You will be given a copy of this Research Subject HIPAA Authorization describing your confidentiality and privacy rights for this study.

By signing this document, you are permitting University of Pennsylvania to use and disclose personal health information collected about you for research purposes as described above.

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

If you have questions, concerns or complaints regarding your participation in this research study or if you have any questions about your rights as a research subject, you should speak with the Principal Investigator listed on page one of this form. If a member of the research team cannot be reached or you want to talk to someone other than those working on the study, you may contact the IRB at the number on page one of this form.

CONTACT FOR FUTURE RESEARCH

There may be studies in the future that may be of interest to you. May we have your permission to contact you in the future to discuss other research projects? The person contacting you would be your physician or a member of this research team. Please initial below to indicate your permission regarding contact for future research.

_____ Yes, you may contact me in the future regarding research projects.

_____ No, you may not contact me in the future regarding research projects.

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

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

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

IRB Approval From: 03-15-2022 To: 03-14-2023

University of Pennsylvania
Institutional Review Board
3600 Civic Center Blvd., 9th Floor
Philadelphia, PA 19104
Ph: 215-573-2540
(Federalwide Assurance # 00004028)

15-Mar-2022

Dr. Heidi Harvie
HHarvie@pennmedicine.upenn.edu
Attn: Lorraine Flick
Lorraine.Flick@pennmedicine.upenn.edu

PRINCIPAL INVESTIGATOR	: Dr. Heidi S Harvie
TITLE	: Treatment for Mixed Urinary Incontinence: Mid-urethral Sling vs. Botox A
SPONSORING AGENCY	: National Institute of Child Health and Human Development/NIH/DHHS
PROTOCOL #	: 842657
REVIEW BOARD	: IRB #4

Dear Dr. Heidi Harvie:

The above referenced protocol, and any applicable consent form(s), HIPAA authorization, recruitment materials and supporting documents were reviewed and re-approved by the above Institutional Review Board on 15-Mar-2022.

Approval by the IRB does not necessarily constitute authorization to initiate the conduct of a human subject research study. You are responsible for obtaining any relevant committee approvals.

This approval is for the period 15-Mar-2022 to 14-Mar-2023.

The following documents were included in this review:

- HSERA Continuing Review, confirmation code: dfficcae, submitted 02/09/2022
- This Cover Letter dated 2.07.22
- Continuing Review Request Form, uploaded 2.07.22
- Adverse Event Report, uploaded 2.07.22,
- Protocol Deviation Report, uploaded 2.07.22
- Protocol V 3.0 dated 11.9.20, uploaded 2.07.22
- Informed Consent Form approved 5.27.20, uploaded 2.07.22
- DSMB Recommendation Letters 5.17.21 and 9.13.21, uploaded 2.24.21
- Investigator's Brochure/product labelling (botoxapkginsert.pdf) uploaded 2.07.22

When enrolling subjects at a site covered by the University of Pennsylvania's IRB, a copy of the IRB approved informed consent form with the IRB approved from/to stamp must be used unless a waiver of written documentation of consent has been granted.

If you have any questions about the information in this letter, please contact the IRB administrative staff. Contact information is available at our website: http://www.upenn.edu/IRB/directory.

Thank you for your cooperation.

Sincerely,

Patrick J Landis, Esq.
Reason: I have reviewed this document
Date: 2022.03.15 15:40:09 -04'00'

IRB Administrator

RESEARCH SUBJECT INFORMED CONSENT AND HIPAA AUTHORIZATION FORM

Protocol Title:	Therapy for Mixed Urinary Incontinence: Mid-urethral Sling vs. Botox A (MUSA)
Principal Investigator:	Heidi Harvie, MD University of Pennsylvania Division of Urogynecology 3400 Spruce St. Dulles 5 Philadelphia, PA 19104
Emergency Contact:	Doctor on Call 215-662-6747
Sponsor	NICHD Pelvic Floor Disorders Network

Research Study Summary for Potential Subjects

You are being invited to participate in a research study. Your participation is voluntary, and you should only participate if you completely understand what the study requires and what the risks of participation are. You should ask the study team any questions you have related to participating before agreeing to join the study. If you have any questions about your rights as a human research participant at any time before, during or after participation, please contact the Institutional Review Board (IRB) at 215-573-2540 for assistance.

