**Partners HealthCare System**
**Research Consent Form**

Subject Identification

**General Template - Drug Clinical Trial**
**Version Date: February 2010**

Protocol Title: Effects of Type A botulinum toxin in obstructed defecation syndrome: a Phase II randomized, parallel group, triple-blind, placebo-controlled trial NCT02160288

Principal Investigator: Liliana Bordeianou, MD, MPH

Site Principal Investigator:

Description of Subject Population: Subjects with constipation/ obstructive defecation syndrome

## 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.

Partners HealthCare System is made up of Partners hospitals, health care providers, and researchers. In the rest of this consent form, we refer to the Partners system simply as "Partners."

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.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

## Why is this research study being done?

We are doing this research study to find out if Type A Botulinum Toxin (Botox) can help improve bowel emptying in people with Obstructed Defecation Syndrome (ODS). We also want to find out if Botox is safe to inject without significant side effects.

Obstructed defecation syndrome (ODS) is a very common cause of constipation. One of the most frequent causes of ODS is a muscle that contracts, instead of relaxing, when you try to move your bowels. The name of this muscle is puborectalis. This leads to complaints (symptoms) like constipation, straining, feeling of incomplete emptying of bowels and the need to use your fingers to help you go. Traditional treatment approaches (fiber, laxatives and enemas) do not always help.

Several small research studies have shown that Botox works in ODS and it helps improve the symptoms of constipation by relaxing the contracted puborectalis muscle. The goal of this study is to find out if this is indeed so**.** We also want to make sure that this injection does not lead to other bowel symptoms.

The U.S. Food and Drug Administration (FDA) has approved Botox injection into the muscles to treat wrinkles, urinary incontinence, chronic headaches, upper limb spasticity, cervical dystonia, strabismus and spasm of the lids, but the FDA has not yet approved Botox to treat ODS.

Over 150 people with ODS taking part in research studies around the world have received Botox so far. Additionally many people have been treated with Botox in the anal muscles for the treatment of other conditions.

In this study, we want to compare Botox with placebo. The placebo looks exactly like Botox, but contains no active ingredient. During this study, you may get placebo instead of Botox. Placebos are used in research studies to see if the results are due to the study drug or other reasons.

We are asking you to take part in this research study because you were diagnosed with ODS and which has not been resolved or managed with traditional treatments.

We plan to enroll 46 people with ODS, all at Massachusetts General Hospital (MGH).

## How long will I take part in this research study?

It will take you about 1 year and 1 month to complete this research study. During this time, we will ask you to make 3 study visits to MGH. We will also ask you to fill in 5 surveys sent to you via mail during this study**.**

## 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.

**Visit 1**

At this visit, we will again review the study with you and answer all questions. If you choose to take part in this study, you will then sign this consent form. Once you have signed the consent form, we will ask you to fill out a questionnaire. In total, this visit will take around 30 minutes. We will then schedule you for the procedure.

Assignment to Study Group

If you qualify for the study, we will assign you by chance (like a coin toss) to the Botox group or the placebo group. You and the study doctor cannot choose your study group. You will have a 1 in 2 chance of being assigned to the Botox group.

You and the study doctor cannot know which study group you are in, but she can find out if necessary.

**Visit 2- Procedure**

This visit will take about 30 minutes. For this visit, you will come to the office.
During this procedure, we will give you an injection of local anesthesia (a medicine to numb the area) followed by the injection of either the placebo or the Botox

Your doctor will pass a small camera (transrectal ultrasound) through your anus to guide the needle into the puborectalis muscle where we want to inject Botox. Next, she will inject a long-acting local anesthetic to numb you. This injection may hurt. After you are numb, your doctor will inject the Botox or placebo at three areas in the puborectalis muscle and external anal sphincter. This entire procedure should take less than 5 minutes.

We do not expect any side effects after this injection. To make sure you recover smoothly, we will watch you in the office till you recover after the injection.

When the effect of the local anesthetic goes away, you may experience discomfort or pain at the site of the injection. The pain will be minimal and you will likely not need pain medication.

