



Multidisciplinary Approach to Pelvic Pain (MAPP)

Trans-MAPP Control Study

Sponsored by: The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institutes of Health (NIH), Department of Health and Human Services (DHHS)

Manual of Procedures (MOP)

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1. INTRODUCTION

1.A. MAPP Overview

The Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) Research Network has been established by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) of the National Institutes of Health (NIH) to better understand the etiology and treated natural history of urologic chronic pelvic pain syndrome (UCPPS), and to identify clinical factors and research measurements to define clinically relevant sub-groups of male and female patients with Interstitial Cystitis (IC)/Painful Bladder Syndrome (PBS), and Chronic Prostatitis (CP)/Chronic Pelvic Pain Syndrome (CPPS) in men, for future clinical trials, and to inform symptom management.

1.B. Rationale for Trans-MAPP Phase II Control Protocol

After the initiation phase for the Trans-MAPP Symptom Patterns Study (SPS), it became clear that many of the hypotheses being proposed required well-characterized healthy “normal” controls that lack urologic pain as well as other study related symptoms/conditions.

Although many operational aspects of this protocol are the same as the MAPP SPS, the differences in inclusion criteria, follow-up, and aspects of informed consent are extensive enough to warrant the preparation of this as a separate “companion” protocol.

1.C. Study Hypotheses

The MAPP Control Study will address the following hypotheses:

- Hypothesis 1.** Variation in a number of objective abnormalities in biological specimens (i.e. potential biomarkers) associated with change in symptom pattern can be identified in UCPPS participants and this variation will be larger than the observed natural variation in healthy control participants.
- Hypothesis 2.** Change in brain structural and functional markers associated with change in UCPPS symptoms over a 6 month period will exceed natural variation in these markers over the same period in a population of healthy controls. Controlled for urinary urgency, healthy controls will have reduced brain activation in response to bladder filling compared to UCPPS patients.
- Hypothesis 3** Healthy controls will demonstrate higher pain thresholds, more efficient conditioned pain modulation, and less temporal summation compared to UCPPS patients.
- Hypothesis 4** Healthy controls will demonstrate more stable levels of pain sensitivity and modulation across repeated testing sessions compared to UCPPS patients.

1.C.1. Specific Aims

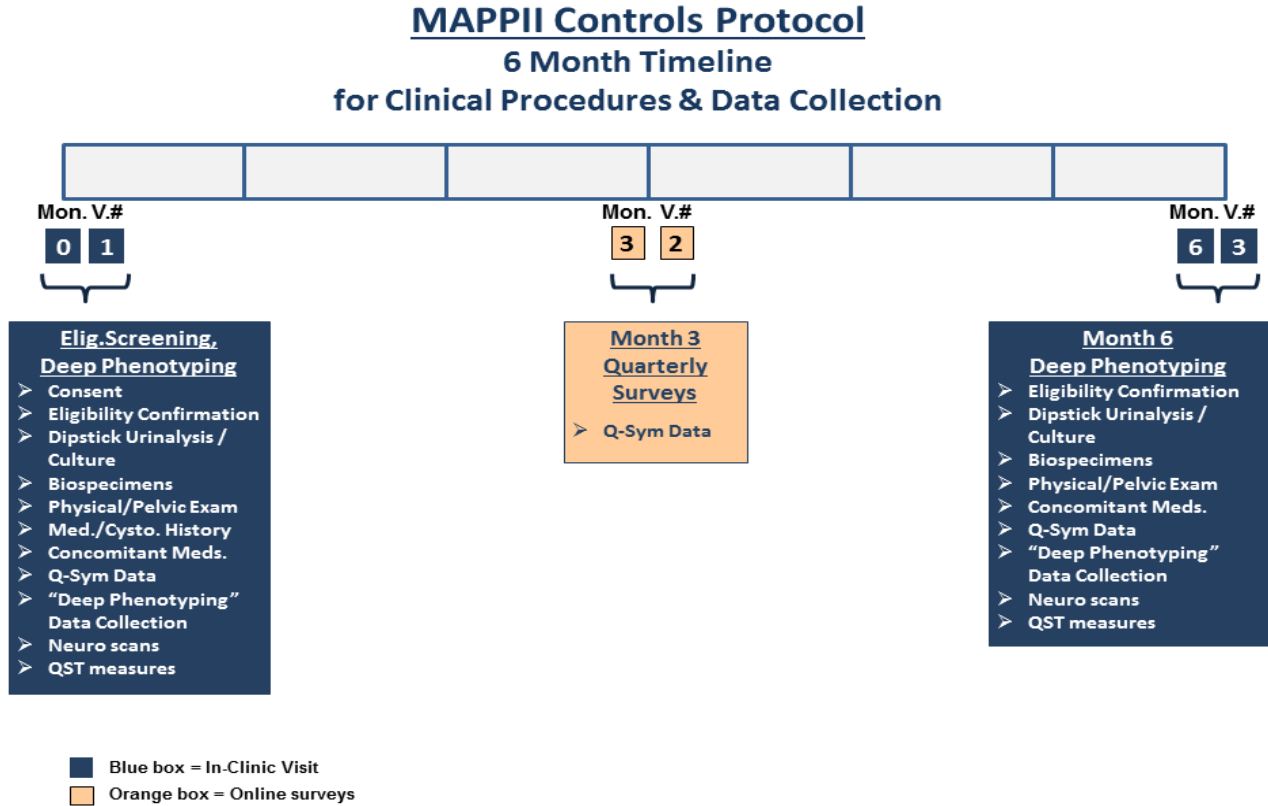
Each of these hypotheses motivates a series of specific aims that will be the focus of the MAPP Control Study Protocol and are outlined below:

- Aims Related to Hypothesis 1: To collect biological samples on these same controls, for comparison with individuals with UCPPS.
- Aims Related to Hypothesis 2: To collect brain MRI data (fMRI functional data, T1-weighted structural data, and diffusion tensor imaging data) at a low urinary urgency state as well as fMRI functional data at a higher urinary urgency state.
- Aims Related to Hypothesis 3: To measure pressure pain sensitivity, conditioned pain modulation, and temporal summation in healthy controls for comparison to UCPPS patients and methodological validation.
- Aims Related to Hypothesis 4: To determine the reliability of the QST measures and the normal variation in sensory profiles in healthy controls over a 6 month period for comparison to UCPPS patients and methodological validation.

1.C.2. Description

The overall design of the Trans-MAPP Control Study includes screening and enrollment of eligible participants during an in-clinic Screening/Eligibility visit (week 0) during which participants will be asked to provide biospecimens, complete a physical exam, a pelvic exam, extensive (“deep”) phenotyping questionnaires, a neuroimaging scan as well as Quantitative Sensory Tests (QST). Sites have the option to conduct Screening/Eligibility in 2 visits (see Section 3.A). After the Week 0 Screening/Eligibility visit participants will be asked to complete a series of online questionnaires 3 months after the initial visit; and to return 6 months from the initial visit for a follow-up/final study visit. During the Month 6 visit, as with the Screening/Eligibility visit, participants will be asked to provide biospecimens, complete deep phenotyping questionnaires, a physical exam, pelvic exam, as well as neuroimaging scans, and QST assessments (**Figure 1**). Participants will also obtain saliva samples after each in clinic visit. Please note that week 0 and month 0 are used interchangeably in this document.

Figure 1. Timeline for MAPP Phase II Controls Study



1.C.3. Specimen Collection for Biomarker and Microbiome Studies

In support of Trans-MAPP Biomarker and Microbiome Studies, blood, urine, rectal, and vaginal swab biosamples will be collected during both the Screening/Eligibility and 6 month clinic visits. Salivary cortisol samples will be collected by participants during the 3 days immediately following both clinic visits (Table 1). The Biomarker Studies will compare clinical biomaterial results between UCPPS patients and controls, utilizing both Discovery and Validation efforts to confirm clinically useful biomarkers.

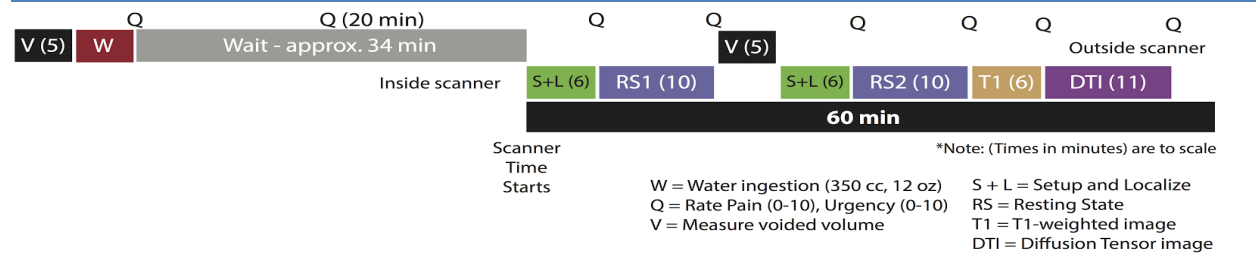
Table 1. MAPPII Controls Schedule of Biologic Specimen Collection

Specimen Type	Specimen Details	Specimen Collection CRF Code	Week 0 (Elig. Screening In-Clinic) V.#1	Month 6 (In-Clinic) V.#3
Blood Collection	Blood specimen, Plasma	PTRAC2	X	X
	Stim Tubes	STIMTR2	X	X
Biomarker Urine	VB2 (~90ml)	UTRAC2	X	X
Saliva	Salivary Cortisol	S3TRAC2	X	X
Microbiome	Urine: VB1, VB2	UFMBTR2 UMMBTR2	X	X
	Rectal Swabs	RSTRAC2	X	X
	Vaginal Swabs	VSTRAC2	X	X

1.C.3.a) Neuroimaging

The Single Session Neuroimaging Protocol will be performed on all MAPP Phase II Control Study eligible participants at the Screening/Eligibility and the Month 6 visits. The Single Session Neuroimaging Protocol includes Structural, Resting State, and Bladder Evoked Response. The standard single session for the fixed volume, fixed time evoked procedure is shown in **Figure 2** below. The participant voids before the start of the scanning session, and is then set up in the scanner. The participant is queried (Q) to rate pain (0 -10) and urgency (0 -7) at fixed time points.

Figure 2. Protocol Overview of Bladder Filling Paradigm Based on Resting State Changes



Further details are provided in the full Neuroimaging protocol [See Appendix D in the Control Protocol].

1.C.3.b) Quantitative Sensory Testing “QST”

To better evaluate the role that the CNS is playing in pain and sensory sensitivity among individuals with UCPPS, a broader and more comprehensive set of quantitative sensory testing (QST) methods will be implemented. QST will be conducted at the Week 0 Screening/Eligibility and Month 6 in-clinic visits on all Control Study participants. The MAPP Phase II QST protocol consists of a “core” battery of four methods that assess generalized and segmental pain sensitivity and modulation.

As in MAPP Phase I, participants will be assessed for generalized mechanical sensitivity using the University of Michigan (UM) MAST system. In addition, the QST core battery will include an evaluation of spinal segmental mechanical sensitivity at the most common referral site of pelvic pain (the suprapubic area), as well as tests of temporal summation and conditioned pain modulation (CPM) [See **Appendix E** QST MOP].

1.D. General Policy

1.D.1. General Protocol Policy

The objectives of the Trans-MAPP Control Study are most likely to be achieved if the protocol does not require alteration. Any changes in the protocol will result in some degree of heterogeneity of the data, which complicates the analyses and may compromise the scientific integrity of the study. However, occasions may arise in which protocol changes are necessary. Therefore, changes in the protocol will be considered only if they are required to ensure participant safety or will significantly enhance the scientific validity of the study.

1.D.2. Initiating a Protocol Change

The Executive Committee must review and approve all protocol amendments or revisions. Proposed protocol changes should be presented in writing to either the Chair of the Executive Committee or to the Data Coordinating Core. The DCC and/or Chair of the Executive Committee will present the proposed amendment to the Executive Committee for review and discussion. If approved by the MAPP Network Executive Committee, amendments must be submitted to the IRB for approval and once approved, be incorporated into the protocol. IRB approval must occur prior to the implementation of an amendment. Amendments that include minor changes to the protocol may undergo expedited review if these changes fit into expedited review criteria. All changes to the informed consent form must also be approved by the IRB.

2. PARTICIPANT ENROLLMENT

2.A. Participant Population and Recruitment

Each Discovery site will be responsible for recruiting 10 -12 healthy controls over a two year period. Each of these Control Study participants will complete the Screening/Eligibility in-clinic visit as well as a Month 6 in-clinic visit. Enrollment at each site will be closed after 10 controls complete the protocol through the Month 6 visit. Thus, the Trans-MAPP Control population will include approximately 60-72 adult healthy controls. Approximately half of the participants will be male. Consequently, the target distribution of study participants across the Discovery sites are summarized as follows:

Table 2. Composition of Trans-MAPP SPS Control Study Participants by Target Factors

Gender	# of Healthy Controls
Females	36
Males	36
Total	72

In addition, each site is requested to recruit controls that have an age and race/ethnicity distribution similar to that of the UCPPS participants in the MAPP SPS Study. The age and race/ethnicity distribution in each protocol will be monitored by the Executive Committee and the DCC, and adjustments made if warranted.

2.B. Identifying Potential Participants

Discovery Sites will use the same general techniques for recruiting control participants as are used for recruiting other research participants, and may include advertising or using individuals who are seen in clinical settings who fulfill the eligibility criteria. Sites will be responsible for assuring that their control participants are approximately the same age, gender, and ethnic composition as their UCPPS patients; this will then ensure that the Trans-MAPP SPS studies that combine individuals from multiple sites will likewise be matched for these demographic characteristics.