The research study is being conducted to find the best way to treat women who have urinary incontinence due to BOTH stress urinary incontinence (SUI) and urgency urinary incontinence (UUI), also known as mixed urinary incontinence (MUI). Stress urinary incontinence is when you leak urine with sneezing, coughing and/or physical activity. Urgency urinary incontinence (also called overactive bladder) is when you feel a sudden, strong desire to pass urine that results in leakage before reaching the toilet.

In this study we are trying to find out which treatment is best to use for women with MUI. Usually, BOTOX ® injections in the bladder are used for treating the urgency part of MUI and a mid-urethral sling (sling) surgery is used for treating the stress part of MUI, but recent studies show that maybe both types of leakage improve in women with MUI after either BOTOX or sling. Both of these procedures are standard of care for your condition and are not experimental. What we are studying is which one works better for women who have MUI.

The study involves several research visits in addition to standard medical care treatments for your condition outlined below. If you agree to join the study, you will first undergo an assessment by your doctor and study personnel to determine if you are eligible for the study. If you are eligible, you will be asked to complete surveys about your health and quality of life. You will be asked to stop any current treatment (such as

- to evaluate and manage research functions.

Who may use and share information about me?

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

- The investigator for the study and the study team
- Other authorized personnel at the University of Pennsylvaniaincluding offices that support research operations
- Other research personnel with access to the databases for research and/or study coordination and as otherwise approved by the IRB
- Greenphire employees who will administer/process Clincards and payments for study participation
- The study Data Coordinating Center, Research Triangle Institute (RTI)
- The sponsor of the study, the NICHD Pelvic Floor Disorders Network (PFDN)

Oversight organizations

- The U. S. Office of Human Research Protections (OHRP)
- The study Data and Safety Monitoring Board

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

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

How long may my personal health information be used?

Your authorization for use of your personal health information for this specific study does not expire.

Your information may be held in a research database. However, the University of Pennsylvania may not re-use or re-disclose information collected in this study for a purpose other than this study unless:

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

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

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

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

Then you will not be able to be in this research study.

A clinical trial management system (CTMS) is used to register your information as a participant in a study and to allow for your research data to be entered/stored for the purposes of data analysis and any other required activity for the purpose of the conduct of the research.

If you are receiving care or have received care within the University of Pennsylvania (outpatient or inpatient) and are participating in a University of Pennsylvania research study, information related to your participation in the research (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your existing EMR maintained by the University of Pennsylvania. Information related to your participation in clinical research will also be contained in the CTMS.

If you have never received care within the University of Pennsylvania and are participating in a University of Pennsylvania research study that uses University of Pennsylvania services, an EMR will be created for you for the purpose of maintaining any information produced from your participation in this research study. The creation of this EMR is required for your participation in this study. In order to create your EMR, the study team will need to obtain basic information about you that would be similar to the information you would provide the first time you visit a hospital or medical facility (i.e. your name, the name of your primary doctor, the type of insurance you have). Information related to your participation in the study (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in this EMR.

Once placed in your EMR or in the CTMS, your information may be accessible to appropriate University of Pennsylvania workforce members that are not part of the research team. Information within your EMR may also be shared with others who are determined by the University of Pennsylvania to be appropriate to have access to your EMR (e.g. Health Insurance Company, disability provider, etc.).

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

- Name
- Contact information: address, email address, telephone number
- Date of birth
- Medical history
- Social Security Number
- Medical Record Number
- Information from your study visits and procedures, including all test results
- Information from your medical records pertaining to any illnesses or medical complications you may have during your participation in the study.

Why is my information being used?

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

- do the research
- oversee the research
- to see if the research was done right

medications or a pessary) for your MUI and keep a bladder diary for 3 days. After this, you will come in for a visit and if you are eligible for the study, you will be assigned by chance (like the flip of a coin) to receive either 100 units of BOTOX through an injection in the bladder or a mid-urethral mesh sling performed surgically. You will be followed after the procedure, including a follow up visit 1 to 4 weeks after the procedure to check for infection or trouble with urinating. For the research study you will then be asked to complete a 3-day bladder diary at 3 months, 6 months and 12-months; come in at 3 months and 6 months; and complete a phone call at 9 months and 12 months after the treatment to assess your symptoms. Each visit will take about 1 hour. The research staff will call you at 9 months and 12 months to assess your symptoms, these phone calls will take about 30 minutes. If you received BOTOX, after 3 months you may be eligible for a second injection of 100 units of BOTOX if needed. After 6 months you may receive other treatments for your MUI if needed, including the alternative treatment (BOTOX or mid-urethral sling). Your participation will last for up to 15 months.