## Follow -up Visit (Visit 3)

Visit 3 will be scheduled one month after the procedure and it will take about 45 minutes. At this visit, we will:

- Do a physical exam
- Ask you questions about your constipation symptoms
- Ask questions to see if you had any side effects or health problems since your last visit
- Ask you to fill out a second questionnaire with similar questions to the first questionnaire
- Evaluate the treatment effects by anorectal manometry, electromyography (EMG) and balloon expulsion test. These are the tests you have had in the past that led to your diagnosis of ODS. You can take part in the study without agreeing to have any of these procedures done. They are optional (not required).

### *Anorectal Manometry, Electromyography (EMG), and Balloon Expulsion Test*

We will ask you to have a special test that measures the function of your sphincter muscle (anorectal manometry). This is often done as part of the initial evaluation for ODS. During this test, we will check your rectum to see if stool is present. If stool is present, we will have you do a Fleet's enema in the office prior to the test. Then a small flexible plastic tube (a manometry catheter) is passed into your rectum through your anal sphincter. The manometry catheter is connected to a machine that records the contractions (squeezing movements) and relaxations of your rectum and anal sphincter. The test will take about 5 minutes and is not painful.

The doctor will then ask you to stay on your left side and a small sponge tipped sensor will be placed into your rectum (EMG). You may experience discomfort from this. We will use it to see whether your puborectalis muscle is able to relax. This takes about 1 minute.

Lastly, a 6 inch-long catheter is placed in the rectum and then filled with air (balloon expulsion test). You will be asked to sit on the toilet and try to expel the balloon. We will time you for 5 minutes. You have completed the test when the balloon passes, or if 5 minutes pass. If you do not pass the balloon, it will be deflated and removed at that time.

These procedures are very safe. You may experience some slight discomfort during the test, and may have a small amount of bleeding before or during the test.

## Long Term Follow-up by Mail or Telephone (3, 6, and 12 months After Visit 2)

You will be contacted by mail three times after your procedure at Visit 2**.**

- We will mail you a home questionnaire to fill out at 3, 6 and 12 months after the procedure. We will ask you to fill out and return to us these surveys. A prepaid envelope will be supplied with the return address on it.
- If you do not complete the questionnaire, we will call you to follow-up and ask you these questions over the phone.

## After You Complete the Study

After you complete the study, we will let you know its results as soon as they become available. We will refer you back to your own doctor for your ongoing medical care.

If you were in the placebo group and the study showed that Botox worked for the people who received it, we will offer you the injection of Botox free of charge.

## Stopping the Study Early

If you decide to stop taking part in the study for any reason, we will ask you to call the office of Lieba Savitt, N.P., at 617-643-5580. She is available Monday-Friday from 9 am-5 pm for any questions or concerns about this research study. She will ask you the reason why you chose to stop taking part in our study. Also, she will ask you to make a final study visit which will take about 30 minutes. At this visit, we will:

- Do a physical exam
- Ask about any side effects or health problems since your last visit
- Give you a questionnaire to fill out

Also, the study doctor may take you out of the study without your permission. This may happen because:

- The Sponsor decides to stop the study
- You can't make the required study visits
- We stop doing the study for other reasons

If this happens, the study doctor will explain why you need to stop taking part in the study. We will ask you to come in for a final study visit as described above.

### Review of Medical Records from Hospital Admissions or Emergency Department Visits

MGH has an electronic system that lets your study doctors know if you are admitted to a Partners Hospital, or if you visit a Partners Hospital Emergency Department for any reason. This alert will let the study doctors know why you are there. We want to make sure the study doctors know about any possible problems or side effects you experience while you are taking part in the study.

## Use of Your Health Information

The Department of General and Gastrointestinal Surgery at MGH 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 Botox alone or in combination with other treatments for ODS and constipation such as biofeedback.

The Department of General and Gastrointestinal Surgery at MGH may use health information that no longer identifies you to do any type of research.

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

### Risks of Taking Botox

Botox injections are relatively safe when performed by an experienced doctor. The most common side effects include discomfort or pain at the injection site. We will numb you before the injection and also give you pain medication to make you comfortable.

