EFFECTIVE

6/8/2021

MCW/FH IRB

Medical College of Wisconsin and Froedtert Hospital
INTRODUCTION TO THE INFORMED CONSENT

Name of Subject: _____

Study Title: Interstitial Cystitis-Examination of the Central Autonomic Network (ICECAN)

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You are invited to take part in this research. You can decide whether to take part in this project or not. You are free to say yes or no. If there is anything that you do not understand, please ask questions.

Definitions

Interstitial Cystitis/Bladder Pain Syndrome- is a type of chronic pain that affects the bladder. Symptoms include feeling the need to urinate right away, needing to urinate often, and pain with sex

Myofascial Pelvic Pain- is a source of chronic pelvic pain in women and men that is defined by short, tight, tender pelvic floor muscles that include palpable nodules or trigger points that cause referred pain. The pain can be continuous or episodic. MPPS can impact urinary, bowel, and sexual function.

Purpose

This project is being done to determine whether brain circuits that control the body affect the clinical course of patients with chronic pelvic pain.

Length

- You will be in this research project for 12 weeks.
- We will also follow up with you 4 weeks after your study completion.

Procedures *or* Activities

After reading and signing this informed consent document, you will be given a pre-screen to determine if you qualify to participate

List of visits:

- On-sire long visits
  - Total Number: 3
  - Total Time: 3 hours per visit

- At-home monitoring
  - Total Number: 12
  - Total Time: 24 hours, 1x/week

Procedures/Activities that will occur at various visits:

Invasive Procedures

- Blood sample collection
- pelvic exam

Non-invasive Procedures

- Medical history questionnaire
- Breathing test
- Heart rate test
- Urine sample collection
- General exam
- Questionnaires

Risks

This is a brief list of the most commonly seen risks The ***full consent form*** after this introduction contains a more complete list of potential research risks.

Device risks:

- redness from patches used to record your heart rate
- you may feel dizzy, nauseated, or get a headache from the breathing test

Non-Physical Risks:

- Your personal information and the data collected from you for this study will be kept confidential and, the extent permitted by law, will not be made publicly available. However, there is a risk of loss of confidentiality of your information. You will read more about the protection of your information later in this form. Please ask the study doctor or study staff if you would like to know more about how your information will be protected while you are in this study.

Benefits

This project may not help you, but we hope the information from this project will help us develop a better understanding of IC/BPS and MPP.

My Other Options

You do not have to join this project. You are free to say yes or no.

- Whether or not you join this project, you are free to seek services from this or other agencies.
- Whether or not you join this project, your usual medical services will not change.

If you have more questions about this project at any time, you can call Thomas Chelimsky, M.D. Principal Investigator at 414-805-5246 OR Gisela Chelimsky, M.D. at 414-266-3690.

If you have questions about your rights as a participant, want to report any problems or complaints, or offer input, you can call the MCW/Froedtert Hospital Research Subject Advocate at 414-955-8844.

CONSENT TO PARTICIPATE IN RESEARCH

A1. INTRODUCTION – WHY ARE WE ASKING YOU TO PARTICIPATE?

You are invited to participate in this research study because you have been diagnosed with chronic pelvic pain (CPP) such as Interstitial Cystitis/Bladder Pain Syndrome (IC/BPS) or Myofascial Pelvic Pain (MPP) and you are not pregnant. If you have been diagnosed with IC/BPS, you may have experienced symptoms such as painful urination and pressure in the pelvis or bladder. If you have been diagnosed with MPP you may have experienced pain and spasm in the pelvic muscles that may spread to other areas like the abdomen, legs and back.

A total of about 180 people are expected to participate in this research at Froedtert Hospital (FH) and Northshore Hospital in Chicago. We expect to enroll up to 150 at FH.

The Directors of the project are Dr. Thomas Chelimsky, Dr. Gisela Chelimsky, Dr. Lisa Conant, Dr. Jeffrey Janata, and Dr. Frank Tu in the departments of Neurology and Gastroenterology at MCW, Case Western Reserve University in Cleveland, and Northshore in Chicago. A research team works with Dr. Chelimsky, and Jeffrey Janata, and Dr. Frank Tu. You can ask who these people are.

The National Institutes of Health (NIH) is funding this study.

A2. DO I HAVE TO PARTICIPATE?

You can decide whether to take part in this research or not. You are free to say yes or no. If you say no, your regular medical care will not change. Even if you join this project, you do not have to stay in it. You may stop at any time.

A3. WHY IS THIS PROJECT BEING DONE?

The purpose of this project is to determine whether brain circuits that control the body affect the clinical course of patients with chronic pelvic pain.

B1. WHAT WILL HAPPEN IF I PARTICIPATE?

Screening procedures: If you are interested in this research study, you will first complete a pre-screen in person or on the phone to see if you are able to participate. An in-person pre-screen takes place in the MCW Neurology Research Rooms or Neurology Clinic at Froedtert Hospital (FH) or OBGYN clinics at Moorland Reserve Health Center, Westbrook Clinic or St. Joseph's Health Center.

If the screening information shows that you meet the requirements, then you will be able to start. If the screening information shows that you cannot be in the research, the research doctor will discuss other options with you and/or refer you back to your regular doctor.

If you are able to participate, you will complete 3 regular on-site long-visits at weeks 0, 4, and 12. The first long-visit (baseline evaluation) may occur either today following consent or at another date convenient for you. The baseline evaluation comprises a general and pelvic examination (no speculum), psychological questionnaires and a background history

questionnaire. You will complete a urine flow measurement, a heart rate recording and a breathing test. You will also be asked to provide a urine sample and a blood sample. The blood sample is optional.

We will also contact you 4 weeks after your study completion to follow-up with you.

Summary of Procedures:
At each long visit, you will complete a physician exam, a set of questionnaires, provide a 24-hour voiding diary and the following tests: breathing test, heart rate test and a "uroflow measurement." You will also complete a pelvic exam at week 0 (visit 1) and week 12 (visit 3).

The first physician exam will include a detailed medical interview and a pelvic exam. This exam may take up to 45 minutes to complete. If the physician questionnaire is unable to be completed during the study visit, the study doctor may complete this with you over the phone at a more convenient time.

You will be asked to complete questionnaires at each long-visit including: Hospital Anxiety and Depression Scale (HADS), State-Trait Anxiety Inventory (STAI), Thoughts About Symptoms (CSQ), Pennebaker Inventory of Limbic Languidness (PILL), Multidimensional Pain Inventory (MPI), Female Genitourinary Pain Index (FGUPI), Perceived Stress Scale (PSS), PROMIS Social Roles and Activities, PROMIS Physical Function, PROMIS Fatigue, PROMISE Sleep Disturbance, the Holmes-Rahe Life Stress Inventory, the MAPP II Interactive Brief Pain Inventory, and the Covid-19 Questionnaire. You will complete the Childhood and Recent Trauma Events Scale (RTES) during your first long visit only.

You can skip any question that you do not feel comfortable answering on any of the forms. Although the first questionnaires will be completed in the clinic to keep your answers private, the next will be completed while you are at home. We cannot guarantee that those responses will be kept private and there is a chance that answers may be seen by those who live in or visit your home. If your score is suggestive of emotional problems, study directors Dr. Thomas Chelimsky or Dr. Gisela Chelimsky or study Co-Investigator and Psychologist, Dr. Lisa Conant will provide you with places to help get treatment for these issues within 1 week of your participation. The researchers are required by law to report any abuse or neglect (or suspicion of abuse or neglect) if you mention it to the researchers or if it is suspected.

You will complete a "breathing test" in the MCW Neurology Research Rooms at FH. To complete this test, you will have wrist straps secured to a table and asked to breathe in deeply and out forcefully through a tube. You will have a small band on your arm to measure your heart rate and blood pressure. You will complete 4 cycles of breathing: two cycles while lying down flat and two cycles while leaning slightly forward.

The heart rate variability (HRV) and active posture change (ACP) recording will take about 20 minutes to complete. You will complete this recording at each long-visit and each week that you are in this study. Heart rate will be recorded with an eMotion Faros 360° portable ECG device. It is small and lightweight, with 3-5 small adhesive electrode patches placed on the skin of your chest and torso. You will lie down flat on a bed and rest for 10 minutes before the recording starts. After that, you will lie down for 5 more minutes while your heartbeat is recorded. You will be asked to stand up as quickly as you can and stand still for an additional 5 minutes. You may sit down if this test becomes too much for you to complete. Coded 24-hour HRV and ACP

recordings will be sent to Dr. Julian Thayer's research group at University of California Irvine for analysis. Your sample will be labeled by a number and will not contain any information that can be used to directly identify you.

A "uroflow measurement" measures the volume of urine, how long it takes to be released from the body and the speed. The uroflow measurement requires you to urinate on a special toilet in the MCW Neurology Research Rooms at FH. The toilet contains sensors that measure the speed of the urine flow and amount of urine. About one hour prior to this test you will be asked to drink a quart of fluid.