Participation in the study may or may not benefit you directly and may result in new knowledge that may help others. Possible risks of participation are loss of confidentiality, boredom and fatigue from completing questionnaires and burden of doing the bladder diaries. The mid-urethral sling procedure and BOTOX injections are standard of care treatments and risks associated with these procedures may be experienced whether you receive these treatments as a part of the study, or outside of the study.

The risks of BOTOX include discomfort from the injections, urinary tract infection, and difficulty emptying your bladder requiring you to use a catheter to empty your bladder. Other rare risks include worsening or unexpected difficulty swallowing or talking, trouble breathing or muscle weakness. There may be unknown side effects or problems that could result in serious illness or even death.

The risks of sling surgery include retention requiring a catheter, urinary tract infection, additional surgery, or exposure of mesh material, and pain. Additional rare risks related to the mid-urethral sling surgery include bleeding requiring a blood transfusion, surgical infection, injury to surrounding organs and medical complications from anesthesia including death.

Your doctor will discuss in more detail the procedures you are assigned to in a separate procedure consent.

Alternatives to this study can include receiving BOTOX or a mid-urethral sling surgery outside the research study. There are also other treatments for urgency incontinence including medications, tibial nerve stimulation and sacral neuromodulation. The other options for stress urinary incontinence include lifestyle modifications, weight loss, pelvic exercises, use of a pessary or support device, or a surgical procedure that does not involve mesh (pubovaginal sling, urethral colpopexy, or urethral bulking injection material). You also may elect not to have any treatment. Additional, detailed information about this research is provided below. Please ask any questions you have before signing this consent.

Please note that there are other factors to consider before agreeing to participate such as additional procedures, use of your personal information, costs, and other possible individual concerns. If you are interested in participating, a member of the study team will review the full information with you. You are free to decline or stop participation at any time during or after the initial consenting process.

Why am I being asked to volunteer?

You are being invited to participate in a research study because you have mixed urinary incontinence (MUI). Your doctor is an investigator in this research study. You do not have to participate in any research study offered by your doctor. If you choose not to participate, you will not lose benefits to which you are otherwise entitled. You may also decide to discuss the study with your family, friends, or family doctor before deciding whether to participate. Being in a research study is different from being a patient. As an investigator, your doctor is interested both in your clinical welfare and in the conduct of this study. If you decide to participate, you will be asked to sign this consent form.

What is the purpose of this research study?

The purpose of this study is to determine the best way to treat women with MUI. Because MUI includes both types of incontinence (stress and urgency), it is difficult to treat. Treatments that might help one type of incontinence may not help the other type. Right now, we do not know the best treatment for women who have not been successful in controlling their leakage with behavioral therapy, physical therapy, pessary and/or medications. In this study, you will receive treatment for your leakage with either BOTOX ® injections in the bladder or mid-urethral sling surgery.

BOTOX® helps to treat UUI by preventing bladder spasms that cause leakage. The use of BOTOX is currently approved by the FDA to treat conditions like overactive bladder including UUI. It is FDA approved to treat UUI at 2 doses: 100 units for those who have UUI without an associated neurological condition and 200 units for those people with UUI and an associated neurological condition like spinal cord injury or multiple sclerosis. In this study, you will receive 100 units of BOTOX®. For the treatment of UUI, BOTOX® is injected into the bladder wall through a cystoscope (a thin telescope passed into the bladder through the urethra or urinary tube). The urethra is the small tube-shaped organ that carries urine from the bladder to the outside. The injection is performed under local anesthesia in the clinic, hospital or surgical center. Repeat injections are usually necessary when the therapy wears off (usually 6 to 12 months). BOTOX® is an effective treatment for UUI, but we do not know if it also helps improve SUI.

A surgical treatment for MUI is a mid-urethral sling (MUS), where a small piece of permanent mesh is placed under the urethra. Mid-urethral slings are generally placed in the operating room under general anesthesia or deep sedation. They are primarily used for treating SUI, but they might also help UUI in women who have MUI. Because it is hard to treat both SUI and UUI at the same time, we need treatments that can help both conditions in women who have MUI. This study is evaluating whether BOTOX® or a sling works better for treating MUI.

If an insurer or employer learns about your participation, and obtains your consent to receive research information, then we may not use the Certificate of Confidentiality to withhold this information. This means that you and your family must also actively protect your own privacy.