In some cases, local newspapers and other media will be used to promote these MAPP research study opportunities. Participants may be self-referred or referred through their primary physician. Possible participants will be introduced to the protocol by study investigators and/or the research coordinator, and asked whether they are interested in participating in the study.

The process of securing local physician approval and contacting the screening candidate will depend on prevailing guidelines of local IRBs, the requirements of each medical facility and the governmental HIPAA Guidelines which became effective in April 2003. Typically, candidates will first learn of the study from an invitational letter signed by the local principal investigator and/or personal physician. Occasionally, some individuals may learn of the study during a routine encounter with a healthcare provider who has agreed to assist in recruitment. Those individuals who express preliminary interest in the study will have a pre-screening telephone/clinic visit to confirm eligibility. Those who remain interested will be scheduled for the Screening/Eligibility visit, at which point a written informed consent is obtained.

2.B.1. Contacting Potential Participants

Once a potential participant is identified, he/she will be contacted via telephone or mail to schedule a screening/eligibility visit.

- Participant refuses contact: Enter this information into the Pre-Screening Case Report Form (CRF) as patient refusal with the reason, if provided. No further contact will be made.
- Participant approves contact: Proceed with scheduling the in-clinic screening/eligibility visit as soon as possible.
- Participant does not reply after 3 weeks: Try contacting the participants again by phone or by mail.

Maintain a telephone log of all attempted and actual contact with potential participants by phone, indicating the following information:

- Contact unsuccessful: If a potential participant is unreachable after several attempts at different times during the day, document as unable to contact individual, with a brief explanation if possible.
- Contact successful: The potential participant has been contacted by phone or mail and is willing to come in for the screening/eligibility study visit.

2.B.2. Obstacles to reaching potential participants

- Wrong or Disconnected numbers

If a phone number is wrong or disconnected, try to contact the individual again by mail.

- When to call

If the potential participant cannot be reached, ask if there is a better time to call or another number where they may be reached.

- How many times to call

Make several attempts to contact all potential participants. Try each number (day, evening, and message) at least twice during each of the following time periods (10:00 am - Noon, Noon - 6:00 pm, 6:00 pm - 8:30 pm, and anytime during the weekend) before leaving a message. If there is still no answer, leave a message such as the following:

Hello, my name is (----). I'm calling on behalf of CENTER NAME about an inquiry (he/she or you) made at our medical center. We would like to speak with (name of potential participant). Would you please call our clinical center at NNN-NNN-NNN and leave your name, your phone number with area code, and a good time to reach you. Thank you very much.

Do not leave more than one message every couple of days. Do not leave repeated messages. Use your best judgment to ascertain if calls are being avoided or simply bad timing. If the potential participant still cannot be reached, file this information and plan to call again in a few weeks.

2.C. Pre-Screening

The first contact with a potential participant will be considered a pre-screening contact and will include an introduction to the study, a review of the eligibility criteria, a description of tests and procedures involved, and a review of the visit schedule. This should be done to ensure not only the participant's potential eligibility, but also her/his willingness and ability to meet the demands/responsibilities of the study.

Pre-screening may be conducted either over the phone or in the clinic. If the initial contact is by phone, the Research Coordinator (RC) placing the call should identify him/herself and inform the potential participant how she/he was selected. Provide information about the study and answer questions. **Do NOT give the potential participant information about study-specific inclusion criteria.**

2.D. Informed Consent

If the pre-screening contact information indicates that the potential participant is eligible and willing, schedule a time for the participant to come in to review and complete the informed consent prior to proceeding with the Week 0 Screening/Eligibility Visit #1. The RC will request that the potential participant bring, if at all possible, a list of his/her medications, (prescription and over-the-counter) to Visit #1, to facilitate filling out the [CMEDCMED2](#) CRF after consent is obtained.

Each Clinical Site is responsible for ensuring that informed consent is obtained from each participant according to the guidelines of its local Institutional Review Board (IRB) and in accordance with the Common Rule (45 CFR Part 46 subpart A, Protection of Human Subjects). The informed consent form must be obtained (signed and dated by the participant) prior to initiation of any study related activity.

The Informed Consent form must provide the following information to each participant:

- A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental.
- A description of any reasonably foreseeable risks or discomforts to the subject.
- A description of any benefits to the subject or to others which may reasonably be expected from the research.
- A disclosure of appropriate alternative procedures or courses of treatment, if any that might be advantageous to the subject.

- A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained.
- For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.
- An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject; and
- A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

An informed consent *must* be obtained from the participant before study information is collected or study procedures performed.

2.D.1. Obtaining Informed Consent

Obtaining informed consent includes:

- The potential participant should receive a copy of the informed consent, either in person, by mail or by fax.
- The RC should allow the potential participant time to consider the study obligations and discuss the study with his/her family members before signing the consent form.
- The informed consent form must be signed in the presence of the PI or the RC, prior to Visit #1 procedures.

2.D.2. Administration of Informed Consent

When the person comes into the clinic for the Week 0 Screening/Eligibility Visit, the consent process including review of the study's informed consent must occur first.

Administration of Informed Consent

Prepare Participant ... Potential participants will be asked to sign the Informed Consent form following the consent discussion. The consent form describes the Trans-MAPP Control Study that includes the Genetic elements of the study as well as all other study assessments. The form contains embedded YES/NO questions for both consent to participate in the study as well as consent to genetic testing, each has its own signature requirements as well as other optional consents to send specimens to the repository as well as to be contacted for future studies. Instruct the participant to read the entire Informed Consent carefully and to raise any questions or concerns that he/she has and to sign it **ONLY** after their questions or concerns have been answered. Participant questions should be answered using lay language.

Provide a comfortable setting...	Review the informed consent form in a comfortable setting where the participant is able to make a free choice without pressure. Ample time should be given to allow the participant to thoroughly read and process the information.
Determine reading comprehension...	Provide the potential participant with a copy of the Informed Consent Form and ask her/him to read a few sentences out loud to ascertain whether the potential participant needs assistance with the written material. If the participant cannot read the written material, he/she is ineligible for the study. Responses to this question should be recorded on the ELIG CRF.
Review study tasks	Review the study tasks described in the Informed Consent Form using lay language.
Answer questions	Ask the participant if they have any questions about the consent form, the study procedures, or their responsibilities. Participant questions should be answered using lay language. Participant to sign it ONLY after their questions or concerns have been answered.
Blood Specimen for DNA...	A separate section and signature page will be required for consent to collect a blood sample for genetic testing and storage of DNA. In order to proceed with eligibility confirmation, participants must sign consent for use of their DNA. However, they may refuse to sign the separate consent for use storage of their DNA at the NIDDK repository consequence to study eligibility.
Genetic Sampling	Discuss the options and implications of participation in the genetic study, and explain the selections contained in the YES/NO question about genetic samples. Participants must respond to this YES/NO question in the Genetic section of the Informed Consent Form. Responses to the YES/NO questions about provision of genetic samples should be recorded on the ELIG CRF.
Present Optional sections	While it is expected that all participants will agree to participate in all parts of the study, female participants may opt out of the vaginal swabs.
Continued followup...	The participant should be made aware of her/his responsibilities throughout the study. Stress the importance of continued follow-up. This is balanced with a discussion of the effect of participant withdrawal on the study.
If consent is refused ...	If the participant refuses to participate in the study, document this on the ELIG CRF and end the study visit.
If consent is delayed...	If the participant wishes to take the Informed Consent Form home before reaching a decision, then she/he may do so. Reschedule the Screening/Eligibility Visit and at the subsequent visit, answer any questions raised by the participant.

Signed/dated...	The Informed Consent Form must be signed and personally dated by the participant and the person “obtaining consent”. Do not ask a participant to sign the consent statement if he/she has any doubts about enrolling or if the clinic staff believes he/she does not understand what his/her participation would involve. Under <i>no</i> circumstance is any study information to be collected or study procedures performed for the specific purpose of the study before the participant has signed the informed consent form.
Maintain original/provide copy to participant...	Maintain the <u>original</u> consent document in the participant’s confidential file with other confidential documentation, and provide a copy of the signed and dated informed consent(s) to the participant. A second copy of all informed consent(s) should be made as a back up and stored together in the “study-confidential file”. In addition, a signed/dated progress note must be made in each participant’s file that the informed consent process took place prior to any study procedures.
Confidentiality...	To ensure confidentiality, do not send copies of the consent form(s) to the DCC or keep any copies of the Informed Consent Form with the case report forms.
Sign/date...	<i>Participant must sign and date the informed consent form prior to proceeding with any of the Week 0 procedures.</i>

2.D.3. Participant Confidentiality

HIPAA

At most sites, participants must sign a Health Insurance Portability and Accountability Act Authorization (HIPAA) in addition to the Informed Consent Form. The HIPAA Authorization may or may not be incorporated into the Trans-MAPP Control Study consent, depending on the policy of the Clinical Center. However, if the HIPAA language is incorporated into the Informed Consent Form, the regulation mandates that it be submitted to the IRB for prior approval. This form describes both the kinds of health information collected in this study and also all of the disclosures of health information that will be made. The form must also list parties to whom disclosures of personal health information will be made.

Additional Confidentiality Concerns

- Consent form(s), HIPAA authorizations and source documentation must be securely maintained in a separate location from the CRFs.
- Recruited study participants are assigned a Participant ID number, a unique study identification number.
- The DCC staff has access to the Participant ID number for data management purposes. All communication between the DCC staff and the Clinical Center staff regarding participant data occurs via the Participant ID number only.

2.D.4. Registering Participants to the Trans-MAPP Control Study

Once consent is obtained, register the participant in the Data Management System (DMS) to obtain a Control Study Participant ID.

2.D.5. Assignment of Participant ID and PIN

Eligible participants who consent to participate will have their name recorded on the Participant ID Log [PTIDLOG] and will be registered in the Trans-MAPP Control Participant Registration module in the DMS (see Sections 8.B.2 and 8.B.3 for details). Participants will be assigned a computer generated participant ID number and PIN provided by the participant registration module at the time of registration. Once a participant ID number and PIN has been assigned, it should never be reassigned for any reason. Participants assigned an ID number and PIN who are ineligible or refuse participation, and who later become eligible or decide to participate will utilize the same ID number and PIN that they were originally assigned. The Participant ID Log [PTIDLOG] should be stored in a secure, locked filing cabinet.

2.D.6. Clinical Centers (CC) and Site Assignments

There are six recruitment Discovery Sites:

CC	SITE	NAME	LOCATION
01	01	Northwestern University Feinberg School of Medicine	Chicago, IL
02	01	University of California (UCLA)/University of Southern California (USC)	Los Angeles, CA
03	01	University of Iowa	Iowa City, IA
04	01	University of Michigan	Ann Arbor, MI
05	01	University of Washington	Seattle, WA
06	01	Washington University	St. Louis, MO

In addition to the above six recruitment sites there are also several non-recruitment Discovery and Core sites:

CC	SITE	NAME	LOCATION
07	01	Data Coordinating Core (DCC), Perelman School of Medicine at The University of Pennsylvania,	Philadelphia, PA
07	02	Children’s Hospital Boston, Harvard Medical School	Boston, MA
07	03	Queen’s University	Kingston, ON
08	01	University of Colorado (TATC)	Aurora, CO
09	01	Cedars-Sinai Medical Center	Los Angeles, CA

2.E. Study Eligibility Criteria

Determining eligibility is a multiple step process involving the review of information collected on case report forms (CRFs) and the immediate results of a urine dipstick analysis, as well as confirmatory results of a urine culture (minimum of 24 hrs incubation) to test for urine pathogens.

The eligibility criteria for healthy controls are based on the same set of criteria for the UCPPS participants in the Trans-MAPP SPS Study, with exception of additional criteria to exclude chronic pelvic pain symptoms, chronic fatigue, and cognitive problems. Eligibility will be reassessed prior to the Month 6 visit.

2.E.1. Inclusion Criteria

Participants are eligible for the Trans-MAPP Control Protocol if they meet the following general and gender-specific criteria listed below:

- Participant has signed and dated the appropriate Informed Consent document.
- Agreed to participate in ALL required study procedures (including Biospecimen collections, Neuroimaging, and Quantitative Sensory Testing).
- Gave permission for use of DNA for genetics studies.
- Gender recorded in Participant Registration module.
- Participant is at least 18 years of age.
- Participant is able to speak, read, and understand English.
- Participant reports a response of **“0” (zero)** on the pain, pressure or discomfort scale (**SYM-Q**, Question #1).
- Participant reports no chronic pain in the pelvic or bladder region, and reports no chronic pain in any other body region.
- Participant reports no urological symptoms that have been evaluated, but are still present.

2.E.2. Exclusion Criteria

Any potential control participant meeting any one of the following criteria will not be eligible for enrollment in the Trans-MAPP Control Study.

- Participant has an on-going symptomatic urethral stricture.
- Participant has an on-going neurological disease or disorder affecting the bladder or bowel fistula.
- Participant has a history of cystitis caused by tuberculosis, radiation therapy or Cytoxan/cyclophosphamide therapy.
- Participant has augmentation cystoplasty or cystectomy.
- Participant has an active autoimmune or infectious disorder (such as Crohn’s Disease or Ulcerative Colitis, Lupus, Rheumatoid Arthritis, Multiple Sclerosis, or HIV).
- Participant has a history of cancer (with the exception of skin cancer).
- Participant has current major psychiatric disorder or other psychiatric or medical issues that would interfere with study participation (e.g. dementia, psychosis, upcoming major surgery, etc.).
- Participant has severe cardiac, pulmonary, renal, or hepatic disease that in the judgment of the study physician would preclude participation in this study.
- Participant has had definitive treatment for acute epididymitis, urethritis, vaginitis.
- Participant has history of unevaluated hematuria, this will require the evaluation of a study physician to determine if this has been appropriately evaluated.
- Participant has had a cystoscopy with hydrodistention or kenalog injection.