Weekly Home Checks will occur once a week for 12 weeks following consent. Each week, you will complete a heart rate recording just before you go to bed. The heart rate recording will help us to study how your heart rate changes throughout the day. You will place the patches on your chest and torso to match the image found on the instruction sheet provided to you as soon as you get up in the morning. A researcher will remind you via skype, email, text or telephone to remind you to complete the recording. The researcher will coach you the first few times you complete this recording until you are comfortable completing it on your own. The researcher will ask you to lie down flat on your bed for 15 minutes. After that, the researcher will instruct you to stand up as quickly as you can in front of your bed for another 5 minutes. You can sit down if you become too dizzy. You will need to bring the Faros 360 device with you to each of your in-person visits. The data from your heart rate recording will be uploaded to a secure server by a member of the research team.

You will complete the following each week from home: a 24-hour heart rate (HR) recording using the eMotion Faros 360° ECG device, the 24-hour voiding diary, answer a set of questions using the ICECAN mobile App installed on a preloaded smartphone, and complete questionnaires (those mentioned previously) that are sent to your personal e-mail account via a secure Internet connection. If in any case you are unable to complete the questionnaires online, you will be asked to return paper copies of the questionnaires at your next in-person follow-up visit.

The 24-hour voiding diary consists of tracking how much liquid comes in and out of your body in a 24-hour period, and how often you void. You will be required to measure the amount of everything you drink. You will also record the time and amount of each void for the 24-hour period. A special measuring "hat" that fits over the toilet seat will help you measure each void.

You will also complete a Daily Flare Question which asks about flare activity, management and if the flares are affecting you. These Flare Questions will be monitored via phone calls and recording in the EMA application on the smartphone.

Once per week, every week for 12 weeks, you will repeat the 24-hr HR recording, as described above, to compare the HRV recording done at home to the one performed at the matching on-site visit.

If you end up not answering some of the EMA questions, we will be asking you the following: At any time during the study, did your pain affect your ability to answer any of the EMA questions? When you didn't answer the EMA questions, what percentage of time was it due to pain? These questions will be asked at each in-clinic visit appointment.

During your follow-up visits at weeks 4 and 12, you will arrive to the MCW Neurology Research Rooms to repeat the following: a review of your symptoms, a brief physician exam, a uroflow measurement, questionnaires, and heart rate recording. You will complete the breathing test in the MCW Neurology Research Rooms with a member of the research team present. You will also complete a repeat pelvic examination at Week 12.

Blood (optional) will be drawn and Urine will be collected (~ 50 mL, a little more than 3 tablespoons) at each in-person visit at weeks 0, 4, and 12. We will determine (1) if immune or inflammatory factors play a role in your pain cycles and (2) if energy production in your cells might be impaired.

A portion of your blood plasma/serum and urine will be sent to Dr. Lori Birder's laboratory at the University of Pittsburgh for additional related analysis. Both of your samples will be labeled by a number and will not contain any information that can be used to directly identify you. This portion of the study is critical for us to gather new information about pelvic pain, which is very poorly understood. We highly encourage you to participate in this portion of the study. However, given how difficult it can be to obtain blood from some people with IC/BPS, we do allow you to opt out of the blood draw portion of this study and still participate in the other parts.

Please **initial** your choice below regarding blood sample collection.

_____ Yes, I agree to provide blood samples for this research project.
INITIALS

_____ No, I do not agree to provide blood samples for this research project.
INITIALS

B2. HOW LONG WILL I BE IN THE PROJECT?

⇒ You will be in this research project for about 12 weeks
⇒ We will also follow-up with you 4 weeks after your study completion.

B3. CAN I STOP BEING IN THE PROJECT?

You may stop at any time. If you decide to leave the project, please let the research team know.

The research doctor may stop your participation in the project at any time for any reason without your consent. He / She will tell you if this happens.

C1. WHAT HEALTH RISKS OR PROBLEMS CAN I EXPECT FROM THE PROJECT?

We watch everyone in the project for unexpected problems and side effects. **You need to tell the research doctor or a member of the research team immediately if you experience any problems or become too upset.**

⇒ **Questionnaires:** The psychological questionnaires may upset you. You can skip any question that you do not want to answer. If your responses are suggestive of emotional problems, a study Investigator will discuss your response(s) and will document this

discussion in your medical record. The Investigator will provide you with places to help get treatment.

⇒ **Physician Exam:** The physician exam includes a tender point evaluation that is standard of care for myofascial pain disorders such as fibromyalgia and may lead to tenderness and pain at the site of contact.

⇒ **Breathing Test:** You may feel anxious, dizzy, nauseated or get a headache from breathing in and out as instructed during the breathing test.

⇒ **Heart Rate Test:** There is a chance that you may develop redness from the patches used to record your heart rate during the heart rate test. These red marks are temporary and generally go away within an hour. If you are allergic to adhesives, you cannot participate in this study.

⇒ **Blood Draw:** The side effects that you might experience as a consequence of donating a blood sample for this project include possible discomfort and bruising at the needle entry site. Rare complications of any venipuncture (drawing blood from a vein) include fainting, arterial puncture, peripheral nerve injury, local infection, and local blood clot. There may be other unanticipated risks, but every precaution will be taken to assure your personal safety and to minimize discomfort. The person drawing your blood will observe you for side effects, but please inform him or her if you experience any discomfort or feel faint.

Another risk may be loss of confidentiality. Every effort will be made to keep your research records confidential but we cannot guarantee it. Depending on the kind of information being collected, if your research information were accidentally seen, it might be used in a way that could embarrass you or affect your ability to get insurance. If you have questions, you can talk to the project director about whether this could apply to you.

C2. RISKS TO WOMEN WHO COULD BECOME PREGNANT

Birth control methods for all subjects
Check with the research doctor about the birth control methods needed for this project and how long to use them. Some methods might not be good enough for this project. If you are having sex that could lead to pregnancy, you should use birth control while you are in this project. This may include:

- Not having vaginal sex (abstinence)
- Taking birth control pills orally
- Having birth control shots or patches such as Depo-Provera
- Surgical sterilization (hysterectomy or tubal ligation)
- Use of an intrauterine device (IUD)
- Use of diaphragm with contraceptive jelly
- Use of condoms with contraceptive foam
- Use of diaphragm with condoms (“double barrier”)
- Limiting sexual activity to a male partner who has had a vasectomy

C3. ARE THERE ANY BENEFITS TO TAKING PART IN THE PROJECT?

This project may not help you, but we hope the information from this project will help us develop a better understanding of IC/BPS and MPP.

D1. ARE THERE ANY COSTS TO BEING IN THE PROJECT?

There are no costs to you for any of the visits or services you receive in this project. If you have questions regarding costs, please contact Dr. Chelimsky.

If you participate in this research, the costs of any necessary emergency medical treatment in the event of a research-related injury will be billed to you or your health insurance.

D2. WILL I BE PAID FOR PARTICIPATING IN THE PROJECT?

You will be paid $250 for completing at least 80% of the required items for the 3 major on-site visits and 12 minor at-home monitoring sessions.

- You will receive a $50 payment on a preloaded credit card after completing all study tasks and Visit 1
- You will receive a $50 payment on a preloaded credit card after completing all study tasks and Visit 2
- You will receive a $150 payment on a preloaded credit card after completing all study tasks, visit 3, and returning the Faros ECG monitor and the pre-loaded Smartphone.
- If you complete the baseline evaluation but are found to not be eligible to participate in this study, you will be mailed a $25 check

You may be given the option to redo a study visit if the study data are incomplete or if you need to stop the study drug. If you redo a visit, you will receive payment for the visit which was repeated in the same amount as mentioned above.

Travel reimbursements

- If travel time is between 1 and 2 hours, you will be paid at a rate of $20 per visit on a preloaded credit card.
- If travel time is between 2 and 4 hours, you will be paid at a rate of $40 per visit on a preloaded credit card.

To pay you, we need your social security number. Any payment may be reportable as income on your taxes.

D3. WHAT OTHER HEALTHCARE CHOICES DO I HAVE?

You do not have to join this project. You are free to say yes or no. Whether or not you join this project, you are free to seek services from this or other agencies. Whether or not you join this project, your usual medical services will not change

D4. WILL I BE GIVEN NEW INFORMATION ABOUT THE PROJECT?

After the project has been completed, we will notify you of when the results will be available to the public.

When research data are collected and analyzed , there is the chance of finding something clinically relevant. There may be benefits to learning such results (such as early detection and treatment of a medical condition), but there are risks as well (such as feeling worried about a finding for which no treatment is required or appropriate).
In this study, you will be informed of any findings of possible clinical significance that may be discovered during review of results from your research data. The results of your research data will not be placed in your medical record.

The results from the data we collect in this research study are not the same quality as what you would receive as part of your health care. The data will not be reviewed by a physician who normally reads such results. We will provide you with this information so that you may discuss it with your primary care physician.

D5. WHAT HAPPENS IF I AM INJURED BECAUSE I TOOK PART IN THE PROJECT?

Emergency medical treatment for injuries directly related to your participation in this research project will be provided to you. You or your health insurance will be billed for the costs of this emergency treatment. MCW will decide on a case by case basis if they will reimburse you or your insurer for emergency treatment costs. If your research-related injury requires medical care beyond this emergency treatment, you or your insurer will be responsible for the costs of this follow-up care.

At this time, there is no plan for any additional financial payments.