You will receive 100 units of Botox. If the dose is too high for you, the medication may cause problems such as leakage of gas or stool against you will (fecal incontinence). This is less common and only happens when very high doses (over 200 units of Botox) are used. Only 8 of 151 patients (5.2%) who have received Botox and were studied experienced fecal incontinence and in most cases it was mild incontinence for gas. Only one out of 151 patients (0.7%) had incontinence for solid feces. The incontinence went away in most cases when the effect of the medication started to fade (within 2-3 months). Tell your doctor if you have any side effect that bothers you or that does not go away.

Although very unlikely, there is a possibility that the effect of Botox may spread to other parts of the body and cause botulism-like signs and symptoms. These problems can happen hours, days, to weeks after an injection of Botox. **Call your doctor or get medical help right away if you have any of these problems after treatment with Botox:**

- Muscle weakness all over the body
- Vision problems
- Trouble speaking or swallowing
- Trouble breathing
- Loss of bladder control

These problems could make it unsafe for you to drive a car or do other dangerous activities.

The FDA has required that a black boxed warning, the strongest warning they require, be placed on the labeling for the drug. It means that medical studies indicate that the drug carries a risk of serious or even life-threatening side effects should the injected medication spread from the site of injection.

There has not been a confirmed serious case of spread of toxin effect away from the injection site when Botox was used at the recommended doses for the diseases in which it is already approved by the FDA.

As with any drug, an allergic reaction can occur. Allergic reactions can be mild or more serious, and can even result in death. 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. If you are having trouble breathing, call 911 immediately.

There may be other risks of Botox that are currently unknown.

## Risks to an Embryo or Fetus, or to a Breastfeeding Infant

The effect of Botox on an embryo or fetus (developing baby still in the womb), or on a breastfeeding infant, is unknown and may be harmful. Because of these unknown risks, 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 12 months or more, you will not need to have a pregnancy test. Also, you will not need to have a pregnancy test if you have had a hysterectomy (surgical removal of your uterus and/or ovaries). All other female subjects must have a negative pregnancy test before receiving Botox.

***For Females***

If you are sexually active female and 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. We recommend that you use two methods contraception for the first three months after your dose of Botox.

Acceptable birth control methods for use in this study are:

- Hormonal methods, such as birth control pills, patches, injections, vaginal ring, or implants
- Barrier methods (such as a condom or diaphragm) used with a spermicide (a foam, cream, or gel that kills sperm)
- Intrauterine device (IUD)
- Abstinence (no sex)

For the first three months after the injection, we recommend that you use a barrier method in addition to another method. If you are unsure which method to use, ask your study doctor.

If you miss a period, or think you might be pregnant during the study, you must tell the study doctor or nurse immediately. If you become pregnant, you must stop taking part in the study. The study doctor may ask for your permission to collect information about the outcome of your pregnancy and the condition of your newborn.

***For Males***

If you are sexually active, and able to father a child, you must agree to use one of the birth control methods listed below. You must use birth control for the entire study. We recommend that you use two methods contraception for the first three months after your dose of Botox.

Acceptable birth control methods that you can use in this study are:

- Condoms with spermicide (a foam, cream, or gel that kills sperm)
- Abstinence (no sex)

Acceptable birth control methods that your partner(s) should use are:

- Hormonal methods, such as birth control pills, patches, injections, vaginal ring, or implants
- Barrier methods (such as a condom or diaphragm) used with a spermicide (a foam, cream, or gel that kills sperm)
- Intrauterine device (IUD)

For the first three months after the injection, we recommend that you use a barrier method in addition to another method. If you are unsure which method to use, ask your study doctor.

If your female partner misses a period, or thinks she might be pregnant during the time you are in the study, you must tell the study doctor or nurse immediately. The study doctor may ask for your partner's permission to collect information about the outcome of her pregnancy and the condition of her newborn. You will **not** have to stop taking part in the study if your partner becomes pregnant.

**Risks of Taking Botox with Other Medications**

Only about 150 adults in studies have received Botox for ODS. Botox has also been used in children with constipation. Botox has been injected into the anus for other reasons (anal fissures) in many patients, and has been injected into other sites on adults. We don't know about all the side effects that can happen when taking Botox with other drugs.

**Risks of Study Injection Procedure**

We do not expect any unusual safety concerns in this study. The small foreseeable discomforts and complications of the office procedures have been listed with their description.