Exclusion Criteria for Males Only

- Diagnosis of unilateral orchalgia, without pelvic symptoms.
- History of transurethral microwave thermotherapy (TUMT), transurethral needle ablation (TUNA), balloon dilation, prostate cryo-surgery, or laser procedure.

- A prostate biopsy or transurethral resection of the prostate (TURP) within the last three months.

Exclusion Criteria for Females Only

- Participant has a positive urine pregnancy test.

Specimen Exclusion Criteria (Males and Females)

- Participant has a positive urine culture.

Fatigue Symptom Eligibility Criteria

- Participant, for at least 3 months in the past year, has persistent fatigue not relieved with rest.
- Participant, for at least 3 months in the past year, has extreme fatigue following exercise or mild exertion.
- Participant, for at least 3 months in the past year, has impaired memory, concentration or attention.

Exclusion Criteria - Urine test results

A clean-catch midstream urine specimen (VB2) will be obtained from all male and female participants during the Week 0 and Month 6 study visits, so that a urine dipstick analysis can be done for all participants, and a urine pregnancy test can be conducted for females of child bearing age excluding those who are post-menopausal and those with a history of hysterectomy.

- If participant has an abnormal dipstick urinalysis indicating abnormal levels of nitrites and/or occult blood that in the opinion of the Principal Investigator warrants exclusion, participant will be ineligible for study participation at the initial visit and withdrawn from study participation. A positive dipstick at the Month 6 visit will also result in the participant being withdrawn.
- If participant has had a positive urine culture in the past 6 weeks, or currently has a midstream urine culture (VB2) ($\geq 100,000$ CFU/ml), with a single uropathogen, the participant will be ineligible for the study, treated and withdrawn from study participation. This must be documented on Urine Culture Result CRF [UCR].
- Keep all specimens and data collected from both eligible and ineligible participants unless a participant requests that his/her data be destroyed, and not utilized for the study.

2.F. Screening Failures

A participant who does not complete the Screening procedures, for whatever reason, will be considered a screening failure, and will **not** be enrolled into the Control Study. All of the completed screening forms, including informed consent form, for participants who are considered screening failures, should be filed at the center in the Source Documentation Binder.

If at any time during the screening process the participant is found to be ineligible, they must be informed of this fact as soon as possible. If the participant does not meet the necessary eligibility criteria, thank the participant for his/her time and effort, explain to the participant that he/she did not meet the study eligibility criteria, provide the designated site-specific reimbursement, and discontinue any further study measures/visits.

A participant who is excluded based on the exclusion criteria cannot be re-screened.

2.G. Study and Participant Documents

Study and participant documents must be made available to the Trans-MAPP Network Study Group, NIH, NIDDK, and/or any agents/representatives of these parties. These documents should be organized as outlined in binders or files and stored in accordance with **security and record retention** regulations until further written notice by the sponsor or the DCC. Each clinical center must maintain the following documents:

Clinic Regulatory Binder (1 per clinical center)

This binder contains all essential documents, such as:

- Trans-MAPP Control Study Protocol
- Trans-MAPP Control Study Case Report Form Templates
- IRB-Approved Informed Consent Forms
- IRB Documents/Correspondence
- IRB Membership List (current for duration of study)
- Laboratory Certifications/Laboratory Normals (current for duration of study)
- CVs of all clinic personnel
- Medical licensure for study physician
- Signature and Delegation of Responsibilities Log [STAFFLOG]
- Clinic Correspondence – Log and other documentation
- Trans-MAPP Control Study Manual of Procedures (MOP)

Note to file: Documents outlined above may be stored in other/additional binders during the course of the study; however a “Note to File” should be placed in any section where this occurs for a reference and as a reminder to replace documents at time of study termination

Case Report Form Binder

This binder contains all data collection forms and select administrative forms completed during the course of the study. No participant identifiers other than participant ID number and participant initials should be contained in this binder.

Source Documentation Binder/Folder (1 per study participant)

Contains all documentation collected to support and verify information contained on the data collection forms. This includes the following original source documents: participant signed informed consent, medical records, laboratory results, contact information, administrative forms not contained in Case Report Form Binder, progress notes, and correspondence. In addition, any copies of applicable source documentation should also be stored in this file. Any study documents containing any participant identifiers beyond participant ID number and participant initials should be contained in this file.

Participant Study Binder (1 per clinical center)

This binder contains Participant ID Assignment Log, a copy of all participant signed informed consents and all financial documents related to the study. Any additional study specific confidential documents

should be contained in this file. At the completion of the study, the Participant Contact Log should be completed and stored in this file. These files must be stored under secure conditions.

3. VISIT SCHEDULE AND ADMINISTRATION

Participants who meet eligibility criteria, and enroll in the study at the Screening/Eligibility visit will complete online assessments at Month 3 and attend a Month 6 in-clinic visit. A complete list of data elements to be collected is provided in **Appendix A: MAPP Phase II Control Study Visit Schedule**. The specific directions for completing each Case Report Form are found in Section 6. of this manual.

As illustrated in **Figure 3**, discrete modules of measures and procedures are scheduled for each in-clinic study visit, as well as Month 3 on-line modules of data capture. These include measures that do not change over time, such as demographic information, “trait measures” (e.g., personality), and early life history measures.

Figure 3. Visit Schedule for Screening/Eligibility (Week 0) and Follow-up Deep Phenotyping (6 months)

	Eligibility & Deep Phenotyping	Quarterly Online Data Collection	Month 6 Deep Phenotyping
PROCEDURES	Week 0	Month 3	Month 6
Eligibility Confirmation Sequence of Procedures	X		X
Microbiome/Biomarker Specimen Collection	M B		M B
Microbiome M			
Biomarker (Blood, Plasma, Stim Tubes, & Urine) B	S		S
Swabs [§] S			
Cortisol C	C		C
Clinical Procedures & Data Collection	M		M
Meds & Tx. Collection M			
Pelvic/Phys. Exam P	P		P
CystoHx C	C		
Online Data Collection	S		Q
Screening Visit Surveys S			
Abbreviated On-line Survey Q	P	Q	P
Phenotyping Surveys P			
Deep Phenotyping Surveys D	D		D
Deep Phenotyping Clinic Data Collection and Procedures*	X		X

[§]optional rectal/vaginal swabs; specific details in protocol
 *Deep Phenotyping Visit: Biospecimen collection, Neuroimaging scans; Clinical CRFs; QST Procs

The Study Visit Schedule (**Appendix A**) describes the types of visits and permissible visit intervals (i.e. visit window) used throughout this manual to describe interaction with study participants. The participant study calendar, which is a tool available in the DMS, will be generated based on the date of the Eligibility CRF completed at the Week 0 Screening/Eligibility Visit #1. All contacts and visits will have a permissible window of contact surrounding them that defines the period of time during which a visit is permissible. If a participant logs into the online participant module at a time that is outside of his/her

visit window, he/she will not be allowed to complete any assessments at that time, but instead will be reminded of the correct date to complete their next online assessment.

Participants are expected to complete Week 0 and Month 6 online questionnaires at the clinic during the same day/visit as they provide the biospecimens for each visit. As such, participants will not have access to the clinic visit online questionnaires until they are in clinic and the survey is initiated by the Research Coordinator. The clinic visit participant online survey will require a Research Coordinator to enter the participant's ID and PIN to initiate the survey. If the participant does not finish the survey during the study visit, the participant will have until the end of that calendar day (11:59pm) to complete the online questionnaires from home/other location of their choice.

The visit window for the Month 3 online computer assessments is ± 1 week. The visit window for the Month 6 visit is ± 2 weeks.

Each Trans-MAPP Control clinic visit has an accompanying checklist/progress note, which lists processes for a particular clinic visit. In addition, the Trans MAPP Control Study schedule (**Appendix A**) is a comprehensive list of the study processes that occur at all visits/online computer assessments.

3.A. Screening/Eligibility Visit #1 (Week 0)

The Screening/Eligibility visit will be conducted as one in-person clinic visit. After the informed consent process is completed, the visit is structured such that essential information required to assess eligibility is acquired prior to the conduct of more intensive and time-consuming procedures required later in the visit. Contact information and a questionnaire assessing eligibility will be completed and a urine dipstick and urine culture will be done. Those persons who are eligible after the initial screening process will be invited to complete the MAPP Control Study "deep" phenotyping assessments.

Key eligibility criteria will be reviewed and confirmed and eligibility CRFs will be completed. Week 0 measures will be collected including medication data, two urine samples, a blood specimen, physical and pelvic exams conducted, and rectal and vaginal swabs will be obtained, and the completion of CRFs related to the participant's urological symptoms and current medications.

During the Screening/Eligibility visit participants will undergo an initial series of Quantitative Sensory Tests (QST_Screen/QST) as well as Neuroimaging scans (NEURO_SCAN2_CON/NEURO_CRF). Please see the Neuroimaging protocol [see Appendix D in the Control Protocol] and QST MOP [**Appendix E**] for additional details regarding both batteries of tests.

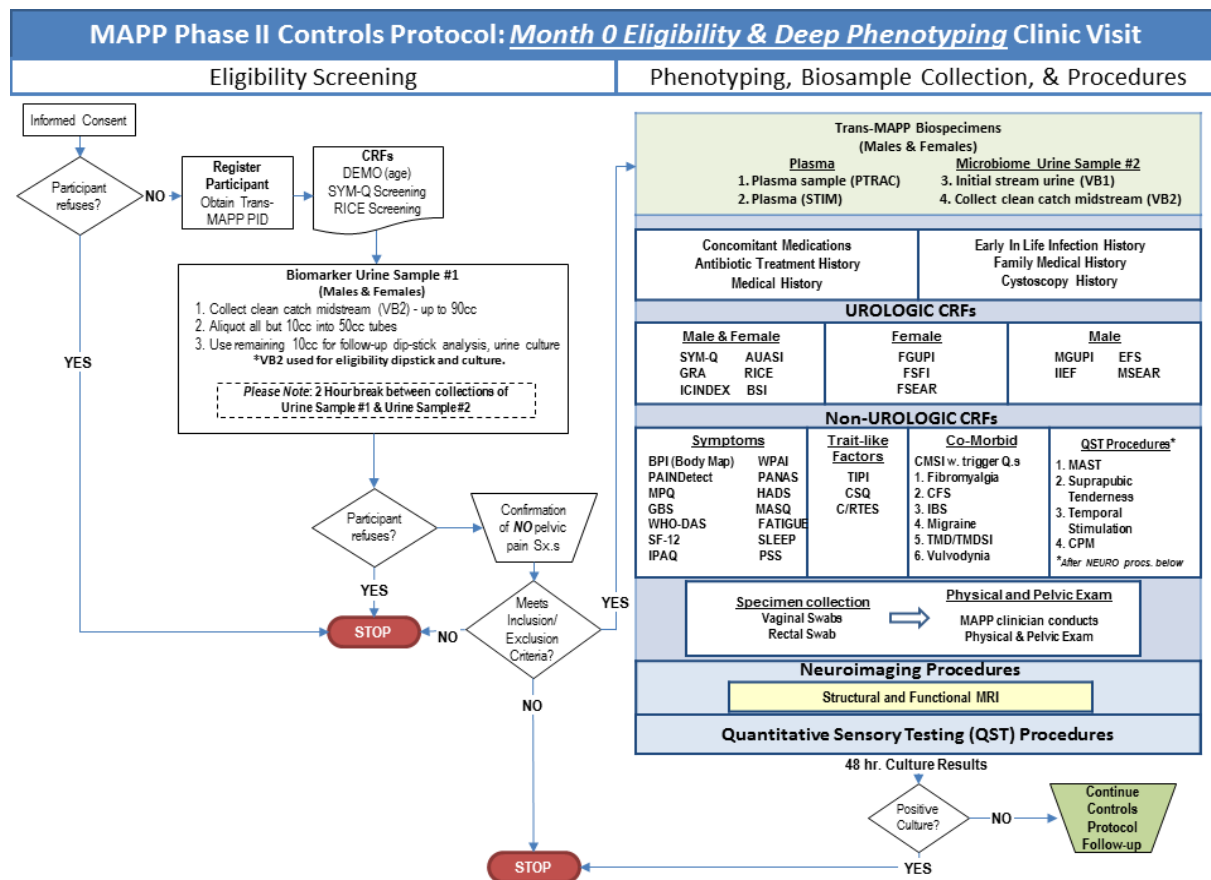
The completion of the Screening/Eligibility visit, followed by a negative 24 hrs (minimum) urine culture result, defines enrollment in the MAPP Control Study.

The entire visit is expected to take approximately 4.5 – 6 hours to complete. As illustrated in **Figure 4**, the eligibility screening session (left-hand panel) is intended to collect the minimally sufficient data to confirm eligibility, so that the extensive baseline phenotyping portion of the visit (right-hand panel) and corresponding assessments (biospecimen collection, neuroimaging, and QST) is initiated only for participants highly likely to be confirmed eligible after the 24 hrs (minimum) urine culture results are known.

All procedures should be done at one clinic visit. Neuroimaging scans must be completed within 48 hours of the Week 0 visit if they cannot be done the same day as the Week 0 visit. It is preferred that neuroimaging occurs prior to QST. If QST occurs first, neuroimaging must occur at least 2 hours after the completion of QST.