If you believe that you have been injured because of your participation in this project, contact the research doctors right away. Contact information: Thomas Chelimsky, MD, 414-955-0619 or Gisela Chelimsky, MD, 414-266-3690.

Nothing in this consent form affects any legal rights you may have nor does it release the investigator, the sponsor, the institution, or its agents from liability for negligence.

D6. WHO CAN ANSWER MY QUESTIONS ABOUT THE PROJECT?

- If you have more questions about this project at any time, you can call Thomas Chelimsky at 414-955-0619 or Gisela Chelimsky at 414-266-3690.
- If you have questions about your rights as a research participant, want to report any problems or complaints, or offer input, you can call the MCW/Froedtert Hospital Research Subject Advocate at 414-955-8844.

E. PERMISSION TO COLLECT, USE AND SHARE HEALTH INFORMATION

E1. What health information will be collected and used for this project?

To be in this research project, the research team needs your permission to access, collect and use some of your health information. If you say no, you cannot be in the project. This information may come from questions we ask, forms we ask you to fill out, or your medical record, as described below. We will only collect and use information needed for the project.

The protected health information (PHI) originates from services you will or have received at one or more of the following locations: the Medical College of Wisconsin (MCW); BloodCenter of Wisconsin (BCW); Children's Hospital of Wisconsin (CHW); any Froedtert Health Affiliate-Froedtert Memorial Lutheran Hospital (FMLH), Inc.; Community Memorial Hospital (CMH) Menomonee Falls, Inc.; St. Joseph's Community Hospital (SJH) West Bend, Inc.; Froedtert & The Medical College of Wisconsin Community Physicians Clinics, Inc. (FMCWCP); the West Bend Surgery Center, LLC; and the Froedtert Surgery Center, LLC.

The health information we will collect and used for this project is:
To do this research study, we need your permission to collect and use some of your health information, or you cannot be in the study. This information may come from questions we ask, forms we ask you to fill out, or your medical records of care you receive from this project. Health information such as your clinical and laboratory information will be collected and shared. Researchers will also access your entire medical record for relevant study data such as your medical history, radiology scans, or lab data to help analyze the data collected. We will only collect and use information needed for the study.

E2. Who will see the health information collected for this project?

The only people allowed to handle your health information are those on the research team at MCW/Froedtert Hospital those on the Institutional Review Board (IRB) and those who check on the research activities to make sure the hospital's rules are followed.

If the costs of any necessary emergency medical treatment in the event of a research-related injury are billed to your health insurance, your health information may need to be disclosed to the insurer for billing purposes.

The research team may share your information with people who are not part of the research team because they planned, pay for, or work with us on this project. The federal Privacy Rule may no longer protect your health information once it leaves MCW/Froedtert Hospital. For this project, we plan to share information with those doctors, researchers or government representatives working with us on this project at the institutions or companies listed here:

- U.S. Food and Drug Administration, Rockville, MD
- Northshore Hospital in Chicago, IL Medical College of Wisconsin & Froedtert Hospital
- Case Western Reserve University in Cleveland, OH
- Multi-Disciplinary Approach to the study of Chronic Pelvic Pain (MAPP) Research Network, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)

Because this project involves the use of drugs and/or devices, the FDA also has the right to inspect all project records.

We may record your research information, including results of tests, procedures or questionnaires done for research, in your Froedtert Hospital and/or Medical College of Wisconsin medical record As a result, this research information may be seen by people allowed to see your medical records for healthcare operations or treatment, by those you allow to see your medical records by giving written permission, and by others when required by law.

We will not use your personal health information for a different project without your permission or the permission of a hospital research review board (IRB). Once all personal identification is removed from your health information, and/or biospecimens, the information and/or biospecimens may be used for future research or distributed to another investigator for future research without additional informed consent from you or your legally authorized representative. The information might also be used or released for other purposes without asking you. Results of the project may be presented in public talks or written articles, but no information will be presented that identifies you.

E3. What are the risks of sharing this health information?

One risk of taking part in a research project is that more people will handle your personal health information collected for this project. The research team will make every effort to protect the information and keep it confidential, but it is possible that an unauthorized person might see it. Depending on the kind of information being collected, it might be used in a way that could embarrass you or affect your ability to get insurance. If you have questions, you can talk to the research doctor about whether this could apply to you.

E4. How long will you keep the health information for this project?

If you sign this form, we plan to keep your information for 10 years after the research project ends in case we need to check it again for this project.

E5. Can I cancel my permission to share this health information?

If you change your mind later and do not want us to collect or share your health information, you need to send a letter to Dr. Thomas Chelimsky or Dr. Gisela Chelimsky at *8701 Watertown Plank Road, Department of Neurology, Milwaukee, WI, 53226*. The letter must say that you have changed your mind and do not want the researcher to collect and share your health information. At that time, we may decide that you cannot continue to be part of the project. We may still use the information we have already collected.

F1. FOR MORE INFORMATION ABOUT THE PROJECT

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.

You can look up this project by referring to the ClinicalTrials.gov number NCT03008382 or by asking the research team for a printed copy.

CERTIFICATE OF CONFIDENTIALITY

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. The study team can use this Certificate to legally refuse to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The study team will use the Certificate to resist any demands for information that would identify you, EXECPT as explained below:

The Certificate cannot be used to resist a demand for information from personnel of the United States federal or state government agency sponsoring the project and that will be used for auditing or program evaluation of agency funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). 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 research. If an insurer, medical care provider, or other person obtains your written consent to receive research information, then the researchers will not use the Certificate to withhold that information.

CONSENT TO PARTICIPATE

By signing my name below, I confirm the following:

- I have read (or had read to me) this entire consent document. All of my questions have been answered to my satisfaction.
- The project's purpose, procedures, risks and possible benefits have been explained to me.
- I agree to let the research team use and share the health information and other information gathered for this project.
- I voluntarily agree to participate in this research project. I agree to follow the procedures as directed. I have been told that I can stop at any time.

IMPORTANT: You will receive a signed and dated copy of this consent form. Please keep it where you can find it easily. It will help you remember what we discussed today.

Subject's Name *please print*	**Subject's Signature**	**Date/Time**

Name of Witness *please print*	**Signature of Witness**	**Date/Time**

Rationale for Use of Witness	
☐ Subject has limited/no literacy ☐ Subject has limited English proficiency ☐ Subject has limited/no vision	☐ Sponsor requirement ☐ Other _____

*** Name of person discussing/ obtaining consent** *please print*	**Signature of person discussing/obtaining consent**	**Date/Time**

** A member of the research team trained and authorized by the Principal Investigator to act on her/his behalf in obtaining informed consent according to the protocol. The Principal Investigator is responsible and accountable for the research project.*

Name of Principal Investigator *please print* __ I participated in consent process __ I acknowledge enrollment of this subject into the project	**Signature of Principal Investigator**	**Date/Time**

Attachment 1 – Details of project schedule and procedures

			Visit 1	Visit 2	Visit 3	4 Weeks Post Visit 3
		Week	0	4	12	16
Schedule of Events	Time to complete					
General exam	180 minutes		x			
Physician Exam	10 minutes		x^	x	x^	
Questionnaires	50 minutes		x	x	x	x*
Heart Rate Test	20 minutes		x	x	x	
Breathing Test	10 minutes		x	x	x	
Participant Incentive			x	x	x	
Home Checks, App & Diary	Variable	Done once a week for 12 weeks				

x^ Physician Exam and a pelvic exam will be completed
x* Study team will contact you to complete a general wellbeing check with you.

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Definitions
Interstitial Cystitis/Bladder Pain Syndrome- is a type of chronic pain that affects the bladder. Symptoms include feeling the need to urinate right away, needing to urinate often, and pain with sex

Myofascial Pelvic Pain- is a source of chronic pelvic pain in women and men that is defined by short, tight, tender pelvic floor muscles that include palpable nodules or trigger points that cause referred pain. The pain can be continuous or episodic. MPPS can impact urinary, bowel, and sexual function.

Metoprolol- a beta-blocking drug related to propranolol, used to treat hypertension and angina.

Placebo- A pill that doesn't contain an active drug ingredient, often called a "sugar pill"

Purpose

This project is being done to determine whether brain circuits that control the body affect the clinical course of patients with chronic pelvic pain.

Length

- You will be in this research project for 25 weeks.
- We will also follow up with you 4 weeks after your study completion.

Procedures

After reading and signing this informed consent document, you will be given a pre-screen to determine if you qualify to participate.

List of visits:

- On-site long visits
  - Total Number: 5
  - Total Time: about 3 hours per visit
- At- home monitoring
  - Total Number: 24
  - Total Time: 24 hours, 1x/week

Procedures that will occur at various visits:

Invasive Procedures

- Blood sample collection
- pelvic exam

Non-invasive Procedures

- Medical history questionnaire
- Breathing test
- Heart rate test
- Urine sample collection
- General exam
- Questionnaires.

Risks

This is a brief list of the most commonly seen side effects. The ***full consent form*** after this introduction contains a more complete list of potential research risks.