You should understand that we will in all cases, take the necessary action, including reporting to authorities, to prevent serious harm to yourself or others (ie: in the case of elder abuse or neglect).

Will information about this study be available to the public?

A description of this clinical trial will be available on www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you.

What may happen to my information collected on this study?

Your information will be de-identified. De-identified means that all identifiers have been removed. The information could be stored and shared for future research in this de-identified fashion. This reduces the risk that future researchers would be able to identify you as we would not share any identifiable information about you with future researchers. This can be done without seeking your consent again in the future, as permitted by law. The future use of your information only applies to the information collected on this study.

Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Pelvic Floor Disorders Network (PFDN) plans to make data generated by PFDN studies available to external researchers in accordance with NIH data sharing policies. Data to be shared include clinical datasets of variables collected via the clinical trial management system, and analysis datasets containing derived variables that would enable a researcher to reproduce published study results. The data will be de-identified to protect study participant confidentiality. PFDN Data Coordinating Center (DCC) statisticians will implement a series of steps to de-identify study datasets in order to minimize the risk of researchers identifying any individuals in the data. This process will be consistent with Health Insurance Portability and Accountability Act (HIPAA), Health and Human Services (HHS) policies for protection of human research subjects, and related requirements for protecting participant confidentiality.

Electronic Medical Records and Research Results

What is an Electronic Medical Record and/or a Clinical Trial Management System?

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

any time by your physician, the study Sponsor, or the Food and Drug Administration (FDA) without your consent because:

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

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

How will my personal information be protected during the study?

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

Information you have provided will be kept in a research record and stored in a locked facility and on a secure, password-protected computer. Research information will not be made a part of your regular medical record. There is no personal information (name, social security number, etc.) about you that is associated with your research data; a study number will indicate your identity on the research records.

Information relating to this study, including your name, medical record number, date of birth and social security number, may be shared with the billing offices of the University of Pennsylvania so that the costs for clinical services can be appropriately paid for by either the study account or by your insurance.

Certificate of Confidentiality

This research has a Certificate of Confidentiality from the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development that protects your privacy.

With this Certificate, we cannot be forced (for example by court order or subpoena) to disclose information that may identify you in any federal, state, local, civil, criminal, legislative, administrative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except to prevent serious harm to you or others, and as explained below.

You should understand that a Certificate of Confidentiality does not prevent you, or a member of your family, from voluntarily releasing information about yourself, or your involvement in this study.

How long will I be in the study?

Including the time required for screening and to schedule your procedures, you will be in the study for up to 15 months. You will be followed in the study for 12 months after your first procedure (BOTOX® or sling). In total, we expect it will take 16 months to enroll all participants and complete the study.

What am I being asked to do?

Baseline / Screening visit – (Research visit - approximately 1 hour).

If you decide you want to be in the study, you will have the following procedures to find out if you qualify to be in this study:

- The study will be explained in detail and you will be asked to read and sign this consent form when you are comfortable.
- You will be asked about any bladder medications you are taking and any previous surgeries for urinary incontinence.
- You will empty your bladder and the coordinator or doctor will check to see if there is any urine remaining in your bladder by ultrasound or by inserting a catheter (thin tube) through the urethra into the bladder.
- Your urine will be checked for infection. If you have a urinary tract infection (UTI), you will be treated by your physician and then re-tested at a follow-up visit to confirm that your UTI has resolved and that you are eligible to continue participation in the study.
- You will be asked to complete health-related questionnaires about your medical and surgical history, urinary incontinence, general health and quality of life.
- If you qualify so far, you will receive a 3-day bladder diary with verbal and written detailed instructions on how to complete the diary. You will record the times that you urinate, leak urine, and what you were doing when any urine leakage occurred. You will return the completed diary by mail or you will bring the diary with you to the Randomization visit.
- If you are currently taking a bladder medication for overactive bladder, you will be asked to stop the medication for 3 weeks before completing the bladder diary and you will be asked to remain off medications during the 9 months of the study.
- If you currently have a pessary or other devices for incontinence, you will be asked to remove the pessary before completing the bladder diary.