If conducting the study in one visit is not feasible, the visit may be conducted in two parts. The following procedures must be done at the initial screening visit: the bulleted screening procedures listed under “Screening Procedures” including microbiome urine sample (VB1 and VB2), the physical and pelvic exams as well as vaginal and rectal swabs. The second screening visit must include the deep phenotyping questionnaires, biomarker urine sample (VB2), blood specimens, at home saliva collection, neuroimaging and QST. These visits must be within 2 weeks of each other. Neuroimaging must take place during the second screening visit.

Figure 4. Month 0 Eligibility & Deep Phenotyping Clinic Visit



Upon completing the Screening/Eligibility assessment, the RC should be able to determine if the participant is potentially eligible for the Trans-MAPP Control Study. If necessary, the RC should confer with the PI on questions related to eligibility, and make an overall decision regarding the participant’s suitability for participation in the study at that visit.

At the screening/eligibility (week 0) visit, the following sequence of steps will occur:

Screening procedures:

- Layered informed consent process; consent obtained for various levels of specimen collection (ICF)
- Contact information provided (Site documentation)
- Demographic information recorded (**DEMO**)
- Symptom assessment via Symptom and Healthcare Utilization Questionnaire (**SYM-Q**). At the Week 0 visit the Sym-Q is administered via paper, however for all other visits Sym-Q is administered online via the participant module.
- RICE Case Definition Questionnaire for Control Participants (**RICE_CON**)
- Eligibility urine specimen
- Urine Culture Result (**UCR**) – confirm negative urine culture from the microbiome VB2 specimen within 48-24 hours of the Week 0 screening visit
 - a clean catch midstream urine specimen will be obtained for the urine dipstick test and 24 hrs (minimum) urine culture (see details in **Appendix B**);
 - a urine dipstick test will be performed for the presence of leukocyte esterase, nitrites, and hematuria;
 - If the dipstick is positive for nitrites, participant is ineligible.
 - For females of childbearing potential, perform a pregnancy test
- Inclusion and Exclusion Criteria - Eligibility Confirmation form (**ELIG_CON**) –complete prior to participant completing online questionnaire battery and exams
- *Neuroimaging Study Eligibility for Control Participants (**ELIG_SCAN2_CON**) – Confirms that Control Participants agree to participate in the neuroimaging component of the study and documents that Control participants do not meet any neuroimaging-specific exclusionary criteria.
- QST Screening (**QST_Screen**) – confirm that QST procedures were reviewed with participant

*Note: Participants with neurostimulators are eligible for the Control Study but are excluded from the Neuroimaging study.

NOTE: The Eligibility [**ELIG_CON**] CRF must be data entered into the Oracle Clinical Module prior to proceeding with the questionnaires and exams, and is absolutely necessary to enter in order to log the participant into the online system to complete the screening/eligibility Participant Survey as well as to generate the participant follow-up calendar.

Assuming that the participant meets all eligibility criteria that can be known prior to the results of the 24 hrs (minimum) urine culture, the participant will begin the biospecimen, phenotyping and physical/pelvic exam portion of the visit.

Week 0 Biospecimens:

- Blood specimens
 - 10mL ACD plasma vacutainers (Plasma and Buffy Coat DNA)
 - STIM TUBES – Three 1 mL blood samples for stimulated cytokines
- Urine specimens
 - Biomarker – VB2
 - Microbiome – VB1, VB2 (collected for screening procedures)
- Vaginal swabs

- Rectal swabs
- Salivary Cortisol (collected by participant after visit)

Note: Collect blood from participant’s non-dominant arm, if possible.

Physical and Pelvic Exam (EXAM2 and PEX_Female/PEX_Male): A physical exam and a pelvic exam will be performed by a MAPP physician (or designated trained clinician) to assess pelvic musculature tenderness. While the pelvic exam is required, the rectal and vaginal swabs are optional and not required to participate in the study.

The following data will be collected by the RC:

- Medical History (MEDHX2)
- Family Medical History (FAMHX)
- Cystoscopy History (CYSTO)
- Antibiotic Treatment History (ABHX)
- Documentation of current medications on Concomitant Medications (CMED2)

The RC will demonstrate to and provide each participant with instructions on how to log onto and complete the online participant questionnaires, as well as answer any questions the participant may have. It is expected to take approximately one hour to complete these CRFs. The RC should then escort eligible participants to a quiet comfortable location where he/she can complete the online questionnaire assessments including:

Urologic CRFs, All Participants

- Global Response Assessment (GRA)
- Interstitial Cystitis Symptom Index (ICSI) and Problem Index (ICPI) forms– (ICINDEX)
- AUA Symptom Index (AUASI)
- RICE Bladder Symptom Impact (BSI)
- Early In Life Infection History (EIL-INF)

Urologic CRFs, Female Participants only:

- Female Genitourinary Pain Index (FGUPI)
- Female Sexual Function Index (~~FSEI~~[FSFI2](#))
- Female Self-Esteem and Relationship Questionnaire (FSEAR)

Urologic CRFs, Male Participants only:

- Male Genitourinary Pain Index (MGUPI)
- International Index of Erectile Function (IIEF)
- University of Washington Ejaculatory Function Scale (EFS)
- Male Self-Esteem and Relationship Questionnaire (MSEAR)

Non-Urological Phenotyping CRFs, All Participants:

- Symptoms and Illness Impact**
- Complex Medical Symptoms Inventory (CMSI2_Screening)
 - Fibromyalgia symptoms module (CMSI2_FM2)

- Brief Pain Inventory: Body Map, Intensity, Interference (BPI2)
- PAIN Detect (PAIN)
- McGill Pain Questionnaire (MPQ)
- Gracely Box Scales (GBS)
- WHO Disability Assessment Schedule (WHO-DAS)
- Medical Outcomes Health Survey (SF-12)
- International Physical Activity Questionnaire (IPAQ)
- Work Productivity & Activity Impairment Questionnaire (WPAI)
- Feelings and Emotions Questionnaire (PANAS)
- Hospital Anxiety and Depression Scale (HADS)
- Multiple Ability Self-Report Questionnaire (MASQ)
- PROMIS Fatigue
- PROMIS Sleep
- Perceived Stress Scale (PSS)
- Traits & Early Life Experience**
 - Ten Item Personality Inventory (TIPI)
 - Catastrophizing Sub-scale (CSQ:CAT)
 - Childhood Traumatic Events Scale; Recent Traumatic Events Scale (C/RTES)
- Co-morbid Symptoms**
 - CMSI, Chronic Fatigue Syndrome (CMSI2_CFS2)
 - CMSI, Irritable Bowel Syndrome (CMSI2_IBS2)
- (PRN per report following CMSI Questionnaire)**
 - CMSI, Migraine (CMSI2_MI2)
 - CMSI, Vulvodynia (CMSI2_VDYN)
 - CMSI, Current TMD Symptoms (CMSI2_TMD2)
 - Gonzalez TMJD Questionnaire (TMDSI)

3.A.1. Completing the Week 0 Visit

After Participant completes the online questionnaires:

- Run Participant CMSI Report from the RC Data Management Tools screen.
- Administer the applicable CMSI modules (Fibromyalgia (**CMSI_FM2**), Chronic Fatigue (**CMSI_CFS2**), Irritable Bowel Syndrome (**CMSI_IBS2**), Migraine (**CMSI_MI2**), Vulvodynia (**CMSI_VDYN2**), Temporomandibular Joint Disorder (**CMSI_TMD2**)) as indicated on the participant report.
- Review the Completeness Report – stress to participant the importance of completing the entire survey/questionnaires. If participant did not complete the entire survey, as indicated on the report, confirm with him/her that they intended to not complete the survey. If not, assist participant in logging back onto the system to complete the survey. Note that it is not mandatory that he/she completes the session.
 - If eligible, transport participant to location where he/she will complete Trans-MAPP Neuroimaging scans (see Appendix D in the Control Protocol). Scans may be conducted within 48 hours of the Week 0 visit.
- Conduct QST procedures – see **Appendix E**

Prior to Participant leaving clinic, provide him/her with:

- Salivette collection kit and shipping materials for 3 day collection
 - Pre-assembled at-home collection kits (see the **Appendix B** for detailed instructions on assembling and distributing kits).
 - A review of the instructions on how to collect and ship the samples from the back of the tracking form [**S3TRAC2**]

Note: RC must complete the header information and the scheduled collection dates on [**S3TRAC2**] and enter this information into the specimen tracking module of the DMS before giving to participant.

- Instruction sheet for accessing and completing the online Participant questionnaires
- A reminder of their study PID# and PIN (this can be included on the Contact Completion Calendar or separate site specific format)
- If visit is split into 2, provide participant with next screening visit date
- The Target window to complete the Month 3 online questionnaires
- The date for next in-clinic (Month 6) visit, if scheduled
- Site specific reimbursement for their time and effort
- Copy of signed informed consent
- Site Contact information for participant questions

Once participant leaves, RC will:

- Properly store biospecimens at the required temperature as indicated in the lab section of the manual of procedures.
- Send urine aliquot for 24 hrs (minimum) urine culture to local lab/clinic.

Confirming Eligibility

After a 24 hrs (minimum) negative urine culture result is confirmed, complete the Enrollment Confirmation [**ENROLL_CON**] CRF to confirm that all Eligibility Criteria have been met.

It is expected that the **ENROLL_CON** CRF as well as all other Screening/Eligibility CRFs are data entered in the DMS within 3 days of the study visit.

3.B. Month 3 Online Assessment

Participants will provide self-reported longitudinal symptom data via web-based internet tools. The following questionnaires will be completed at Month 3:

- | | |
|----------------------------------|--|
| Urologic Questionnaires | <ul style="list-style-type: none">• Symptom & Healthcare (SYM-Q)• Global Response Assessment (GRA)• Interstitial Cystitis Symptom Index and Problem Index (ICINDEX)• RICE Case Definition Questionnaire for Controls (RICE_CON) |
| Female Participants only: | <ul style="list-style-type: none">• Female Genitourinary Pain Index (FGUPI) |
| Male Participants only: | <ul style="list-style-type: none">• Male Genitourinary Pain Index (MGUPI) |

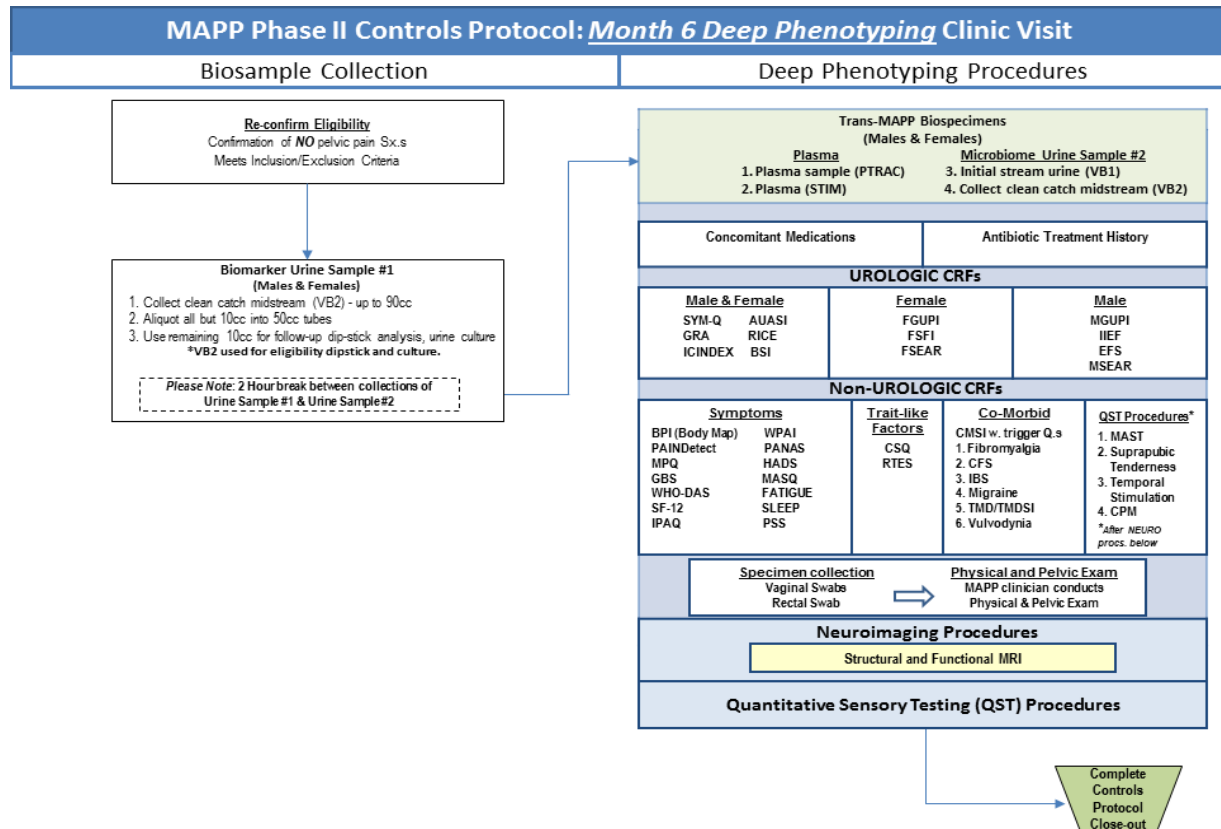
- Non-Urologic Questionnaires:**
- Complex Medical Symptoms Inventory (CMSI2_Follow-Up)
 - Fibromyalgia symptoms module (CMSI_FM2)
 - Brief Pain Inventory: Body Map, Intensity, Interference (BPI2)
 - Pain Detect (PAIN)
 - WHO Disability Assessment Schedule (WHO-DAS)
 - Hospital Anxiety and Depression Scale (HADS)
 - PROMIS Fatigue (FATIGUE)
 - PROMIS Sleep (SLEEP)
 - Perceived Stress Scale (PSS)

3.C. Deep Phenotyping In-clinic Visit at 6 Months

Participants will have an in-clinic visit at 6 months (**Figure 5**) that includes phenotyping, biospecimen collection, physical and pelvic exams, neuroimaging, and QST assessments. All data collection and procedures should be completed within a 72 hour timeframe. Neuroimaging scans must be completed within 48 hours of the Month 6 visit if they cannot be done the same day as the Month 6 visit. It is preferred that neuroimaging occurs prior to QST. If QST occurs first, neuroimaging must occur at least 2 hours after the completion of QST.