Metoprolol risks:

- diarrhea, stomach cramping, nausea, vomiting, rashes, blurred vision, muscle cramping, fatigue, depression, heart failure or heart block in patients with heart problems, headaches, dizziness, nightmares, shortness of breath in asthmatics, sexual dysfunction and may cause low or high glucose

Device Risks:

- redness from patches used to record your heart rate
- you may feel dizzy, nauseated, or get a headache from the breathing test

Non-Physical Risks:

- Your personal information and the data collected from you for this study will be kept confidential and, the extent permitted by law, will not be made publicly available. However, there is a risk of loss of confidentiality of your information. You will read more about the protection of your information later in this form. Please ask the study doctor or study staff if you would like to know more about how your information will be protected while you are in this study.

Benefits

We don't know if this project will help you. Your condition may get better but it could stay the same or even get worse.

My Other Options

You do not have to join this project. Your other options may include:

- Joining a different project
- Routine care for this condition
- Getting no treatment for this condition

If you have more questions about this project at any time, you can call Thomas Chelimsky, M.D. Principal Investigator at 414-805-5246 OR Gisela Chelimksy, M.D. at 414-266-3690.

If you have questions about your rights as a participant, want to report any problems or complaints, or offer input, you can call the MCW/Froedtert Hospital Research Subject Advocate at 414-955-8844.

CONSENT TO PARTICIPATE IN RESEARCH

A1. INTRODUCTION – WHY ARE WE ASKING YOU TO PARTICIPATE?

You are invited to participate in this research study because you have been diagnosed with chronic pelvic pain (CPP) such as Interstitial Cystitis/Bladder Pain Syndrome (IC/BPS) or Myofascial Pelvic Pain (MPP) and you are not pregnant. If you have been diagnosed with IC/BPS, you may have experienced symptoms such as painful urination and pressure in the pelvis or bladder. If you have been diagnosed with MPP you may have experienced pain and spasm in the pelvic muscles that may spread to other areas like the abdomen, legs and back.

A total of about 180 people are expected to participate in this research study at Froedtert Hospital (FH) and Northshore Hospital in Chicago. We expect to enroll 150 participants from FH.

The Directors of the project are Dr. Thomas Chelimsky, Dr. Gisela Chelimsky, Dr. Lisa Conant, Dr. Jeffrey Janata, and Dr. Frank Tu in the departments of Neurology and Gastroenterology at MCW, Case Western Reserve University in Cleveland, and Northshore in Chicago. A research team works with Dr. Chelimsky, Dr. Jeffrey Janata and Dr. Frank Tu. You can ask who these people are.

The National Institutes of Health (NIH) is funding this study.

A2. DO I HAVE TO PARTICIPATE?

You can decide whether to take part in this research or not. You are free to say yes or no. If you say no, your regular medical care will not change. Even if you join this project, you do not have to stay in it. You may stop at any time.

A research project is different from routine medical care in three ways: 1) there are extra risks that we will tell you about in this form; 2) you may have some extra medical tests and visits; 3) the research procedures, tests and visits follow a set plan that must be kept.

A3. WHY IS THIS PROJECT BEING DONE?

This drug has been approved by the U.S. Food and Drug Administration, and in this study we want to learn more about how it can affect the brain circuits that control the body and thereby affect the clinical course of patients with chronic pelvic pain.

B1. WHAT WILL HAPPEN IF I PARTICIPATE?

Screening procedures: If you are interested in this research study, you will first complete a pre-screen in person or on the phone to see if you are able to participate. An in-person pre-screen takes place in the MCW Neurology Research Rooms or Neurology Clinic at Froedtert Hospital (FH) or OBGYN clinics at Moorland Reserve Health Center, Westbrook Clinic or St. Joseph's Health Center.

If the screening information shows that you meet the requirements, then you will be able to start. If the screening information shows that you cannot be in the research, the research doctor will discuss other options with you and/or refer you back to your regular doctor.

If you are able to participate, you will complete 5 regular on-site long-visits at weeks 0, 4, 12, 16 and 24. We will also contact you 4 weeks after your study completion to follow-up with you.

The first long visit (baseline evaluation) may occur either today following consent or at another date convenient for you. The baseline evaluation comprises a general and pelvic examination (no speculum), psychological questionnaires and a background history questionnaire. You will complete a pregnancy test (if you are still menstruating), a urine flow measurement, a heart rate recording and a breathing test. You will also be asked to provide a urine sample and a blood sample. The blood sample is optional.

If you join this project, you will be given one of two drugs without knowing exactly which one (a "blinded" project). If you ask to see your health records during this "blinded" project, the research team cannot tell you which drug you are being given. This is because the research team also remains "blinded" about which drug the pharmacy has randomly assigned to you. You would have to wait until the time given below. We cannot do the project unless you agree. However, if the blinded information is needed to treat you, it will be provided to the research doctor.

- What are the blinded options? You will get one of these drugs: metoprolol or placebo
- When can you find out which drug you were given? You can find out at the project end date in June 2021.

Starting at Week 4, you will be randomized to a group that will receive 8 weeks of either placebo (contains no real medicine and we do not expect it will do anything for your health) or metoprolol (a pill that reduces the impact of the brain's "fight or flight" circuits). Metoprolol is in the class of "beta-blockers" commonly used for mild blood pressure control and migraine.

Randomized means that you are put into a group by chance, like flipping a coin. A computer decides the group you are put into. Neither you nor the researcher will choose what group you will be in. You will have an equal chance of being placed in either group. Using randomization helps to improve the chance of determining which (if either) treatment is better. Neither you nor the researcher will know which group you are in, only the pharmacy will know.

You will be asked to stop taking the metoprolol or placebo from Weeks 12 to 16. After that, you will be asked to take the other medication (metoprolol or placebo, whichever you did not receive the first time) for 8 weeks. For example, if you were randomized to start taking metoprolol during Weeks 4-12, you will switch to start taking the placebo for Weeks 16-24.

Summary of Procedures:
At each long visit, you will complete a physician exam, a set of questionnaires, and the following tests: breathing test, heart rate test and a "uroflow measurement." You will also complete a pelvic exam on visits 1, 3 and 5.

The first physician exam will include a detailed medical interview and a pelvic exam. This exam may take up to 45 minutes to complete. If the physician questionnaire is unable to be completed during the study visit, the study doctor may complete this with you over the phone at a more convenient time.

You will be asked to complete questionnaires at each long-visit including: Hospital Anxiety and Depression Scale (HADS), State-Trait Anxiety Inventory (STAI), Thoughts About Symptoms (CSQ), Pennebaker Inventory of Limbic Languidness (PILL), Multidimensional Pain Inventory (MPI), Female Genitourinary Pain Index (FGUPI), Perceived Stress Scale (PSS), PROMIS Social Roles and Activities, PROMIS Physical Function, PROMIS Fatigue, PROMISE Sleep Disturbance, the Holmes-Rahe Life Stress Inventory, the MAPP II Interactive Brief Pain Inventory, and the Covid-19 Questionnaire. You will complete the Childhood and Recent Trauma Events Scale (RTES) during your first long visit only.

You can skip any question that you do not feel comfortable answering on any of the forms. Although the first questionnaires will be completed in the clinic to keep your answers private, the next will be completed while you are at home. We cannot guarantee that those responses will be kept private and there is a chance that answers may be seen by those who live in or visit your home. If your score is suggestive of emotional problems, study directors Dr. Thomas Chelimsky or Dr. Gisela Chelimsky or study Co-Investigator and Psychologist, Dr. Lisa Conant will provide you with places to help get treatment for these issues within 1 week of your participation. The researchers are required by law to report any abuse or neglect (or suspicion of abuse or neglect) if you mention it to the researchers or if it is suspected.

You will complete a “breathing test” in the MCW Neurology Research Rooms at FH. To complete this test, you will have wrist straps secured to a table and asked to breathe in deeply and out forcefully through a tube. You will have a small band on your arm to measure your heart rate and blood pressure. You will complete 4 cycles of breathing: two cycles while lying down flat and two cycles while leaning slightly forward.

The heart rate variability (HRV) and active posture change (ACP) recording will take about 20 minutes to complete. You will complete this recording at each long-visit and each week that you are in this study. Heart rate will be recorded with an eMotion Faros 360° portable ECG device. It is small and lightweight, with 3-5 small adhesive electrode patches placed on the skin of your chest and torso. You will lie down flat on a bed and rest for 10 minutes before the recording starts. After that, you will lie down for 5 more minutes while your heartbeat is recorded for 5 minutes. You will be asked to stand up as quickly as you can and stand still for an additional 5 minutes. You may sit down if this test becomes too much for you to complete. Coded 24-hour HRV and ACP recordings will be sent to Dr. Julian Thayer’s research group at University of California Irvine for analysis. Your sample will be labeled by a number and will not contain any information that can be used to directly identify you.

A “uroflow measurement” measures the volume of urine, how long it takes to be released from the body and the speed. The uroflow measurement requires you to urinate on a special toilet in the MCW Neurology Research Rooms at FH. The toilet contains sensors that measure the speed of the urine flow and amount of urine. About one hour prior to this test you will be asked to drink a quart of fluid.