We will give you an injection with a long-acting local anesthetic to numb you before injecting Botox. Injecting the anesthetic through your rectum may hurt. Next, we will inject Botox or placebo at three sites in the contracting puborectalis muscle and external anal sphincter. This injection may also feel uncomfortable, or even hurt.

We do not expect any other complications after this injection. We will keep you in the office for 30 minutes after the injection, to make sure you don't experience any side effects, drowsiness or other immediate complications.

After the effect of the anesthetic passes, you may experience discomfort or pain at the site of the injection. We will give you pain medication to control it. If necessary, we can give you a prescription for pain medication.

**Psycho-social (non-medical) risks**

Psychosocial risks may include loss of productivity from appointments. We tried to limit the number of appointments you have to attend for our study to three (one for consent, one for the injection and one a month later). Therefore, we ask you that you agree to us contacting you by mail or phone to monitor the response of your disease to medication and possible side effects.

You may experience frustration if your symptoms do not improve and you need to undergo further treatments and investigations.

Some people may feel frustrated because the study doctors don't let them see the results of their tests. We will share with you the results of all tests you undergo as part of this study once the study is over.

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

You may not benefit from taking part in this research study. If you receive Botox, your constipation symptoms and quality of life could improve after the injection. If the results of the study show that Botox works and you received placebo, we will offer you a Botox injection at the end of the study.

Other people with ODS may benefit in the future from what we learn in this study**.** Only a few easy-to-administer and fast-acting options are available for the treatment of ODS. If Botox works, it could improve the suffering and discomfort caused by this condition.

## What other treatments or procedures are available for my condition?

You do not have to take part in this research study to be treated for ODS. Other treatments or procedures that are available for ODS include:

1. Treatment with medication (laxatives, enemas or fiber supplements)
2. Treatment with biofeedback therapy
3. Surgical procedures including colostomy or illeostomy

Talk with the study doctor if you have questions about any of these treatments or procedures.

## Can I still get medical care within Partners 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 within Partners 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.

Also, it is possible that we will have to ask you to drop out of the study before you finish it. If this happens, we will tell you why. We will also help arrange other care for you, if needed.

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

We will not pay you to take part in this study.

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

The Department of General and Gastrointestinal Surgery at MGH is providing the Botox and placebo at no cost. Study funds will pay for the injections, study visits and procedures that are done only for research.

Although study funds will pay for the injection and study procedures, 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 your 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 doctors and study staff. If necessary, we will arrange for you to speak with someone in Patient Financial Services about these costs.

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

We will offer you the care needed to treat any injury that directly results from taking part in this research study. We reserve the right to bill your insurance company or other third parties, if appropriate, for the care you get for the injury. We will try to have these costs paid for, but you may be responsible for some of them. For example, if the care is billed to your insurer, you will be responsible for payment of any deductibles and co-payments required by your insurer.

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. The researcher's name and phone number are listed in the next section of this consent form.

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

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

Dr. Liliana Bordeianou is the person in charge of this research study. You can call her at 617-643-0541, Monday-Friday from 9 am-5 pm. The MGH 24hours/day contact information is 24-hour contact: MGH: 617-726-2000 beeper 14039.

You can also call Lieba Savitt, N.P., at 617-643-5580; she is available Monday-Friday from 9 am-5 pm for questions about this research study, including scheduling your appointments or study visits. She is also the person you should call if you want to withdraw from the research study.

You can also call Holly Milch, N.P., at 617-643-5580. She is available Monday-Friday from 8am-4pm with questions about the research study, including reporting adverse effects and scheduling your appointments or study visits.

If you want to speak with someone **not** directly involved in this research study, please contact the Partners Human Research Committee office. You can call them at 617-424-4100.

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?

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:

- Partners research staff involved in this study
- 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 study and their ethics boards
- A group that oversees the data (study information) and safety of this research
- Non-research staff within Partners who need this information to do their jobs (such as for treatment, payment (billing), or health care operations)

- The Partners ethics board that oversees the research and the Partners research quality improvement programs.
- 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)
- Other:

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 Partners, 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.

## 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.

# Informed Consent and Authorization

**Statement of Study Doctor or Person 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 or Person 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.

Consent Form Version Date: 11/28/2016