Approximately 2-3 weeks prior to the Month 6 visit, contact the participant to reassess eligibility. If the participant no longer meets eligibility criteria, withdraw the participant and do not conduct the Month 6 visit.

Figure 5. Month 6 Deep Phenotyping Clinic Visit



At the Month 6 visit, the following sequence of steps will occur:

- Biomarker urine specimen (VB2) (See **Appendix B**: Biospecimen Collection Manual)
- Eligibility Follow up/Dipstick Urinalysis and Urine Culture Result (**UCR**) –Eligibility Confirmation form completed to document status of urine culture results for participants who have not had a negative urine culture within the preceding 6 weeks,
 - a clean catch midstream urine specimen will be obtained for the urine dipstick test and 24 hrs (minimum) urine culture;
 - a urine dipstick test will be performed for the presence of leukocyte esterase, nitrites, and hematuria;
 - For females of childbearing potential, perform a pregnancy test
 - A participant with a positive dipstick will be withdrawn.
- Brief clinical diagnostics will also be collected via the **CDX** CRF including: Height, weight, waist circumference, blood pressure, urine culture results, specimen collection, and negative pregnancy test or verbal confirmation based on your site requirements.
- Reconfirm Neuroimaging Eligibility
- Research Coordinator will review with the participant his/her medical history and history of family member diagnosis of IC/BPS and/or CP/CPPS.
- Online Symptom assessment via Symptom and Healthcare Utilization Questionnaire (**SYM-Q**).
- Antibiotic Treatment History (**ABHX**)
- Documentation of current medications on Concomitant Medications (**CMED2**)

Month 6 Biospecimens/Exam:

- Blood specimens
 - 10mL ACD plasma vacutainers (Plasma and Buffy Coat DNA)
 - STIM TUBES – Three 1 mL blood samples for stimulated cytokines
- Urine specimens
 - Biomarker – VB2 (to confirm eligibility)
 - Microbiome – VB1, VB2
- Vaginal swabs
- Rectal swabs
- Salivary Cortisol (collected by participant after the visit)

Note: Collect blood from participant’s non-dominant arm, if possible.

Physical and Pelvic Exam (EXAM2 and PEX_Female/PEX_Male): A physical exam and a pelvic exam will be performed by a MAPP physician (or designated trained clinician) to assess pelvic musculature tenderness. While the pelvic and physical exam is required, the rectal and vaginal swabs are optional.

The RC will demonstrate to and provide each participant with instructions on how to log onto and complete the online participant questionnaires, as well as answer any questions the participant may have. It is expected to take approximately one hour to complete these CRFs. The RC should then escort eligible participants to a quiet comfortable location where he/she can complete the online questionnaire assessments including:

Urologic CRFs, All Participants

- Interstitial Cystitis Symptom Index (ICSI) and Problem Index (ICPI) forms– (ICINDEX)
- AUA Symptom Index (AUASI)
- RICE Case Definition Questionnaire for Control Participants (RICE_CON)
- RICE Bladder Symptom Impact (BSI)

Urologic CRFs, Female Participants only:

- Female Genitourinary Pain Index (FGUPI)
- Female Sexual Function Index (~~FSFI~~FSFI2)
- Female Self-Esteem and Relationship Questionnaire (FSEAR)

Urologic CRFs, Male Participants only:

- Male Genitourinary Pain Index (MGUPI)
- International Index of Erectile Function (IIEF)
- University of Washington Ejaculatory Function Scale (EFS)
- Male Self-Esteem and Relationship Questionnaire (MSEAR)

Non-Urological Phenotyping CRFs, All Participants:

- | | |
|---|--|
| Symptoms and Illness Impact | <ul style="list-style-type: none">• Complex Medical Symptoms Inventory (CMSI2_Screening)• Fibromyalgia symptoms module (CMSI2_FM2)• Brief Pain Inventory: Body Map, Intensity, Interference (BPI2)• PAIN Detect (PAIN)• McGill Pain Questionnaire (MPQ)• Gracely Box Scales (GBS)• WHO Disability Assessment Schedule (WHO-DAS)• Medical Outcomes Health Survey (SF-12)• International Physical Activity Questionnaire (IPAQ)• Work Productivity & Activity Impairment Questionnaire (WPAI)• Feelings and Emotions Questionnaire (PANAS)• Hospital Anxiety and Depression Scale (HADS)• Multiple Ability Self-Report Questionnaire (MASQ)• PROMIS Fatigue• PROMIS Sleep• Perceived Stress Scale (PSS) |
| Traits & Early Life Experience | <ul style="list-style-type: none">• Catastrophizing Sub-scale (CSQ:CAT)• Recent Traumatic Events Scale (RTES) |
| Co-morbid Symptoms
(PRN per report following
CMSI Questionnaire) | <ul style="list-style-type: none">• CMSI, Chronic Fatigue Syndrome (CMSI2_CFS2)• CMSI, Irritable Bowel Syndrome (CMSI2_IBS2)• CMSI, Migraine (CMSI2_MI2)• CMSI, Vulvodynia (CMSI2_VDYN)• CMSI, Current TMD Symptoms (CMSI2_TMD2)• Gonzalez TMJD Questionnaire (TMDSI) |

3.C.1. Completing the Month 6 Visit

After participant completes the online questionnaires:

- Run participant CMSI Report from the RC Data Management Tools screen.
- Review the Completeness Report – stress to participant the importance of completing the entire survey/questionnaires. If participant did not complete the entire survey, as indicated on the report, confirm with him/her that they intended to not complete the survey, if not, assist participant in logging back onto the system to complete the survey, however please remember that it is not mandatory that he/she completes the session.
- Administer the applicable CMSI modules (Fibromyalgia (CMSI2_FM2), Chronic Fatigue (CMSI2_CFS2), Irritable Bowel Syndrome (CMSI2_IBS2), Migraine (CMSI2_MI2), Vulvodynia (CMSI2_VDYN2), Temporomandibular Joint Disorder (CMSI2_TMD2)) as indicated on the participant report.
- Conduct QST Procedures– see **Appendix E**
- Transport participant to location where he/she will complete Trans-MAPP Neuroimaging scans (see Appendix D in the Control Protocol)

Prior to participant leaving clinic, provide him/her with:

- Salivette collection kit and shipping materials for 3 day collection
 - Pre-assembled at-home collection kits (see **Appendix B**).
 - A review of the instructions on how to collect and ship the samples from the back of the tracking form [S3TRAC2]

Note: RC must complete the header information and the scheduled collection dates on [S3TRAC2] and enter this information into the DMS before giving to participant.

- Instruction sheet for accessing and completing the online Participant questionnaires
- A reminder of their study PID# and PIN (this can be included on the Contact Completion Calendar or separate site specific format)
- Site specific reimbursement for their time and effort
- Site Contact information for participant questions

Once participant leaves, RC will:

- Ship the collected Plasma Specimen and the Home Collection Linking Form to the TATC and enter shipping details into the DMS
- Properly store the other biospecimens at the required temperature as indicated in the lab section of the manual of procedures.
- Send urine aliquot for 24 hrs (minimum) urine culture to local lab/clinic.

3.D. Cortisol Salivary Sample Collection

Following the Week 0 and Month 6 visits, salivary cortisol will be measured twice daily (morning (4-9am) and bedtime (8pm-12am)). Saliva specimens will be collected at home by the participant during the 3 day period following the Week 0 visit. Participants will be asked to collect 2 samples a day for 3 days according to the salivette instructions on the back of the “3 Day Salivette Collection Form,” to record the collection date and time of every sample on this form, and to refrigerate all salivettes in the refrigerator until shipped in the pre-labeled envelope included in the kit.

4. BIOLOGICAL SPECIMENS

Biologic specimens collected at Week 0 and Month 6 include urine, blood, saliva, and rectal and vaginal swabs. The schedule of these collections is summarized in **Table 3**. Please see the Biospecimen collection CRFs and **Appendix B** for additional details regarding collection, storage, and shipment of the biospecimens.

Table 3: Schedule of Biologic Specimen Collection

Blood Collection	Blood specimen 10mL ACD plasma vacutainers (Plasma and Buffy Coat DNA)		Week 0 (Screening/Eligibility) and 6 Month visits
	STIM TUBES Blood for stimulated cytokines 3 x 1 mL whole blood in TruCulture tubes pre-loaded with LPS, FSL-1 or Null (no treatment)		Monday, Tuesday, Wednesday, and Thursday clinic visits only Week 0 (Screening/Eligibility) and 6 Month visits
Biomarker Urine	Spot urine specimen Biomarker/VB2 (~90mL)		Week 0 (Screening/Eligibility) and 6 Month visits
Saliva	Salivary cortisol samples		2 times a day, waking and bedtime 3 day period after Week 0 (Screening/Eligibility) visit 3 day period after Month 6 visit
Microbiome	Urine (VB1 ~20 mL, VB2 ~30-40mL)	Female/Male Week 0 (Screening/Eligibility) and 6 Month visits	
	Rectal Swabs ²	Female/Male: Week 0 (Screening/Eligibility) and 6 Month visits	
	Vaginal Swabs ³	Female: Week 0 (Screening/Eligibility) and 6 Month visits	

5. INTERNET SITE DESIGN AND OPERATION

The Trans-MAPP internet site will be the primary data collection tool for longitudinal assessment for the online surveys. A number of steps will be taken to assist in participant tracking and retention:

- The site will be designed to be attractive, engaging, and as user-friendly as possible
- Places to contact, via phone or email, for help for site operation or anything else regarding the study will be clear on every page
- If a participant misses a data collection time-point, the primary enrollment site will follow-up with the participant via email, phone, or mail
- Reminders for upcoming assessments will be emailed from the Discovery Sites to each participant, with an easy link to the participant’s own data collection page. Two weekly follow-up emails will be sent automatically after a missed contact.
- Repeated attempts will be made by the Discovery Sites to contact difficult-to-reach participants, and at each time-point, participants will be asked for their most recent phone number, email and physical address

6. CASE REPORT FORMS (CRFS) AND CRF-RELATED PROCEDURES

6.A. Acquisition of Forms from the DCC

The CRFs are provided to the Clinical Centers in electronic format as Adobe portable document format (PDF) files. The RCs at the Clinical Centers are responsible for printing all RC-completed data collection forms and administrative forms for the visits which they conduct. To streamline the printing process, the RC-completed forms necessary for each visit are grouped together in one packet, and are presented in the order they should be completed. For some visits, instructions on the CRFs or Visit Checklists specify when particular CRFs should be completed. For example, at the Week 0 visit, forms collecting eligibility criteria and symptom questionnaires should be completed prior to the administration of physical exams or other study procedures.

Note: The CRFs refer to Week 0 as “Month 0.” These are the same visit.

Each CRF has a code name located in **bold** at the bottom right of the page. Each form is dated at the bottom left corner to identify the version of the CRF. This is important should a form be revised at a later date. Please refer to the Data Entry Form and Administrative Form version logs, included as cover sheets to the master CRF packet, to ensure that you are using the correct form versions.

6.B. General Instructions for the Completion of CRFs

The following guidelines are applicable to all CRFs being completed for this study:

***PLEASE NOTE:** It is imperative that all header information on ALL PAGES on ALL CRFs be completed, even if a particular page (or pages) of a CRF is blank.

Two types of forms are used in this study: Data Forms and Administrative Forms:

- Data Forms contain participant data that are entered into the database.
- Administrative Forms are used for processing Data Forms, tracking data flow and in scheduling study procedures and appointments. Administrative Form data are not entered into the database.

The RC and PT should always verify the forms in a packet against the corresponding Visit Checklist and the Visit Schedule (included with the master CRF packet) to confirm that all forms are available before the participant arrives for a clinic visit. Individual CRFs not included in a visit packet can be printed from the Adobe .PDF files available via the study website prior to the visit. As CRF amendments occur, the DCC will notify the clinical centers and make updated versions available within the application files.

All CRFs should be completed in **black** ink. Do not use pencil or blue or red ink. Always use participant’s initials, not full name. **Print** legibly and clearly. All questions must be answered (all fields completed), as specified on the CRF. Be concise, however, avoid using abbreviations and symbols. **UNK** should be written in any space left unanswered. When the participant is not sure of an answer, they should use a “**best estimate**” rather than not answer the question. It is important that the RC complete **ALL INFORMATION ON ALL PAGES** of the CRF Master Heading **before** continuing with the form to ensure easy identification in case of separated pages. Master headings are at the top of each CRF page. The Master Heading elements include: **the Participant ID (PID), a Participant Identification Number (PIN),**

the Discovery Site number, Clinical Center number, CRF Date, and Visit Number. The Personnel Identification number (“RC ID”) of the study staff member completing the form is located at the bottom of all applicable forms which the RC completes. The RC ID number should be completed following form review. Do not write comments in the margins or on the reverse side of the forms. A legible source document **must** exist for all data recorded on the CRF.