Weekly Home Checks will occur once a week for 24 weeks following consent. Each week, you will complete a heart rate recording just before you go to bed. The heart rate recording will help us to study how your heart rate changes throughout the day. You will place the patches on your chest and torso to match the image found on the instruction sheet provided to you as soon as you get up in the morning. A researcher will remind you via skype, email, text or telephone to complete the heart rate recording. The researcher will coach you the first few times you

complete this recording until you are comfortable completing it on your own. The researcher will ask you to lie down flat on your bed for 15 minutes. After that, the researcher will instruct you to stand up as quickly as you can in front of your bed for another 5 minutes. You can sit down if you become too dizzy. You will need to bring the Faros 360 device with you to each of your in-person visits. The data from your heart rate recording will be uploaded to a secure server by a member of the research team.

You will complete the following each week from home: a 24-hour heart rate (HR) recording using the eMotion Faros 360° ECG device, the 24-hour voiding diary, answer a set of questions using the ICECAN mobile App installed on a preloaded smartphone, and complete questionnaires (those mentioned previously) that are sent to your personal e-mail account via a secure Internet connection. If in any case you are unable to complete the questionnaires online, you will be asked to return paper copies of the questionnaires at your next in-person follow-up visit.

The 24-hour voiding diary consists of tracking how much liquid comes in and out of your body in a 24-hour period, and how often you void. You will be required to measure the amount of everything you drink. You will also record the time and amount of each void for the 24-hour period. A special measuring “hat” that fits over the toilet seat will help you measure each void.

You will also complete a Daily Flare Question which asks about flare activity, management and if the flares are affecting you. These Flare Questions will be monitored via phone calls and recording in the EMA application on the smartphone.

Every week for 24 weeks you will repeat the 24-hr HR recording, as described above, to compare the HRV recording done at home to the one performed at the matching on-site visit.

If you end up not answering some of the EMA questions, we will be asking you the following: At any time during the study, did your pain affect your ability to answer any of the EMA questions? When you didn't answer the EMA questions, what percentage of time was it due to pain? These questions will be asked at each in-clinic visit appointment.

During your follow-up visits at weeks 4, 12, 16, and 24, you will arrive to the MCW Neurology Research Rooms to repeat the following: a review of your symptoms, a brief physician exam, a uroflow measurement, questionnaires, and heart rate recording. You will complete the breathing test in the MCW Neurology Research Rooms with a member of the research team present. You will also complete a repeat pelvic examination at Weeks 12 and 24.

Blood will be drawn (optional) and urine will be collected (~ 50 mL, a little more than 3 tablespoons) at each in-person visit at weeks 0, 4, 12, 16, and 24. We will determine (1) if immune or inflammatory factors play a role in your pain cycles and (2) if energy production in your cells might be impaired.

A portion of your blood plasma/serum and urine will be sent to Dr. Lori Birder’s laboratory at the University of Pittsburgh for additional related analysis. Both of your samples will be labeled by a number and will not contain any information that can be used to directly identify you. This portion of the study is critical for us to gather new information about pelvic pain, which is very poorly understood. We highly encourage you to participate in this portion of the study. However,

given how difficult it can be to obtain blood from some people with IC/BPS, we do allow you to opt out of the blood draw portion of this study and still participate in the other parts.

Please **initial** your choice below regarding blood sample collection.

_____ Yes, I agree to provide blood samples for this research project.
INITIALS

_____ No, I do not agree to provide blood samples for this research project.
INITIALS

B2. HOW LONG WILL I BE IN THE PROJECT?

⇒ You will be in this research project for about 25 weeks.
⇒ You will take the drug/placebo for a total of 16 weeks.
⇒ We will also follow-up with you 4 weeks after your study completion.

B3. CAN I STOP BEING IN THE PROJECT?

You are free to withdraw from the project at any time. If you leave, your regular medical care will not change. If you are thinking about leaving, please tell the research doctor.
⇒ You will be asked to return any unused research drug and its containers.

The research doctor may take you out of this project at any time. This would happen if:

- They think it is in your best interest.
- You do not follow the project rules.
- The whole project is stopped.

If this happens, the research doctor will tell you.

B4. ARE THERE ANY SPECIAL INSTRUCTIONS WHILE I AM IN THE PROJECT?

It is important that you stay on the same medication regimen while you are participating in this study unless directed by your physician. Please notify the study Principal Investigators if your regimen changes.

C1. WHAT HEALTH RISKS OR PROBLEMS CAN I EXPECT FROM THE PROJECT?

There are risks to taking part in any research project. There is a risk that you may get metoprolol and that it does not help your condition or may make it worse. There also may be problems (side effects) we do not know about yet, from metoprolol itself, or how it combines with other drugs you are taking. If we learn about new important side effects, we will tell you.

We watch everyone in the project for problems (side effects). **You need to tell the research doctor or a member of the research team immediately if you experience any problems, side effects, or changes in your health.** If you have:

- Shortness of breath

- Wheezing
- Swelling of the hands, feet, ankles, or lower legs
- Unusual weight gain
- Fainting
- Rapid, pounding, or irregular heartbeat

Call Dr. Thomas Chelimsky immediately at 414-955-0619. In an emergency, call 911.

C2. RISKS OF Metoprolol

Metoprolol itself may cause problems (side effects). Side effects may be mild or very serious. Some can last a long time or never go away.

The side effects that other people have experienced so far with metoprolol are:

- *Dizziness or lightheadedness*
- *Diarrhea*
- *Blurred Vision*
- *Muscle cramping*
- *Fatigue*
- *Headaches*
- *Nightmares*
- *Sexual dysfunction*
- *Low or high glucose*
- *Tiredness*
- *Depression*
- *Nausea*
- *Dry mouth*
- *Stomach pain*
- *Vomiting*
- *Gas or bloating*
- *Heartburn*
- *Constipation*
- *Rash or itching*
- *Cold hands and feet*
- *Runny nose*
- *Heart failure or heart block in patients with heart problems*
- *Shortness of breath in asthmatics*

C3. OTHER RISKS OF THIS RESEARCH PROJECT

Other procedures that are part of the research also involve some risks: There is a chance that you may develop redness from the patches used to record your heart rate during the heart rate test. These red marks are temporary and generally go away within an hour. If you are allergic to adhesives, you cannot participate in this study.

You may feel anxious, dizzy, nauseated or get a headache from breathing in and out as instructed during the breathing test.

The physician exam includes a tender point evaluation that is considered to be standard of care for myofascial pain disorders such as fibromyalgia and may lead to tenderness and pain at the site of contact.

You may develop pain/bruising at the site of your blood draw. You also may feel dizzy during/after having your blood drawn.

The psychological questionnaires may upset you. You can skip any question that you do not want to answer. If your responses are suggestive of emotional problems, a study Investigator will discuss your response(s) and will document this discussion in your medical record. The Investigator will provide you with places to help get treatment.

C4. REPRODUCTIVE RISKS

Risks to women who could become pregnant
The drug Metoprolol in this project might affect a baby, before or after the baby is born. We do not know if the metoprolol causes harm to a baby, so we do not want anyone who might be pregnant to enter the project. You should not become pregnant or nurse a baby while in this project. You must tell the research doctor right away if you think you are pregnant. You will be asked to have a pregnancy test to be sure you are not pregnant at the start of the project

Birth control methods for all subjects
Check with the research doctor about the birth control methods needed for this project and how long to use them. Some methods might not be good enough for this project. If you are having sex that could lead to pregnancy, you should use birth control while you are in this project. This may include:

- Not having vaginal sex (abstinence)
- Taking birth control pills orally
- Having birth control shots or patches such as Depo-Provera
- Surgical sterilization (hysterectomy or tubal ligation)
- Use of an intrauterine device (IUD)
- Use of diaphragm with contraceptive jelly
- Use of condoms with contraceptive foam
- Use of diaphragm with condoms (“double barrier”)
- Limiting sexual activity to a male partner who has had a vasectomy

You should continue using birth control for 1 month after stopping the test drug metoprolol.

C5. ARE THERE ANY BENEFITS TO TAKING PART IN THE PROJECT?

This study could help you, as we believe beta-blockers may change the brain circuits that control your body and therefore your pain responses, be we do not know this, and there is no guarantee. That is why we are doing the study. We believe the information from this study will help us develop a better understanding of brain circuits that affect chronic pelvic pain.

D1. ARE THERE ANY COSTS TO BEING IN THE PROJECT?

There are no costs to you for any of the visits, drugs or services you receive in this project. All costs will be paid by the project. If you have questions regarding costs, please contact Dr. Chelimsky.

If you participate in this research, the costs of any necessary emergency medical treatment in the event of a research-related injury will be billed to you or your health insurance.

D2. WILL I BE PAID FOR PARTICIPATING IN THE PROJECT?

You will receive $400 for completing at least 80% of the required items for the five major visits at the sites and 25 minor at-home monitoring sessions

- You will receive a $50 payment on a preloaded credit card after completing all study tasks and Visit 1
- You will receive a $60 payment on a preloaded credit card after completing all study tasks and Visit 2
- You will receive a $70 payment on a preloaded credit card after completing all study tasks and Visit 3
- You will receive a $80 payment on a preloaded credit card after completing all study tasks and Visit 4
- You will receive a $140 payment on a preloaded credit card after completing all study tasks and Visit 5 and returning the Faros ECG monitor and the pre-loaded Smartphone.

You may be given the option to redo a study visit if the study data are incomplete or if you need to stop the study drug. If you redo a visit, you will receive payment for the visit which was repeated in the same amount as mentioned above.