Randomization visit (Research visit - approximately 1 hour)
Randomization & Treatment:
After you have completed your bladder diary, you will return to the office. At this visit the following will take place:

- Your completed bladder diary will be reviewed by study staff.
- You will complete some questionnaires about how much your urinary incontinence bothers you and how your incontinence has affected your activities and quality of life.
- Your urine will be checked for infection. If you have a urinary tract infection (UTI), you will be treated by your physician and then re-tested at a follow-up visit to confirm that your UTI has resolved and that you are eligible to continue participation in the study.

- If you are still eligible and willing to participate, you will be taught how to pass a thin tube (catheter) through the urinary tube into your bladder.
- If the study staff confirms that you qualify and you still want to participate in the study, you will be assigned by chance (like the flip of a coin) to receive initial treatment with:

BOTOX® injection procedure with 100 units
OR
Mid-urethral sling surgery

- You will have an equal chance of receiving either the BOTOX® or sling. Neither you nor the researcher(s) can choose the group to which you will be assigned.
- You will be told which treatment you are assigned. Some of the study staff will not know which treatment you are receiving.

Procedure visit (Standard of care - 1 to 3 hours)
You will undergo mid-urethral sling surgery or BOTOX injection per standard of care according to the group you are assigned to.

- You will come to the clinic, hospital or surgical center for your BOTOX® injection or mid-urethral sling surgery with your surgeon according to standard of care.
- Both BOTOX® 100 units and sling surgery are standard of care treatments for women with MUI and are not considered experimental. The procedures will be performed according to standard practice and billed to you or your insurance whether you participate in this research study or not. Because we currently do not know which procedure might be better for treating MUI, we are studying both treatments.
    - A sling surgery is performed under anesthesia in the operating room. You will receive preoperative intravenous antibiotic to help prevent infection. A mesh sling will be placed under the midportion of your urethra (the tube through which the urine comes out of the bladder) through an approximately one 1-inch incision in the vagina and two ¼-inch incisions either above your pubic bone or in your groin.
    - A BOTOX injection is performed in the office under local anesthesia. First a catheter will be placed in your bladder and an anesthetic solution will be instilled in order to provide numbing of the bladder. A camera (cystoscope) with an attached needle will be used to inject 15 to 20 different sites with BOTOX into your bladder. You will take an antibiotic pill before you leave to help prevent a UTI and you will take an antibiotic for three days after your injection.

2 weeks after-procedure visit (Standard of care - approximately 30 minutes)
Two weeks after your procedure, you will return to the clinic for a routine post-operative check with your surgeon. This visit is considered routine care. You will also see the research staff:

- You will be asked if you have had any changes in your health and medications.
- You will empty your bladder and the coordinator or doctor will check to see if there is any urine remaining in your bladder by ultrasound or by inserting a catheter (thin tube) through the urethra into the bladder.

manage any side effects, unless you are told that certain tests are supplied at no cost. Before you decide to be in the study, you should check with your health plan/insurance company to find out exactly what they will pay for.

You are still responsible for any deductibles or applicable co-pays for routine office visits, scans and blood work. Examples of routine procedures and drugs that may be billed to you or your insurance company include the following: urine analysis, urine culture, Botox injection procedures, mid-urethral sling procedures, medications and catheterizations. If your bladder symptoms get worse after surgery, or if other complications after surgery occur, all costs associated with the treatment of these complications are considered part of your standard clinical care and will be billed to you or your insurance company. Please talk to your doctor and study team about putting you in touch with a financial counselor to determine exactly what the deductible and co-pay will be for you; this depends on your insurance.

Will I receive the results of research testing?

As part of this study, the study team may ask you to have certain tests. Bladder testing or a cough stress test are part of your regular care. He/she will use these test results both to treat you and to complete this research. These test results will be recorded in your medical record and will be reported to the Pelvic Floor Disorders Network (PFDN) Data Coordinating Center (DCC). Results of tests and studies done solely for this research study and not as part of your regular care will not be included in your medical record. They will only be kept in your research record. You are permitted access to information (including information resulting from your participation in this research study) contained within your medical records.

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

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

There are no plans for the University of Pennsylvania to pay you or give you other compensation for the injury. If you feel this injury was caused by medical error on the part of the study doctors or others involved in the study, you have the legal right to seek payment, even though you are in a study. You do not give up your legal rights by signing this form.

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

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

This study is expected to end after all participants have completed all visits, and all information has been collected. Your participation in this study may also be stopped at

injections and sling surgery have the potential to improve urine leakage and we hope the information learned from this study will benefit other women with your condition in the future.