Errors should be corrected on the CRFs by crossing out the error with a single line and entering the correct information. *Always* initial and date the change. Circle the correct answer for clarification, if necessary. **Never** use correction fluid.

The RC is responsible for reviewing all of the completed forms at the respective visits. All personal identifying information must be removed from lab or procedure reports prior to forwarding copies to the DCC/TATC, if it is applicable/necessary for this to be done. All source documentation sent to the DCC must have all personal identifying information obliterated (“blacked out”) and the study identifying information (Participant ID and Participant Initials) should be recorded. Making a photocopy after blacking out the name assures complete confidentiality.

6.B.1. Forms Completion

In general, the RC completes all CRFs, unless otherwise specified on the form (participants are also directed to complete some forms, as specified in the form’s instructions). Upon completion and review of the RC-completed forms, record the RC ID at the bottom of each CRF. The RC should review all forms for legibility, accuracy, and completeness *before* they are entered into the database or sent to the TATC. The Visit Checklists will assist in documenting the review, entry, and verification process. If the RC identifies an error while reviewing the forms, the error should be corrected on the current form by crossing out the error with a single line in black ink, entering the correct information and initialing and dating the change. The RC should circle the correct answer for clarification, if necessary.

6.B.2. Personnel Identification Numbers (PI ID/RC ID)

Each PI and Clinical Center staff member (RCs) involved in data collection, review, and/or CRF data entry will be assigned a 4-digit ID (“RC ID”). This number is entered in the last question on select RC-completed forms, and refers to the staff member conducting the visit and completing the form.

6.B.3. Participant Completed Forms

For those forms completed by the participant, the RC will instruct the participant in form use and completion. The RC should be readily available to assist the participant with any questions. If the RC believes that the participant may have difficulty reading the forms, the RC may interview the participant to complete the forms. Since the participant may find some of the information on the forms to be sensitive, whenever possible, the participant should be encouraged to complete the forms alone.

The RC should review the participant-completed forms for completeness and legibility before the participant leaves the clinic in case additional information or clarification is required.

6.B.4. Participant Interview Completed Forms

For those forms completed by the RC through Participant Interview, the RC will collect and record information obtained from direct interview.

In completing the forms, the RC clarifies any participant answer that is unclear or incomplete. The interviewer should have the participant elaborate or reconsider an incomplete or inappropriate answer without leading the participant or influencing the content of the answer; thereby, creating a possibly biased answer.

Some questions addressed in the CRFs are personal and may be considered very sensitive by the participant. When a participant shows reluctance in answering a question, the interviewer should reassure the participant regarding the confidentiality of the response and explain the importance of the question.

6.B.5. Header Information on CRF:

Participant ID (PID): This is generated by the Registration Module and logged by the RC in the **PTLOG** at each Discovery Site. It is a six-digit number that is unique to the Discovery Site and the participant. Once assigned, a participant's ID is not deleted or transferred to another study participant.

Participant Initials: The first letter from the first, middle and last name of the participant is noted in the space provided for the initials. If a participant does not have or use a middle initial, the first letter of her first and last name is used.

Participant Identification Number (PIN): The Participant Identification Number (PIN) is a secondary identifier used to confirm the participant for which data corresponds. The Participant ID (PID) and Participant Identification Number (PIN) must correspond on all CRFs for a participant.

Discovery Site Number: Each Discovery Site will be assigned a unique two-digit Discovery Site Number that permanently identifies it for the duration of the study.

Clinical Center: Each sub-site of a Discovery Site will be assigned a 2-digit number Clinical Center number so that it may be identified in conjunction with the Discovery Site number as a secondary unique identifier of the origin of the data recorded on each CRF.

Visit Number: Visit numbers have been identified in the protocol when specific events happen during the course of the study. Visit numbers range from 01-03. ***Please Note:** The Data Management System also has "Visit 0" which is used exclusively as a unique data collection module for collection of **Concomitant Medications**, CMEDs, across **ALL VISITS**. The CMED₂ form is maintained as a running log of all medications which the participant reports taking at each visit.

CRF Date: This is the date the CRF is completed. In most cases, the date of the visit/contact.

RC and PI ID: Each RC and PI must have a unique 4-digit identifier. The DCC uses the unique ID to link specific data to a particular person in times when data clarification is needed.

6.C. Specific Instructions for Completing Data Entry CRFs

This section provides specific instructions on how to complete each Data Entry CRF. **Please note the forms are listed in the order of CRFs completed by the RC and CRFs completed by the participant.** If, after consulting this section, you are still unsure of how to complete a form, please contact Clinical Data Management at the DCC.

Case Report Forms – Data Entry Forms	
Form Name	Form Code
<u>CRFs completed by Research Coordinator:</u>	
Screening/Eligibility forms:	
Demographics	DEMO
Eligibility for Control Participants	ELIG2_CON
Neuroimaging Study Eligibility for Control Participants	ELIG_SCAN2_CON
Urine Culture Result	UCR
Enrollment for Controls	ENROLL_CON
Medical History, Treatment, and Physical Exam:	
Medical History	MEDHX2
Family Medical History	FAMHX
Concomitant Medications	CMED2
Cystoscopy History for Control Participants	CYSTO_CON
Antibiotics Treatment History	ABHX
Physical Exam	EXAM2
Pelvic Exam (Female & Male)	PEX_Female/PEX_Male
Brief Clinical Diagnostics for Control Participants	CDX_CON
Co-morbid Diagnostic Modules completed per answers given on Complex Medical Symptom Inventory:	
Fibromyalgia Diagnostic Module	CMSI2-FM2
Chronic Fatigue	CMSI2-CFS2
Irritable Bowel Syndrome	CMSI2-IBS2
Vulvodynia	CMSI2-VDYN2
Migraine	CMSI2-MI2
Temporomandibular Joint Disorder (TMJD)	CMSI2-TMD2
Gonzalez TMJD Questionnaire	TMDSI
Specimen Tracking CRFs:	
Plasma Specimen Tracking	PTRAC2
STIM Tubes Specimen	STIMTR2
Urine Specimen Tracking	UTRAC2
Microbiome Universal Urine Specimen Tracking (VB2)	UUMBTR2
Microbiome Urine Specimen Tracking (Female/Male)	UFMBTR2 UMMBTR2
Rectal Swab Specimen Tracking	RSTRAC2
Vaginal Swab Specimen Tracking	VSTRAC2
Home Saliva Collection, 3 day	S3TRAC2
Neuroimaging CRFs	
Neuroimaging Day of Scan MRI Screening Procedures (Administrative)	MR_SCREEN
Neuroimaging Day of Scan Data & Procedures Status Confirmation	NEURO_SCAN2_CON
Neuroimaging Data Collection CRF	NEURO_CRF
Quantitative Sensory Testing Procedures	
Quantitative Sensory Testing Screening	QST_SCREEN
Quantitative Sensory Testing CRF	QST

Case Report Forms – Data Entry Forms	
Form Name	Form Code
PRN forms (filled out as-needed):	
Study Stop	SSTOP
Consent Withdrawal	CONWITHDR2
Reinstatement of Consent	RECON2
Procedural or Unanticipated Problems	PUP

Case Report Forms – Data Entry Forms	
Form Name	Form Name
<u>CRFs completed by Participant via online survey:</u>	
Urologic Domain CRFs, Females and Males	
Symptom & Health Care Utilization Questionnaire	SYM-Q
Global Response Assessment	GRA
Interstitial Cystitis Symptom Index	ICINDEX
Interstitial Cystitis Problem Index	
AUA Symptom Index	AUASI
RICE Case Definition Questionnaire for Control Participants	RICE_CON
RICE Bladder Symptom Impact	BSI
Early In Life Infection History	EIL-INF
Urologic Domain CRFs, Females Only	
Female Genitourinary Pain Index	FGUPI
Female Sexual Function Index	FSFI FSFI2
Female Self-Esteem & Relationship Questionnaire	FSEAR
Urologic Domain CRFs, Males Only	
Male Genitourinary Pain Index	MGUPI
International Index of Erectile Function	IIEF
U. Washington Ejaculatory Function Scale	EFS
Male Self-Esteem & Relationship Questionnaire	MSEAR
Non-Urologic Domain CRFs	
Complex Medical Symptoms Inventory	CMSI2_Screening CMSI2_Follow-Up
Fibromyalgia Diagnostic Module (ACR 2010)	CMSI2-FM2
BPI (<i>Body Map</i> , Intensity, Interference)	BPI2_Female
BPI (<i>Body Map</i> , Intensity, Interference)	BPI2_Male
PAIN Detect	PAIN
McGill Pain Questionnaire	MPQ
Gracely Box Scales	GBS
WHO Disability Assessment Schedule	WHO-DAS
SF-12 Health Status Questionnaire	SF-12
International Physical Activity Questionnaire	IPAQ
Work Productivity & Activity Impairment Questionnaire	WPAI
PANAS	PANAS
Hospital Anxiety and Depression Scale	HADS
Multiple Ability Self-Report Questionnaire	MASQ
PROMIS - Fatigue - Short Form	FATIGUE
PROMIS - Sleep - Short Form	SLEEP
Perceived Stress Scale	PSS
Ten-Item Personality Inventory	TIPI
Thoughts About Symptoms	CSQ
Childhood/Recent Traumatic Events Scale	CTES / RTEs

6.D. CRFs completed by Research Coordinator:

6.D.1. Screening/Eligibility forms:

[DEMO] DEMOGRAPHICS

Purpose: To collect demographic data on a participant, as well as family history of PBS/IC and/or CPPS/CP.

Who: Research Coordinator

When: Week 0

General Directions

Question #7 Annual family income is to be recorded in US dollars.

Question #11 A partner can be someone of the same sex.

[SYM-Q] SYMPTOM & HEALTHCARE UTILIZATION QUESTIONNAIRE

Purpose: To collect information regarding the participant’s assessment of symptom changes, specifically pain, urinary symptoms, and non-urinary symptoms. To capture the participant’s mood, single most bothersome symptom, and health care utilization. For female participants the most recent menstrual period is documented.

Who: Participant

When: Screening Week 0, Month 3, Month 6

At Week 0, participant completes **SYM-Q** and RC enters in the DMS. At Months 3 and 6, participant completes online.

[ELIG2_CON] ELIGIBILITY CONFIRMATION FOR CONTROL PARTICIPANTS

Purpose: To determine and ensure the participant’s eligibility for entry into the study for **Control Participants**. All Inclusion Criteria responses must be “Yes” to be eligible for enrollment. All exclusion/deferral responses must be “No” for the participant to be eligible for enrollment.

Who: Research Coordinator

When: Week 0

General Directions:

To be eligible for the study, participants must consent to provide DNA specimens (blood and cheek swab) and blood and urine specimens. Participants must also agree to participate in ALL Control Study procedures including the pelvic exam, Neuroimaging and QST.

Data entry instructions:

For ALL Control Participants, the **ELIG2_CON** must be the first form entered in the DMS. If a participant is found to be *ineligible* enter ONLY the **ELIG2_CON** form and no other screening/eligibility CRFs.

[ELIG_SCAN2_CON] ELIGIBILITY CONFIRMATION, NEUROIMAGING STUDY*

Purpose: To confirm that a potential Participant for the MAPP Neuroimaging study is eligible to be scanned and to participate in the Neuroimaging study.

Who: Research Coordinator

When: Week 0

Note: Participants with a neurostimulator are excluded from the Neuroimaging Study but may still participate in the MAPP Control Study if they are eligible.

[UCR] URINE CULTURE RESULT

Purpose: To confirm that the participant does not have a midstream urine culture $\geq 100,000$ CFU/ml, with a single uropathogen, per urine culture test results. If a participant does have a midstream urine culture $\geq 100,000$ CFU/ml, with a single uropathogen, then the participant is ineligible.

Who: Research Coordinator

When: Week 0

[ENROLL_CON] ENROLLMENT CONFIRMATION

Purpose: To confirm that a participant has successfully enrolled in the study, or to document why a participant has not enrolled following eligibility screening.

Who: Research Coordinator

When: Week 0

General Directions:

Data on this form will be used for monthly accrual reports and for visit scheduling purposes, so all applicable fields must be completed for all participants.

6.D.2. Medical History, Treatment, and Physical Exam:

[MEDHX2] MEDICAL HISTORY

Purpose: To obtain information about the participant's medical history.

Who: Research Coordinator completes form with information obtained from participant interview

When: Week 0

General Directions

Responses on MEDHX2 may be verified with participant's medical records, if available, at the Clinical Center or another treatment facility. Medical records are not required.

[FAMHX] FAMILY MEDICAL HISTORY

Purpose: To obtain information about the participant's first degree blood relatives' history of common chronic pain and common psychiatric disorders.

Who: Participant

When: Week 0

General Directions

Ensure that the participant understands that first-degree blood relatives include only the following: parents, grandparents, aunts, uncles, siblings, children.

If the answer to Q.#1 is “No” or “Don’t know” please leave the rest of the form blank.

If the answer to Q.#1 is “Yes”, ensure that the Participant completes, to the best of his or her ability, the table on page 2 of the **FAMHX** form.

[CMED2] CONCOMITANT MEDICATIONS

Purpose: To collect information from the participant in order to record all concomitant medications/supplements/vitamins/herbal remedies currently taken by the participant, while in the study.

Who: Research Coordinator

When: *Please note: The CMED2 form is managed within its own Visit in the DMS at Visit #0 as a running log of all medications recorded at Screening Week 0 and all subsequent visits.