If you complete the baseline evaluation but are found to not be eligible to participate in this study, you will be mailed a $25 check.

Travel reimbursements:

- If travel time is between 1 and 2 hours, you will be paid at a rate of $20 per visit on a preloaded credit card
- If travel time is between 2 and 4 hours, you will be paid at a rate of $40 per visit on a preloaded credit card

To pay you, we need your social security number. Any payment may be reportable as income on your taxes.

D3. WHAT OTHER HEALTHCARE CHOICES DO I HAVE?

You do not have to join this project. You are free to say yes or no. If you do not join this project, your research doctor can discuss other healthcare choices with you.

The drug offered to you may also be available without being in any research project.

The research doctor can explain both the possible benefits and the risks of other options that are available to you.

D4. WILL I BE GIVEN NEW INFORMATION ABOUT THE PROJECT?

If we learn any important new information about metoprolol that might change your mind about being in the project, we will tell you about it right away. You can then decide if you want to stay in the project.

When research data are collected and analyzed, there is the chance of finding something clinically relevant. There may be benefits to learning such results (such as early detection and treatment of a medical condition), but there are risks as well (such as feeling worried about a finding for which no treatment is required or appropriate).

In this study, you will be informed of any findings of possible clinical significance that may be discovered during review of results from your research data. The results of your research data will not be placed in your medical record.

The results from the data we collect in this research study are not the same quality as what you would receive as part of your health care. The data will not be reviewed by a physician who normally reads such results. We will provide you with this information so that you may discuss it with your primary care physician.

After the project has been completed, we will notify you of when the results will be available to the public.

D5. WHAT HAPPENS IF I AM INJURED BECAUSE I TOOK PART IN THE PROJECT?

Emergency medical treatment for injuries directly related to your participation in this research project will be provided to you. You or your health insurance will be billed for the costs of this emergency treatment. MCW will decide on a case by case basis if they will reimburse you or your insurer for emergency treatment costs. If your research-related injury requires medical care beyond this emergency treatment, you or your insurer will be responsible for the costs of this follow-up care.

At this time, there is no plan for any additional financial payments.

If you believe that you have been injured because of your participation in this project, contact the research doctors right away. Contact information: Thomas Chelimsky, MD, 414-955-0619 or Gisela Chelimsky, MD, 414-266-3690.

Nothing in this consent form affects any legal rights you may have nor does it release the investigator, the sponsor, the institution, or its agents from liability for negligence.

D6. WHO CAN ANSWER MY QUESTIONS ABOUT THE PROJECT?

- If you have more questions about this project at any time, you can call Thomas Chelimsky at 414-955-0619 or Gisela Chelimsky at 414-266-3690.
- If you have questions about your rights as a research participant, want to report any problems or complaints, or offer input, you can call the MCW/Froedtert Hospital Research Subject Advocate at 414-955-8844.

E. PERMISSION TO COLLECT, USE AND SHARE HEALTH INFORMATION

E1. What health information will be collected and used for this project?

To be in this research project, the research team needs your permission to access, collect and use some of your health information. If you say no, you cannot be in the project. This information may come from questions we ask, forms we ask you to fill out, or your medical record, as described below. We will only collect and use information needed for the project.

The protected health information (PHI) originates from services you will or have received at one or more of the following locations: the Medical College of Wisconsin (MCW); BloodCenter of Wisconsin (BCW); Children's Hospital of Wisconsin (CHW); any Froedtert Health Affiliate-Froedtert Memorial Lutheran Hospital (FMLH), Inc.; Community Memorial Hospital (CMH) Menomonee Falls, Inc.; St. Joseph's Community Hospital (SJH) West Bend, Inc.; Froedtert & The Medical College of Wisconsin Community Physicians Clinics, Inc. (FMCWCP); the West Bend Surgery Center, LLC; and the Froedtert Surgery Center, LLC.

The health information to be collected and used for this project is:

To do this research study, we need your permission to collect and use some of your health information, or you cannot be in the study. This information may come from questions we ask, forms we ask you to fill out, or your medical records of the care you receive from this project. Health information such as your clinical and laboratory information will be collected and shared. Researchers will also access your entire medical record for relevant study data such as your medical history, radiology scans, or lab data to help analyze the data collected. We will only collect and use information needed for the study.

E2. Who will see the health information collected for this project?

The only MCW/Froedtert Hospital employees allowed to handle your health information are those on the research team, those on the Institutional Review Board (IRB) and those who check on the research activities to make sure the hospital's rules are followed.

If the costs of any necessary emergency medical treatment in the event of a research-related injury are billed to your health insurance, your health information may need to be disclosed to the insurer for billing purposes.

The research team may share your information with people who don't work at MCW/Froedtert Hospital because they planned, pay for, or work with us on this project. The federal Privacy Rule may no longer protect your health information once it leaves MCW/Froedtert Hospital. For this project, we plan to share information with those doctors, researchers or government representatives working with us on this project at the institutions or companies listed here:

- U.S. Food and Drug Administration, Rockville, MD
- Northshore Hospital in Chicago, IL Medical College of Wisconsin & Froedtert Hospital
- Case Western Reserve University in Cleveland, OH

- Multi-Disciplinary Approach to the study of Chronic Pelvic Pain (MAPP) Research Network, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)

Because this project involves the use of drugs and/or devices, the FDA also has the right to inspect all project records.

We may record your research information, including results of tests and procedures done for research, in your Froedtert Hospital and/or Medical College of Wisconsin medical record. As a result, this research information may be seen by people allowed to see your medical records for healthcare operations or treatment, by those you allow to see your medical records by giving written permission, and by others when required by law.

We will not use your personal health information for a different project without your permission or the permission of a hospital research review board (IRB). Once all personal identification is removed from your health information and/or biospecimens, the information and/or biospecimens may be used for future research or distributed to another investigator for future research without additional informed consent from you or your legally authorized representative. The information might also be used or released for other purposes without asking you. Results of the project may be presented in public talks or written articles, but no information will be presented that identifies you.

E3. What are the risks of sharing this health information?

One risk of taking part in a research project is that more people will handle your personal health information collected for this project. The research team will make every effort to protect the information and keep it confidential, but it is possible that an unauthorized person might see it. Depending on the kind of information being collected, it might be used in a way that could embarrass you or affect your ability to get insurance. If you have questions, you can talk to the research doctor about whether this could apply to you.

E4. How long will you keep the health information for this project?

If you sign this form, we plan to keep your information for 10 years after the research project ends in case we need to check it again for this project.

E5. Can I cancel my permission to share this health information?

If you change your mind later and do not want us to collect or share your health information, you need to send a letter to Dr. Thomas Chelimsky or Dr. Gisela Chelimsky at *8701 Watertown Plank Road, Department of Neurology, Milwaukee, WI, 53226*. The letter must say that you have changed your mind and do not want the researcher to collect and share your health information. At that time, we may decide that you cannot continue to be part of the project. We may still use the information we have already collected.

F1. FOR MORE INFORMATION ABOUT THE PROJECT

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.

You can look up this project by referring to the ClinicalTrials.gov number NCT03008382 or by asking the research team for a printed copy.

CERTIFICATE OF CONFIDENTIALITY

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. The study team can use this Certificate to legally refuse to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The study team 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 federal or state government agency sponsoring the project and that will be used for auditing or program evaluation of agency funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). 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 research. If an insurer, medical care provider, or other person obtains your written consent to receive research information, then the researchers will not use the Certificate to withhold that information.

CONSENT TO PARTICIPATE

By signing my name below, I confirm the following:

- I have read (or had read to me) this entire consent document and attachment 1. All of my questions have been answered to my satisfaction.
- The project's purpose, procedures, risks and possible benefits have been explained to me.
- I agree to let the research team use and share the health information and other information gathered for this project.
- I voluntarily agree to participate in this research project. I agree to follow the procedures as directed. I have been told that I can stop at any time.

IMPORTANT: You will receive a signed and dated copy of this consent form. Please keep it where you can find it easily. It will help you remember what we discussed today.

Subject's Name *please print*	**Subject's Signature**	**Date/Time**

Name of Witness *please print*	**Signature of Witness**	**Date/Time**
Rationale for Use of Witness ☐ Subject has limited/no literacy ☐ Subject has limited English proficiency ☐ Subject has limited/no vision	☐ Sponsor requirement ☐ Other _____	

*** Name of person discussing/ obtaining consent** *please print*	**Signature of person discussing/obtaining consent**	**Date/Time**

** A member of the research team trained and authorized by the Principal Investigator to act on her/his behalf in obtaining informed consent according to the protocol. The Principal Investigator is responsible and accountable for the research project.*

Name of Principal Investigator *please print* __ I participated in consent process __ I acknowledge enrollment of this subject into the project	**Signature of Principal Investigator**	**Date/Time**

Attachment 1 – Details of project schedule and procedures

			Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	4 Weeks Post Visit 5
		Week	0	4	12	16	24	28
Schedule of Events	Time to complete							
General exam	180 minutes		x					
Physician Exam	10 minutes		x^	x	x^	x	x^	
Questionnaires	50 minutes		x	x	x	x	x	
Heart Rate Test	20 minutes		x	x	x	x	x	
Breathing Test	10 minutes		x	x	x	x	x	
Participant Incentive			x	x	x	x	x	
Home Checks, App & Diary	Variable	Done once a week for 24 weeks						x*

x^ Physician Exam and a pelvic exam will be completed
x* Study team will contact you to complete a general wellbeing check with you.