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

Alternatives to this study can include receiving BOTOX or a mid-urethral sling surgery outside the research study. There are also other treatments for urgency urinary incontinence (medications, tibial nerve stimulation and sacral neuromodulation). The other options for stress urinary incontinence include use of a pessary or support device, or a surgical procedure that does not involve mesh (pubovaginal sling, retropubic colpopexy, or urethral bulking injection material). You also may elect to not have any treatment. Ask your doctor to talk with you about the other options.

Will I be paid for being in this study?

To compensate you for your time and travel, you will receive up $275 for participating in this research. The amount will depend on the number of visits you attend in the study:

- $75 after completion of the procedure
- $50 after completion of the 3- month visit
- $75 after completion of the 6- month visit
- $75 after completion of the final 12- month call

Payment will be made in the form of a debit card called a Clincard. Reimbursement payments will be loaded on your Clincard after completion of the above study contacts.

Please note: In order to be compensated for your participation in this study, you must provide your Social Security Number. Additionally, please note that the we are required to report to the IRS any cumulative payments for participation in research studies that exceed a total of $600 in a calendar year.

Will I have to pay for anything?

The sling surgery and Botox ® injection procedures and physician visits are considered part of standard clinical care and will be billed to your insurance in the usual manner. As usual for any medical procedure, if there are portions of the cost that your insurance does not cover, you will be billed in the usual manner for any surgery you may choose to have. You are advised to consult your insurance company before having any operation.

Those tests (e.g., pregnancy, urine dip, bladder emptying) and visits which are only for research will be paid for by the study. In order to make sure that tests and studies done solely for research purposes are charged correctly, we will carefully monitor your procedure and clinic charges as long as you are participating in this study. Please ask your provider if you would like to know more about which tests and studies are being done solely for research purposes.

You and/or your health plan/insurance company will need to pay for the costs of your condition while in this study, including the cost of tests, procedures, or medicines to

- Your urine will be checked for infection. If you have a urinary tract infection (UTI), you will be treated by your physician.
- You will be given a bladder diary to complete for the 3-month visit

3 and 6 months after-procedure visits (Research visit - approximately 1 hour)
At 3 and 6 months after surgery, you will return for a visit with the research staff. At this visit:

- You will be asked if you have had any changes in your health and medications.
- You will complete some questionnaires asking you about your bladder symptoms and quality of life.
- Your completed bladder diary will be collected.
- You will empty your bladder and the coordinator or doctor will check to see if there is any urine remaining in your bladder by ultrasound or by inserting a catheter (thin tube) through the urethra into the bladder.
- Your urine will be checked for infection. If you have a urinary tract infection (UTI), you will be treated by your physician.
- The research staff or doctor will answer any questions you might have.
- If you received BOTOX and the injection is not giving you adequate control of your urinary leakage, after 3 months you may be eligible to receive additional 100 units of Botox®.

9 and 12 months after-procedure call (Research call- approximately 30 minutes)
At 9 and 12 months after surgery, you will have a call with the research staff. At this call:

- You will be asked if you have had any changes in your health and medications.
- You will complete some questionnaires asking you about your bladder symptoms and quality of life.
- The research staff or doctor will answer any questions you might have.
- After 6 months you may receive other treatments for your MUI if needed, including additional BOTOX or the alternative treatment (BOTOX or mid-urethral sling).

Botox Procedure visit (Standard of care - 1 to 3 hours)

- You will come to the clinic, hospital or surgical center for your BOTOX® injection with your surgeon according to standard of care.
- BOTOX® 100 units is a standard of care treatment for women with MUI and is not considered experimental. The procedure will be performed according to standard practice and billed to you or your insurance whether you participate in this research study or not.
    - A BOTOX injection is performed in the clinic, hospital or surgical center under local anesthesia. First a catheter will be placed in your bladder and an anesthetic solution will be instilled in order to provide numbing of the bladder. A camera (cystoscope) with an attached needle will be used to inject 15 to 20 different sites with BOTOX into your bladder. You will take an antibiotic pill before you leave to help prevent a UTI and you will take an antibiotic for three days after your injection.

2 weeks after-procedure visit (Standard of care - approximately 30 minutes)

If you received additional injections of BOTOX, you will return for a routine post-operative check with your surgeon 2 weeks after the injection. This visit is considered routine care. You will also see the research staff:

- You will be asked if you have had any changes in your health and medications.
- You will empty your bladder and the coordinator or doctor will check to see if there is any urine remaining in your bladder by ultrasound or by inserting a catheter (thin tube) through the urethra into the bladder.
- Your urine will be checked for infection. If you have a urinary tract infection (UTI), you will be treated by your physician as part of your routine clinical care.