CMED2 is completed at Week 0, Month 6, and PRN Monthly if medication changes are reported by the participant.

General Directions:

Medications refer to prescription or non-prescription drugs, over-the-counter drugs, vitamins, nutritional supplements or herbal remedies. Document names, doses and frequency of use.

The information for this CRF is obtained from the participant’s report of the most recent dose(s) of over-the-counter medications and/or prescriptions.

****The participant should bring to each clinic contact all containers for medications currently being taken.***

Line #: This is a 3-digit sequential number which begins with “001”, “002”, “003”, etc.

Drug Code #: This is the code that is been obtained from the **Medication Reference/Drug Dictionary** tool in the Data Management System application.

Drug Name: This is the generic name for the medication/treatment, generated from the **Medication Reference/Drug Dictionary** tool.

Medication Start Date: The most recent date the participant reports taking the medication to be recorded.

Medication Stopped?: This checkbox confirms the continuation or discontinuation of medications.

For Urologic or Pelvic Pain Symptoms:

Confirm with the participant if each medication was taken due to any urologic or pelvic pain symptoms.

Additional CMED pages, without Question #1, have been provided if multiple pages are needed to record multiple concomitant medications for a visit.

If a drug code for a concomitant medication that the participant has recorded is unavailable in the Medication Reference Tool on the web application, the RC should call the Clinical Data

Manager at the DCC. If the Clinical Data Manager is unable to locate the information for the RC, the medication and other relevant data will be recorded on a log maintained at the DCC and the Clinical Data Manager will develop a code and enter the data in CMED2 at the DCC.

[CYSTO_CON] CYSTOSCOPY HISTORY

Purpose: To record cystoscopy details within 24 months of study start. If available, images from the cystoscopy should be provided in digital format to the DCC.

Who: Research Coordinator

When: Week 0

[ABHX] ANTIBIOTICS TREATMENT HISTORY

Purpose: To capture the participant’s use of antibiotic medications over the previous 6 month period.

Who: Research Coordinator

When: Week 0 and Month 6

[EXAM2] PHYSICAL EXAM

Purpose: To obtain information about the participant’s study specific health status through a physical examination of abdominal and genitourinary systems.

Who: Investigator completed or his/her approved designee. Upon completion, the RC should review this form for completeness.

When: Week 0 and Month 6

General Directions

Questions #1 and #2: It is *preferable* that height and weight be measured without shoes.

Question #3: Please utilize below guidelines for measuring umbilical waist circumference:

- Participant should be standing with arms held slightly away from the body.
- Technician stands to the right side of the person. Locate the lateral border of the right ilium.
- Draw a horizontal line just above just above the uppermost lateral border of the right ilium and then cross the line to indicate the midaxillary line of the body.
- Standing to the right, place a measuring tape around the trunk in a horizontal plane at the level marked on the side of the trunk. Hold the zero end below the measurement value.
- Do the first waist measurement.
- Repeat the waist measurement. The second measurement should be within 1 cm of the first.
- Record the first of the 2 measurements. If the second measurement is not within 1 cm, repeat measurement until 2 results are within 1 cm. Record the first of the 2 measurements.

[PEX_FEMALE, PEX_MALE] PELVIC EXAM FOR FEMALES AND MALES

Purpose: To record pain symptoms detected during a MAPP-specific pelvic exam.
Who: Clinician trained in MAPP-specific pelvic exam procedures.
When: Week 0 and Month 6

General Directions

Please note, this form must be completed **only** by a **clinician trained in the MAPP-specific pelvic exam procedures** and during the same time as the physical exam procedures. Please see the administrative forms **PEX_Female_Procedures/PEX_Male_Procedures** for further instructions.

[CDX_CON] CLINICAL DIAGNOSTICS -FOLLOW-UP

Purpose: To capture clinical diagnostic details including height, weight, umbilical circumference, blood pressure, urine culture results, and confirmation that female participants are not currently pregnant.
Who: Research Coordinator
When: Month 6

General Directions

Note: if a female participant confirms she is pregnant during follow-up, she must be withdrawn from the study.

6.D.3. Co-morbid Diagnostic Modules completed per answers given on Complex Medical Symptom Inventory

[CMSI2_CFS2] COMPLEX MEDICAL SYMPTOMS INVENTORY – CFS

Purpose: To capture data about the participant’s symptoms related to chronic fatigue syndrome, if reported per the CMSI Questionnaire
Who: Research Coordinator
When: If applicable, Week 0 and Month 6

[CMSI2_IBS2] COMPLEX MEDICAL SYMPTOMS INVENTORY – IBS

Purpose: To capture data about the participant’s symptoms related to irritable bowel syndrome, if reported per the CMSI Questionnaire
Who: Research Coordinator
When: If applicable, Week 0 and Month 6

[CMSI2_VDYN2] COMPLEX MEDICAL SYMPTOMS INVENTORY - VULVODYNIA

Purpose: To capture data about the female participant’s symptoms related to vulvodynia, if reported per the CMSI Questionnaire
Who: Research Coordinator
When: If applicable, Week 0 and Month 6

[CMSI2_MI2] COMPLEX MEDICAL SYMPTOMS INVENTORY - MIGRAINE

Purpose: To capture data about the participant’s symptoms related to migraine, if reported per the CMSI Questionnaire

Who: Research Coordinator

When: If applicable, Week 0 and Month 6

[CMSI2_TMD2] COMPLEX MEDICAL SYMPTOMS INVENTORY - TMJ

Purpose: To capture data about the participant’s symptoms related to temporomandibular joint disorder, if reported per the CMSI Questionnaire

Who: Research Coordinator

When: If applicable, Week 0 and Month 6_

[TMDSI] GONZALEZ TMJD QUESTIONNAIRE

Purpose: To capture data about the participant’s symptoms related to temporomandibular joint disorder, if reported per the CMSI Questionnaire

Who: Research Coordinator

When: If applicable, Week 0 and Month 6

6.D.4. Specimen Tracking CRFs:

[PTRAC2] PLASMA SPECIMEN TRACKING

Purpose: To document collection and shipping details regarding the plasma specimens to be sent to the TATC. Please see the CRF for further instructions.

Who: Research Coordinator

When: Week 0 and Month 6

[STIMTR2] STIM TUBES SPECIMEN

Purpose: To document collection and shipping details regarding the STIM Tube specimens to be sent to the TATC. Please see the CRF for further instructions.

Who: Research Coordinator

When: Week 0 and Month 6

[UTRAC2] URINE SPECIMEN TRACKING

Purpose: To document collection and shipping details regarding the urine specimens to be sent to the TATC. Please see the CRF for further instructions.

Who: Research Coordinator

When: Week 0 and Month 6

[UUMBTR2] MICROBIOME UNIVERSAL URINE SPECIMEN TRACKING (VB2)

Purpose: To document collection and shipping details regarding the urine specimens from participants for the Microbiome studies to be sent to the TATC.

Who: Research Coordinator

When: Week 0 and Month 6

Please see the CRF for further instructions. Also, please see the detailed instructions sheet included in the specimen collection kit, provided by the TATC, which is to be given to the participant to ensure the most sterile and accurate specimen collection methods. Please contact the TATC to re-order these kits well in advance of any participants' screening Week 0 and/or Month 6 Clinic Visits if supply of these kits runs low.

[UFMBTR2, UMMBTR2] MICROBIOME URINE SPECIMEN TRACKING (FEMALE/MALE)

Purpose: To document collection and shipping details regarding the urine specimens from male and female participants, respectively, for the Microbiome studies to be sent to the TATC.

Who: Research Coordinator

When: Week 0 and Month 6

Please see the CRF for further instructions. Also, please see the detailed instructions sheet included in the specimen collection kit, provided by the TATC, which is to be given to the participant to ensure the most sterile and accurate specimen collection methods. Please contact the TATC to re-order these kits well in advance of any participants' Screening Week 0 and/or Month 6 Clinic Visits if supply of these kits runs low.

[RSTRAC2] RECTAL SWAB SPECIMEN TRACKING

Purpose: To document collection and shipping details regarding the rectal swab specimens to be sent to the TATC. Please see the CRF for further instructions.

Who: Research Coordinator

When: Screening Week 0

[VSTRAC2] VAGINAL SWAB SPECIMEN TRACKING

Purpose: To document collection and shipping details regarding the vaginal swab specimens to be sent to the TATC. Please see the CRF for further instructions.

Who: Research Coordinator

When: Screening Week 0

[S3TRAC2] HOME SALIVA COLLECTION, 3 DAY

Purpose: To document collection and shipping details regarding the home saliva specimens to be sent to the TATC. Please see the CRF for further instructions regarding home collections and shipment to the TATC.

Who: Research Coordinator completes when distributed to the participant. Participant completes shipping procedures from home.

When: Week 0 and Month 6

[NEURO_SCAN2_CON] NEUROIMAGING DAY OF SCAN DATA & PROCEDURES STATUS CONFIRMATION

Purpose: To confirm details about scanning procedures and timing of events on the day of the Neuroimaging scan.

Who: Research Coordinator

When: Week 0 and Month 6

Q1: If Q1 is Yes, Q2 must also be Yes.

Q6: Do not complete Qs 6a-6e UNLESS Q6 is No.

[NEURO_CRF] NEUROIMAGING DATA COLLECTION CRF

Purpose: To confirm details about voiding, water ingestion, and pain testing procedures performed during the Neuroimaging scan.

Who: Research Coordinator

When: Week 0 and Month 6

[QST_SCREEN] QUANTITATIVE SENSORY TESTING SCREENING

Purpose: To assess participants' ability to participate in some or all of the QST procedures and to provide the participants with some information about and guidelines for conduct of the QST procedures.

Who: Research Coordinator

When: Week 0 and Month 6

[QST] QUANTITATIVE SENSORY TESTING

Purpose: To record the results of the Quantitative Sensory Testing Procedure results obtained from the MAST, Algometer, Temporal Summation, and Conditioned Pain Modulation procedures.

Who: Research Coordinator

When: Week 0 and Month 6

6.D.5. PRN CRFs

[SSTOP] STUDY STOP POINT

Purpose: To record the date the participant completed the study or the date and the primary reason for a participant's termination prior to the Month 6 visit.

Who: Research Coordinator and Principal Investigator

When: 6-month visit, or at time of early study withdrawal.

General Directions

The Study Stop Point [SSTOP] form is completed at the end of the 6-Month Visit (Visit #3), the last study contact. It is also completed at the time of withdrawal if a participant opts to withdraw from the study early. If the participant withdraws in-between visits, in the DMS, select the next in-clinic visit # in order to access the SSTOP CRF.

Qx #1: Indicate if the participant has successfully completed the trial. If the answer is “No”, the reason for not successfully completing the trial must be indicated. **Only one most applicable and appropriate reason must be checked.** Reasons include, but are not limited to:

- ◆ No longer willing to follow the protocol/interested in participating
- ◆ Lost to follow-up
- ◆ Participant has personal constraints
- ◆ Medical Condition/Event
- ◆ Physician’s discretion
- ◆ Other

Female Participants only:

- ◆ Female participant is pregnant

Q2: Number of Participant’s final contact: If the participant withdraws in-between visits/contacts, please use the visit number of the participant’s most recent completed visit/contact. For example, if the participant wishes to no longer participate between visits 2 and 3, please use Visit #2. This visit number does not have to be the same as the CRF visit number.

Qx #s 5 and 6: The PI and the RC **must** sign and date the Study Stop Point [SSTOP] form.

[CONWITHDR2] CONSENT WITHDRAWAL

Purpose: To document the withdrawal of consent for a participant’s biospecimen(s) to be used for the purposes of this study and/or other studies.

Who: Research Coordinator

When: Visit at which the participant informs the study staff of the wish to withdraw consent of the use of biospecimen(s).

General Directions:

If a participant wishes to withdraw consent for the use of biospecimens, all fields on this CRF must be completed as appropriate, the biospecimens must be destroyed, and documentation detailing when the specimens were destroyed must be kept with the participant’s study records.

[RECON2] REINSTATEMENT OF CONSENT

Purpose: To confirm reinstatement of consent for a participant’s biospecimens to be used.

Who: Research Coordinator

When: Visit at which the participant provides the study staff with consent that biospecimen(s) may be used.

[PUP] PROCEDURAL OR UNANTICIPATED PROBLEMS

Purpose: To collect information concerning any Procedural or Unanticipated Problems (PUPs) that the participant experiences during the course of the trial. PUPs may occur at clinic contacts and in relation to study procedures (such as blood draw, for example), or in the intervals between clinic contacts while the Participant is enrolled in the study.

- Who:** Research Coordinator and/or PI completes. The RC and/or PI determines the study-relatedness and grades the severity of the PUP using the codes provided on the form.
- When:** **The PUP form is completed on an as-needed basis in the event of an procedural or unanticipated problems that occur, whether they are related to the study or not. Please note that Procedural or Unanticipated Problems may be related to a Protocol Deviation and/or Violation. Please note the codes in the legend to record a PUP as a Protocol Deviation and/or Violation.**

General Directions

The following items are listed in the order in which they appear on the form. When completing the form, please refer to the PUP codes at the bottom of the form.

