audio recordings will be shown under his direction to students, researchers, doctors, or other professionals and persons.
Please indicate under what conditions Dr. Michael S. Okun has your permission to use the photograph(s), video and/or audio recordings, and sign and date below.

☐ The following will be **destroyed once the study is closed** (initial next to all that apply):

____ photograph(s) _____ video recording(s) _____ audio recording(s)

☐ As described in the Informed Consent Form, and for the purposes of **education at the University of Florida Health Science Center**. The PI may keep the following for an indefinite period of time in a locked file, in a password protected computer server drive, or as an encrypted electronic file (initial next to all that apply):

____ photograph(s) _____ video recording(s) _____ audio recording(s)

☐ As described in the Informed Consent Form; for the purposes of **education at the University of Florida Health Science Center; and for presentations at scientific meetings outside the University**. The PI may keep the following for an indefinite period of time in a locked file, in a password protected computer server drive, or as an encrypted electronic file (initial next to all that apply):

____ photograph(s) _____ video recording(s) _____ audio recording(s)

_____ _____

Signature Date

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# Consent to Notify Primary Care Physician (PCP) of Enrollment in Clinical Study

Would you like your PCP to be informed of your enrollment in this clinical study? If yes, a letter will be sent that briefly describes the study and what your participation entails. If no, we will not communicate details of this study to your PCP.

☐ Yes, please inform my PCP of my enrollment in this study.

☐ No, please do not inform my PCP of my enrollment in this study.

_____ _____

Signature Date

# Certificate of Confidentiality – NIH Funded Request

To help us protect your privacy, we have requested a Certificate of Confidentiality from the National Institutes of Health. With this Certificate, the researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

You have been informed that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information. That is, if you give written consent for the release of information, we cannot withhold that information and we cannot hold responsibility for how that person may use your information.

The Certificate of Confidentiality does not prevent the researchers from disclosing voluntarily, without your consent, information that would identify you as a participant in the research project under the following circumstances. If we learn about child abuse, elder abuse, or intent to harm yourself or others, we will report that information to appropriate authorities.