EFFECTIVE

6/8/2021

MCW/FH IRB

Medical College of Wisconsin and Froedtert Hospital
INTRODUCTION TO THE INFORMED CONSENT

Name of Subject: _____

Study Title: Interstitial Cystitis-Examination of the Central Autonomic Network (ICECAN)

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Watertown Plank Road Milwaukee,
WI 53226

You are invited to take part in this research. You can decide whether to take part in this project or not. You are free to say yes or no. If there is anything that you do not understand, please ask questions.

Definitions

Interstitial Cystitis/Bladder Pain Syndrome- is a type of chronic pain that affects the bladder. Symptoms include feeling the need to urinate right away, needing to urinate often, and pain with sex

Myofascial Pelvic Pain- is a source of chronic pelvic pain in women and men that is defined by short, tight, tender pelvic floor muscles that include palpable nodules or trigger points that cause referred pain. The pain can be continuous or episodic. MPPS can impact urinary, bowel, and sexual function.

Purpose

This project is being done to understand how the brain controls the bodies of women who are not diagnosed with IC or MPP compared to women who are diagnosed with IC/BPS or MPP.

Length

- You will be in this research project sub-study for about 4.5 hours while you complete the safety forms, pregnancy tests (if applicable) and fMRI scans.

Procedures *or* Activities

If you choose to participate in this research sub-study, you will first complete an MRI safety form to make sure that it is safe for you to participate in this study.

List of visits:

- MRI Visits
  - Total Number: 3
  - Total Time: 4.5 hours

Procedures/Activities that will occur at various visits:

Invasive Procedures
- None

Non-invasive Procedures
- Pregnancy Tests
- MRI Scans
- MRI Experience Questionnaire

Risks

This is a brief list of the most commonly seen risks The ***full consent form*** after this introduction contains a more complete list of potential research risks.

Device risks:

- Headaches
- Tinnitus
- Claustrophobia

Benefits

This project will not help you, but we hope the information from this project will help us develop a better understanding of IC/BPS and MPP.

My Other Options

You do not have to join this project. You are free to say yes or no.

- Whether or not you join this project, you are free to seek services from this or other agencies.
- Whether or not you join this project, your usual medical services will not change.

If you have more questions about this project at any time, you can call Thomas Chelimsky, M.D. Principal Investigator at 414-805-5246 or Gisela Chelimsky, M.D. at 414-266-3690.

If you have questions about your rights as a participant, want to report any problems or complaints, or offer input, you can call the MCW/Froedtert Hospital Research Subject Advocate at 414-955-8844.

CONSENT TO PARTICIPATE IN RESEARCH

A1. INTRODUCTION – WHY ARE WE ASKING YOU TO PARTICIPATE?

You are being invited to participate in this research because you have been diagnosed with Interstitial Cystitis (IC), Myofascial Pelvic Pain (MPP) and you are not pregnant. We believe the brain plays a major role in this type of pain and would like to learn more about what it is doing. A total of 18 women who have not been diagnosed with IC/BPS or MPP and 36 women who have been diagnosed with IC/BPS or MPP.

A total of about 54 people are expected to participate in this research study at the Medical College of Wisconsin/Froedtert Hospital.

The Directors of the project are Dr. Thomas Chelimsky, Dr. Gisela Chelimsky, Dr. Sumana Koduri, and Dr. Camila Bomtempo in the Departments of Neurology, Pediatric Gastroenterology, and the Department of OB/GYN. A research team works with them. You can ask who these people are.

The National Institute of Health, a government agency, is funding the research.

A2. DO I HAVE TO PARTICIPATE?

You can decide whether to take part in this research or not. You are free to say yes or no. If you say no, your regular medical care will not change. Even if you join this project, you do not have to stay in it. You may stop at any time.

A3. WHY IS THIS PROJECT BEING DONE?

The purpose of this project is to understand how the brain controls the bodies of women who are not diagnosed with IC or MPP compared to women who are diagnosed with IC/BPS or MPP.

B1. WHAT WILL HAPPEN IF I PARTICIPATE?

MRI (Magnetic Resonance Imaging) is a way for us to see inside your body. MRI uses a powerful magnet, radio waves and a computer to produce detailed pictures of organs, bones and other internal body structures. For the MRI, you will lie on a table inside a scanner tube for about 60 minutes, while the scanner moves the reading unit over the areas of your body to be scanned.

If you choose to participate in this research sub-study, you will first complete an MRI safety form to make sure that it is safe for you to participate in this study. If you are able to participate, you will complete a pregnancy test prior to each scan (if applicable) and a total of 3 fMRI scans. You will complete one scan within the four weeks prior to visit 2, another 12 weeks later and the last one 24 weeks into this study. Each fMRI session will take about 60 minutes to complete. The MRI Experience Questionnaire (MEQ) is completed after the fMRI procedure to assess your experience during the MRI.

As a precaution, you will complete a pregnancy test (if applicable) and an MRI safety screening form at each visit before you enter the scanner room. This test must be negative for you to safely continue with the scan. You will also be given the option of lying in a mock (fake) scanner to prepare yourself for the fMRI before completing it.

Information collected in clinic (form you fill out, information about your symptoms) may be used for research.

There is no penalty for not participating.

B2. HOW LONG WILL I BE IN THE PROJECT?

You will be in this research project for about 4.5 hours while you complete the safety forms, pregnancy tests (if applicable) and fMRI scans.

B3. CAN I STOP BEING IN THE PROJECT?

You may stop at any time. If you decide to leave the project, please let the research team know.

You may stop at any time, including during the MRI scan.

The research doctor may stop your participation in the project at any time for any reason without your consent. He / She will tell you if this happens.

C1. WHAT HEALTH RISKS OR PROBLEMS CAN I EXPECT FROM THE PROJECT?

We watch everyone in the project for unexpected problems. **You need to tell the research doctor or a member of the research team immediately if you experience any problems or become too upset.**

There is a chance that you could be injured if you fail to tell the research staff that you have any of the following and try to complete the fMRI session:

• A pacemaker or any other metal, such as an aneurysm clip, ear implants, or nerve stimulator in your body. If you do have any of these things then you cannot have an MRI and will be considered ineligible for the study. It is also important to know if you have any metal on your body. If a piece of metal (such as a tool or key) is released into the MRI room, you could be injured.

Certain risks and discomforts may be associated with fMRI.

• There is no exposure to X-rays or radioactivity during MRI (Magnetic Resonance Imaging), and the risk of injury is very low. However, MRI is not safe for everyone. Serious injury or death can result if you go into the scanner with certain metal objects in, on, or attached to your body. For example, it is not safe to have an MRI scan if you have a cardiac pacemaker or defibrillator.
• The loud "banging" sounds made by the MRI scanner may cause you to have a headache or to develop ringing in your ears called tinnitus. To reduce this risk, we will provide you with earplugs.

• The loud “banging” sounds made by the MRI scanner can cause hearing damage, but with earplugs properly worn, there is no known risk of permanent hearing damage. Rarely, you may find that your hearing is less sensitive for several days after an MRI scan. When this occurs, hearing should return to normal within a few days.
• You may experience some discomfort because you are lying still for a long time, or because of the padding used to keep your head from moving. You may also become hot or dizzy.
• You may also experience claustrophobia (fear of closed or narrow spaces) in the MRI scanner. The scanner operator will be in constant contact with you, and you can be removed quickly from the scanner if necessary.
• In addition, there may be some unknown or unanticipated risks or discomforts in addition to those specified above because some of the procedures are relatively new and are attempts to advance medical knowledge. Every known precaution will be taken to ensure your personal safety and to minimize discomfort.

Many questions will be asked as part of your safety screening. If you prefer not to answer a question because it causes you to be upset, you may tell the study team member and not provide that information. If your responses are suggestive of emotional problems, a study Investigator will discuss your response(s) and will document this discussion in your medical record. The Investigator will provide you with places to help get treatment.

Another risk may be loss of confidentiality. Every effort will be made to keep your research records confidential but we cannot guarantee it. Depending on the kind of information being collected, if your research information were accidentally seen, it might be used in a way that could embarrass you or affect your ability to get insurance. If you have questions, you can talk to the project director about whether this could apply to you.

C2. RISKS TO WOMEN WHO COULD BECOME PREGNANT

The MRI in this project might affect a baby, before or after the baby is born. We do not know if the MRI would cause harm to a baby, so we do not want anyone who might be pregnant to enter the project. You should not become pregnant or nurse a baby while in this project. You must tell the research doctor right away if you think you are pregnant. You will be asked to have a pregnancy test to be sure you are not pregnant at the start of the project.

If you become pregnant during the project, you will be dropped from participation for safety reasons. We ask that you inform the research doctor immediately. The research doctor will ask you for written permission to obtain information from you or your obstetrician on your pregnancy and the health of the baby.