What are the possible risks or discomforts?

Participation in this study may involve some risks or discomforts. Because this is a research study, there may be some unknown risks that are currently unforeseeable.

It is possible that the study procedures you receive may not be effective in treating your UUI or SUI symptoms or could make them worse. Additionally, below is a list of risks related to specific study procedures and medications.

Risks of randomization: You will be assigned to a study group at random (by chance). Your assignment is based on chance rather than a medical decision made by the researchers. The study group you are assigned to might not be the group you would prefer to be in. Your assigned study group might also prove to be less effective or have more side effects than the other study group, or other treatments available for your condition.

Risks of Botox® injection: Your surgeon will talk to you about the risks involved with your BOTOX injection. The risks of the procedure are the same whether or not you choose to participate in the study. This procedure is considered to be an accepted procedure for UUI and the procedure itself is not experimental. The risk of urinary tract infection is about 25-30%, and all women will be given an antibiotic to reduce the chance that a urinary tract infection will develop. Research suggests that up to 20% of women may have temporary difficulty emptying the bladder completely and need to insert a small tube into the bladder (catheterizing) several times per day to drain it. Rare risks of BOTOX® (1 in 1000) include: nausea, vomiting, dry mouth, trouble swallowing, weakness of muscles resulting in difficulty breathing, and paralysis. While some of these side effects are very serious and could cause death, they have never been described in patients receiving BOTOX® treatment for urinary problems.

Risks of mid-urethral sling surgery: Your surgeon will talk to you about the risks involved with your mid-urethral sling surgery. The risks of the mid-urethral sling surgery are the same whether or not you choose to participate in the study. This procedure is considered to be an accepted surgical procedure for SUI and the surgery itself is not experimental. The risk of urinary tract infection is about 5-10% and risk of wound infection is about 1%; all women will be given an antibiotic to reduce the chance that an infection will develop. Other risks of mid-urethral sling surgery include injury to the bladder, bowel, blood vessels, or nerves, bleeding, and problems related to the

anesthesia (all <1% for major problems). Some women experience urinary problems after the procedure, including difficulty urinating or urgency symptoms, these can be temporary or persistent (about 10-15%). Although recent research suggests that women with MUI have improvement in incontinence, up to 15% of women may need additional treatment for urinary incontinence after a sling. Recent research suggests that 1-6% of women may need to return to the operating room to remove or revise the sling because of a mesh exposure or problems urinating.

Risks of stopping your bladder medication or pessary treatment: To be eligible for MUSA, if you are taking bladder medication for overactive bladder or using a pessary or other device for stress incontinence, you will need to stop the treatment for 3 weeks before you can fill out the bladder diary. If you are eligible for the study and you choose to enroll in the study, you will be asked to stay off of your bladder medication and all other treatments (as mentioned above) for incontinence during the study, until 6 months after surgery. During this time, you may notice that your incontinence symptoms return. Please feel free to discuss any concerns you have about stopping your medical or pessary treatment with your doctor.

Risks of questionnaires: The quality of life questionnaires contain items that are of a personal nature and may make you uncomfortable or embarrassed. For example, some questions will ask about your sexual activity. You may refuse to answer any question that you do not want to answer.

Reproductive risks: The effects of the treatment procedures may pose some unforeseeable risks on the reproductive system (eggs) or to the developing fetus. For this reason, participants in this study should not become pregnant. We require that all participants who are able to become pregnant agree to either abstain from sexual intercourse or use a reliable, effective contraception for this period, such as hormonal contraceptive, intrauterine device (IUD), diaphragm with spermicide, contraceptive sponge or use of condom by the partner.

After you have been enrolled in this study, pregnancy testing will be performed before you undergo a procedure (either sling or BOTOX). If you have a positive pregnancy test, your doctor may withdraw you from the study. If you become pregnant or if there is any chance of pregnancy (e.g., late menstrual period), please contact the study personnel immediately so that we may provide medical assistance and counseling.

What if new information becomes available about the study?

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

What are the possible benefits of the study?

Participation in the study may or may not benefit you directly. This study may help the investigator(s) learn more about the best options for treating MUI. You may or may not have a decrease in the amount of urinary leakage you are experiencing. Both Botox®