Birth control methods for all subjects
Check with the research doctor about the birth control methods needed for this project and how long to use them. Some methods might not be good enough for this project. If you are having sex that could lead to pregnancy, you should use birth control while you are in this project. This may include:

- Not having vaginal sex (abstinence)
- Taking birth control pills orally
- Having birth control shots or patches such as Depo-Provera
- Surgical sterilization (hysterectomy or tubal ligation)

- Use of an intrauterine device (IUD)
- Use of diaphragm with contraceptive jelly
- Use of condoms with contraceptive foam
- Use of diaphragm with condoms ("double barrier")
- Limiting sexual activity to a male partner who has had a vasectomy

C3. ARE THERE ANY BENEFITS TO TAKING PART IN THE PROJECT?

This project will not help you, but we hope the information from this project will help us develop a better understanding of IC/BPS and MPP.

D1. ARE THERE ANY COSTS TO BEING IN THE PROJECT?

There are no costs to you for any of the visits or services you receive in this project. If you have questions regarding costs, please contact Dr. Chelimsky. If you participate in this research, the costs of any necessary emergency medical treatment in the event of a research-related in jury will be billed to you or your health insurance.

D2. WILL I BE PAID FOR PARTICIPATING IN THE PROJECT?

You will be paid a total of $225. $75 after completion of each scanning visit on a preloaded credit card. To pay you, we need your social security number. Any payment may be reportable as income on your taxes.

D3. WHAT OTHER HEALTHCARE CHOICES DO I HAVE?

You do not have to join this project. You are free to say yes or no. Whether or not you join this project, you are free to seek services from this or other agencies. Whether or not you join this project, your usual medical services will not change

D4. WILL I BE GIVEN NEW INFORMATION ABOUT THE PROJECT?

After the project has been completed, we will notify you of when the results will be available to the public.

When research data are collected and analyzed , there is the chance of finding something clinically relevant. There may be benefits to learning such results (such as early detection and treatment of a medical condition), but there are risks as well (such as feeling worried about a finding for which no treatment is required or appropriate).

In this study, you will be informed of any findings of possible clinical significance that may be discovered during review of results from your research data. The results of your research data will not be placed in your medical record.

The results from the data we collect in this research study are not the same quality as what you would receive as part of your health care. The data will not be reviewed by a physician who normally reads such results. We will provide you with this information so that you may discuss it with your primary care physician.

D5. WHAT HAPPENS IF I AM INJURED BECAUSE I TOOK PART IN THE PROJECT?

Emergency medical treatment for injuries directly related to your participation in this research project will be provided to you. You or your health insurance will be billed for the costs of this emergency treatment. MCW will decide on a case by case basis if they will reimburse you or your insurer for emergency treatment costs. If your research-related injury requires medical care beyond this emergency treatment, you or your insurer will be responsible for the costs of this follow-up care.

At this time, there is no plan for any additional financial payments.

If you believe that you have been injured because of your participation in this project, contact the research doctors right away. Contact information: Dr. Thomas Chelimsky at 414-805-5246 or Dr. Gisela Chelimsky at 414-266-3690.

Nothing in this consent form affects any legal rights you may have nor does it release the investigator, the sponsor, the institution, or its agents from liability for negligence.

D6. WHO CAN ANSWER MY QUESTIONS ABOUT THE PROJECT?

- If you have more questions about this project at any time, you can call Dr. Thomas Chelimsky at 414-805-5246, Dr. Gisela Chelimsky at 414-266-3690.

- If you have questions about your rights as a research participant, want to report any problems or complaints, or offer input, you can call the MCW/Froedtert Hospital Research Subject Advocate at 414-955-8844.

E. PERMISSION TO COLLECT, USE AND SHARE HEALTH INFORMATION

E1. What health information will be collected and used for this project?

To be in this research project, the research team needs your permission to access, collect and use some of your health information. If you say no, you cannot be in the project. This information may come from questions we ask, forms we ask you to fill out, or your medical record, as described below. We will only collect and use information needed for the project.

The protected health information (PHI) originates from services you will or have received at one or more of the following locations: the Medical College of Wisconsin (MCW); BloodCenter of Wisconsin (BCW); Children's Hospital of Wisconsin (CHW); any Froedtert Health Affiliate-Froedtert Memorial Lutheran Hospital (FMLH), Inc.; Community Memorial Hospital (CMH) Menomonee Falls, Inc.; St. Joseph's Community Hospital (SJH) West Bend, Inc.; Froedtert & The Medical College of Wisconsin Community Physicians Clinics, Inc. (FMCWCP); the West Bend Surgery Center, LLC; and the Froedtert Surgery Center, LLC.

The health information we will collect and use for this project is:
Health information collected during this project, such as safety screening form and fMRI scans. Researchers will also access your medical record for relevant study data such as your medical history, radiology scans, or lab data to help analyze the data collected. The brain scans will not

be used to diagnose any existing brain disorders.

E2. Who will see the health information collected for this project?

The only people allowed to handle your health information are those on the research team at MCW/Froedtert Hospital, those on the Institutional Review Board (IRB) and those who check on the research activities to make sure the hospital's rules are followed.

If the costs of any necessary emergency medical treatment in the event of a research-related injury are billed to your health insurance, your health information may need to be disclosed to the insurer for billing purposes.

The research team may share your information with people who are not part of the research team because they planned, pay for, or work with us on this project. The federal Privacy Rule may no longer protect your health information once it leaves MCW/Froedtert Hospital. For this project, we plan to share information with those doctors, researchers or government representatives working with us on this project at the institutions or companies listed here:

• U.S. Food and Drug Administration, Rockville, MD
• Northshore Hospital in Chicago, IL
• Case Western Reserve University in Cleveland, OH
• Multi-Disciplinary Approach to the study of Chronic Pelvic Pain (MAPP) Research Network, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)

Because this project involves the use of drugs and/or devices, the FDA also has the right to inspect all project records.

We may record your research information, including results of tests, procedures or questionnaires done for research, in your Froedtert Hospital and/or Medical College of Wisconsin medical record. As a result, this research information may be seen by people allowed to see your medical records for healthcare operations or treatment, by those you allow to see your medical records by giving written permission, and by others when required by law.

We will not use your personal health information for a different project without your permission or the permission of a hospital research review board (IRB). Once all personal identification is removed from your health information and/or biospecimens, the information and/or biospecimens may be used for future research or distributed to another investigator for future research without additional informed consent from you or your legally authorized representative. The information might also be used or released for other purposes without asking you. Results of the project may be presented in public talks or written articles, but no information will be presented that identifies you.

E3. What are the risks of sharing this health information?

One risk of taking part in a research project is that more people will handle your personal health information collected for this project. The research team will make every effort to protect the information and keep it confidential, but it is possible that an unauthorized person might see it. Depending on the kind of information being collected, it might be used in a way that could

embarrass you or affect your ability to get insurance. If you have questions, you can talk to the research doctor about whether this could apply to you.

E4. How long will you keep the health information for this project?

If you sign this form, we plan to keep your information for 10 years after the research project ends in case we need to check it again for this project.

E5. Can I cancel my permission to share this health information?

If you change your mind later and do not want us to collect or share your health information, you need to send a letter to Dr. Thomas Chelimsky or Dr. Gisela Chelimsky at *8701 Watertown Plank Road, Milwaukee, WI 53226*. The letter must say that you have changed your mind and do not want the researcher to collect and share your health information. At that time, we may decide that you cannot continue to be part of the project. We may still use the information we have already collected.

F1. FOR MORE INFORMATION ABOUT THE PROJECT

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. You can look up this project by referring to the ClinicalTrials.gov number NCT03008382 or by asking the research team for a printed copy.

CERTIFICATE OF CONFIDENTIALITY

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. The study team can use this Certificate to legally refuse to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The study team will use the Certificate to resist any demands for information that would identify you, EXECPT as explained below:

The Certificate cannot be used to resist a demand for information from personnel of the United States federal or state government agency sponsoring the project and that will be used for auditing or program evaluation of agency funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). 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 research. If an insurer, medical care provider, or other person obtains your written consent to receive research information, then the researchers will not use the Certificate to withhold that information.

CONSENT TO PARTICIPATE

By signing my name below, I confirm the following:

- I have read (or had read to me) this entire consent document. All of my questions have been answered to my satisfaction.
- The project's purpose, procedures, risks and possible benefits have been explained to me.
- I agree to let the research team use and share the health information and other information gathered for this project.
- I voluntarily agree to participate in this research project. I agree to follow the procedures as directed. I have been told that I can stop at any time.

IMPORTANT: You will receive a signed and dated copy of this consent form. Please keep it where you can find it easily. It will help you remember what we discussed today.

Subject's Name *please print*	**Subject's Signature**	**Date/Time**

Name of Witness *please print*	**Signature of Witness**	**Date/Time**
Rationale for Use of Witness ☐ Subject has limited/no literacy ☐ Subject has limited English proficiency ☐ Subject has limited/no vision	☐ Sponsor requirement ☐ Other _____	

*** Name of person discussing/ obtaining consent** *please print*	**Signature of person discussing/obtaining consent**	**Date/Time**

** A member of the research team trained and authorized by the Principal Investigator to act on her/his behalf in obtaining informed consent according to the protocol. The Principal Investigator is responsible and accountable for the research project.*