- Visit Number:** The Visit Number in the header will be the current visit number, if the PUP is being reported during a scheduled visit window. If a participant contacts the RC between scheduled visits, the **next** visit number is entered (i.e., if the CRF is completed between Visit #03 and Visit #04, the Visit Number would be 04).
- CRF Date:** CRF Date will be entered in the database as the date of the visit number to which it corresponds even if the PUP(s) may have been recorded between visits. Contacts made with the participant may be recorded on the Comments Sheet (**COMM**), identifying the PUP(s) and the date of contact when the participant reported the PUP(s).
- Question #1:** Any PUP(s) reported by the participant are recorded for the current visit and this question is checked as “Yes”. Question 1a. must confirm the total number of PUPs being recorded and the details of each must be recorded in the space(s) provided in the panel(s) on the form. A second page is available if more than two PUPs are reported at one visit.
- Problem #:** This is a 3-digit sequential number starting with ‘001’, ‘002’, ‘003’, etc. This number repeats during the study **only** if documentation of a continuation of the event being recorded is necessary at a subsequent visit. Each newly reported PUP is recorded with the next, new, sequential number.
- PUP Code:** The PUP Code consists of three letters and two numbers, as listed in the PUP Code panel on the form. The three letters are abbreviations for PUPs as follows: SPC-Specimen collection-related; PRO-Procedure-related; MIS-Miscellaneous, and PDV-Protocol Deviation and/or Violation.
- Date of Onset:** Record the date of onset of the symptoms that the participant experienced that resulted in the PUP, even if the date lasted one day or less. If the PUP is continued from a previous visit and considered a follow-up, re-record the date of onset and be sure to use the original Problem # for the PUP.
- Treatment for PUP:** The RC will code whether the participant received any form of **treatment from a physician or other health care provider** for the PUP. Only physician/health care provider prescribed/recommended treatment is recorded.
- Comments:** Describe the PUP(s) based on the information provided by the participant. Anything transcribed directly from the participant should be set apart by quotation marks. Treatments, if prescribed by the physician, should also be

described in this space. Attempts should be made by the RC to include all pertinent information, for monitoring and reporting purposes at the DCC.

* Also, any supporting documentation of the PUP should be maintained in the Participant’s Source Documentation.

PI ID: This must be completed on all PUP forms. It is a **4 digit number chosen by the PI** or PI’s designee.

All PUP forms are signed and dated by the PI. When recording a new PUP, complete the entire PUP record in each panel. If the PUP is not yet resolved, follow-up should continue at each visit until the event is resolved. Because of this, the RC should review all previously reported PUPs at every visit.

Additional PUP pages, without Question #1 and including additional PUP panels, have been provided if multiple pages are needed to record multiple PUPs for a visit.

6.E. CRFs completed by Participant via online survey:

[SYM-Q] SYMPTOM ASSESSMENT QUESTIONNAIRE (FOR BASELINE AND FOLLOW-UP)

Purpose: To collect information regarding the participant’s assessment of symptom changes, specifically pain, urgency and frequency. To capture the participant’s mood, single most bothersome symptom, and health care utilization. For female participants the most recent menstrual period is documented.

Who: Participant

When: Week 0, Month 3, Month 6

At Week 0, participant completes **SYM-Q** and RC enters in the DMS. At Months 3 and 6, participant completes online.

[GRA] GLOBAL RESPONSE ASSESSMENT

Purpose: To record current symptom status and change in symptoms over the course of the study.

Who: Participant

When: Week 0, Month 3, Month 6

[ICINDEX] IC SYMPTOM & PROBLEM INDEX

Purpose: To collect information on the participant's assessment of IC/PBS symptoms and problems related to these symptoms.

Who: Participant

When: Week 0, Month 3, Month 6

[AUASI] AUA SYMPTOM INDEX

Purpose: To capture details about the severity of urinary symptoms in the previous month from the visit at which the form is administered.

Who: Participant

When: Week 0 and Month 6

[RICE_CON] RICE CASE DEFINITION QUESTIONNAIRE

Purpose: To capture information about symptoms related to pelvic pain, urgency, and frequency in the 3 months prior to the visit at which the form is administered. The RICE form is a companion CRF in the MAPP network to forms and data being collected for the RICE (RAND Interstitial Cystitis Epidemiology) study.

Who: Participant

When: Week 0, Month 3, Month 6

[BSI] RICE BLADDER SYMPTOM IMPACT

Purpose: To capture how the severity of symptoms impact quality of life.

Who: Participant

When: Week 0 and Month 6

[EIL-INF] EARLY IN LIFE INFECTION HISTORY

Purpose: To record data about bladder infection history, kidney infection history, and family history of urinary tract infections.

Who: Participant

When: Week 0

6.F. CRFs for Female Participants ONLY

[FGUPI] FEMALE GENITOURINARY PAIN INDEX

Purpose: To collect information regarding the female participant's assessment of pain and urinary symptoms. Four domains are evaluated: pain/discomfort, urination, impact of symptoms, and quality of life.

Who: Female Participant

When: Week 0, Month 3, Month 6

[FSFI/FSFI2] FEMALE SEXUAL FUNCTION INDEX©

Purpose: To collect information regarding the participant's changes in domains of female sexual functioning during the study.

Who: Female Participant

When: Week 0 and Month 6

[FSEAR] FEMALE SELF-ESTEEM AND RELATIONSHIP QUESTIONNAIRE

Purpose: To collect information about the female participant's perspectives of sexual function and partner relationship.

Who: Female Participant

When: Week 0 and Month 6

6.G. CRFs for Male Participants ONLY

[MGUPI] MALE GENITOURINARY PAIN INDEX (FOR FOLLOW-UP CONTACTS)

Purpose: To collect information regarding the male participant’s assessment of pain and urinary symptoms. Four domains are evaluated: pain/discomfort, urination, impact of symptoms, and quality of life.

Who: Male Participant

When: Week 0, Month 3, Month 6

[IIEF] INTERNATIONAL INDEX OF ERECTILE FUNCTION

Purpose: To capture data about male sexual function.

Who: Male Participant

When: Week 0 and Month 6

[EFS] UNIVERSITY OF WASHINGTON EJACULATORY FUNCTION SCALE

Purpose: To capture data about the severity of the male participant’s symptoms related to ejaculation.

Who: Male Participant

When: Week 0 and Month 6

[MSEAR] MALE SELF-ESTEEM AND RELATIONSHIP QUESTIONNAIRE

Purpose: To collect information about the male participant’s perspectives of sexual function and partner relationship.

Who: Male Participant

When: Week 0 and Month 6

6.H. Non-urologic CRFs

[CMSI_SCREENING, CMSI_FOLLOW-UP] COMPLEX MEDICAL SYMPTOMS INVENTORY QUESTIONNAIRE

Purpose: To report the occurrence of symptoms related to Fibromyalgia, Chronic Fatigue Syndrome, Irritable Bowel Syndrome Temporomandibular Joint Disorder, Migraine, and (if applicable for female participants) Vulvodynia. Data related to other symptoms and disorders are also captured on this form.

Who: Participant

When: **CMSI_Screening** at Week 0
CMSI_Follow-Up at Month 3 and Month 6

[CMSI_FM2] COMPLEX MEDICAL SYMPTOMS INVENTORY - FIBROMYALGIA

Purpose: To capture data about the participant’s symptoms related to fibromyalgia. Data from this form will be used to identify Non-Urological symptoms as well as to create a “pain profile” in conjunction with the body map on the BPI form and responses on the PAIN form.

Who: Participant

When: Week 0, Month 3, Month 6

[BPI2_MALE/FEMALE] BRIEF PAIN INVENTORY

Purpose: To utilize the body map in order to capture areas the participant feels pain. The BPI form also captures data regarding the intensity of pain and interference of pain in the participant’s quality of life.

Who: Participant

When: Week 0, Month 3, Month 6

[PAIN] PAIN DETECT

Purpose: To record general pain symptom details and ratings for types of pain experienced around the body.

Who: Participant

When: Screening Week 0, Month 3, Month 6

[MPQ] MCGILL PAIN QUESTIONNAIRE

Purpose: To capture pain ratings for the intensity of general types of pain.

Who: Participant

When: Week 0 and Month 6

[GBS] GRACELY BOX SCALES

Purpose: To capture pain symptom ratings for intensity and unpleasantness in the past 24 hours.

Who: Participant

When: Week 0 and Month 6

[WHO-DAS] WHO DISABILITY ASSESSMENT SCHEDULE

Purpose: To capture ratings of quality of life as a result of difficulties due to health conditions in the past 30 days.

Who: Participant

When: Week 0, Month 3, Month 6

[SF12] HEALTH STATUS QUESTIONNAIRE ®

Purpose: To collect information regarding the participant’s assessment of their general quality of life as related to their health, and as measured by various types of activities and emotional concerns.

Who: Participant

When: Week 0 and Month 6

[IPAQ] INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE

Purpose: To capture details about physical activity in the past 7 days.

Who: Participant

When: Week 0 and Month 6

[WPAI] WORK PRODUCTIVITY & ACTIVITY IMPAIRMENT QUESTIONNAIRE

Purpose: To record and rate the impact of health problems on the ability to work and do regular activities over the past 7 days

Who: Participant

When: Week 0 and Month 6

[PANAS] PANAS

Purpose: To capture data about various feelings and emotions the participant has felt over the past week.

Who: Participant

When: Week 0 and Month 6

[HADS] HOSPITAL ANXIETY AND DEPRESSION SCALE

Purpose: To collect information regarding the participant’s changes in the emotional component of their illness during the study.

Who: Participant

When: Week 0, Month 3, Month 6

[MASQ] MULTIPLE ABILITY SELF-REPORT QUESTIONNAIRE

Purpose: To rate the ability/difficulty to perform every-day types of activities that might be affected by symptoms.

Who: Participant

When: Week 0 and Month 6

[FATIGUE] PROMIS - FATIGUE - SHORT FORM

Purpose: To capture data about the participant’s feelings of fatigue in the 7 days prior to the visit at which the form is administered.

Who: Participant

When: Week 0, Month 3, Month 6

[SLEEP] PROMIS - SLEEP - SHORT FORM

Purpose: To capture data about the participant’s patterns and quality of sleep in the 7 days prior to the visit at which the form is administered.

Who: Participant

When: Week 0, Month 3, Month 6

[PSS] PERCEIVED STRESS SCALE

Purpose: To indicate feelings and thoughts during the past month.
Who: Participant
When: Week 0, Month 3, Month 6

[TIPI] TEN ITEM PERSONALITY INVENTORY

Purpose: To rate personality traits per the scale provided.
Who: Participant
When: Week 0

[CSQ] THOUGHTS ABOUT SYMPTOMS

Purpose: To capture data about mechanisms the participant uses to cope or deal with symptoms.
Who: Participant
When: Week 0 and Month 6

[CTES/RTES] CHILDHOOD/RECENT TRAUMATIC EVENTS SCALE

Purpose: To capture data about traumatic events in the participant’s past.
Who: Participant
When: Week 0. At Month 6, only **RTES** is completed.

6.I. Specific Instructions for Completing Administrative CRFs

This section provides specific instructions on how to complete each Administrative CRF. Please note the forms are listed alphabetically by Form Name. If, after consulting this section, you are still unsure of how to complete a form, please contact Clinical Data Management at the DCC.

Case Report Forms – Administrative Forms	
Form Code	Form Name (in alphabetical order by Form Name)
STAFFLOG	Clinical Center Staff “Signature and Delegation of Responsibilities” Log
CCORRESP	Clinic Correspondence Log
COMM	Comments Sheet
PTCONT	Participant Contact Information
PCORRESP	Participant Correspondence Log
PTLOG	Participant ID Assignment Log
PROGRESS	Progress Notes
QST_INSTR	QST Instructions
VISIT1 - 3	Visit #1 - 3 Checklists

[STAFFLOG] CLINICAL CENTER STAFF “SIGNATURE AND DELEGATION OF RESPONSIBILITIES” LOG

Binder: Clinic Regulatory Binder
 All personnel working on the Trans-MAPP Control Study must sign the Clinical Center Staff “Signature and Delegation of Responsibilities” Log [STAFFLOG].

The PI should indicate delegation of study responsibilities by initialing in the column associated with the task he or she is delegating and signing and dating each row. This form should be updated regularly as new staff are added or removed.

[CCORRESP] CLINIC CORRESPONDENCE LOG

Binder: Source Documentation Binder

All correspondence between the clinic and the DCC should be recorded on the Clinic Correspondence Log. Refer to the Correspondence Type codes listed at the bottom of each page for the type. “From” and “To” should indicate the names of the persons involved in the correspondence. Refer to the Status Codes listed at the bottom of each page for the status, and update the status as appropriate.

[PTCONT] PARTICIPANT CONTACT INFORMATION

Binder: Source Documentation Binder

The Participant Contact Information [PTCONT] form should be completed by the participant at Visit #1 and is strictly confidential. This form should never be forwarded to the DCC. If a participant’s information changes throughout the course of the study, she should complete a new form.

[PCORRESP] PARTICIPANT CORRESPONDENCE LOG

Binder: Source Documentation Binder

All correspondence between the clinic and the participant *must* be tracked on the Participant Correspondence Log [PCORRESP] form. Any communication, no matter how insignificant it may seem, should be recorded on this log.

[COMM] COMMENTS SHEET

Purpose: To record any relevant information for a visit or a CRF. It can be attached to the CRF or an alternative used to record “Progress Notes” for a visit.
Who: RC and/or PI completed.
When: This CRF is completed on an as needed basis.

[PTLOG] PARTICIPANT ID ASSIGNMENT LOG

Binder: Part of the Clinic Regulatory Binder, but stored separately

The Participant ID Assignment Log [PTLOG] contains a list of all of the participant IDs and identifies the name and initials of the participant assigned to each ID. This log is strictly confidential and must be kept in a secure location.

[PROGRESS] PROGRESS NOTES

Binder: Source Documentation Binder

The Progress Notes [PROGRESS] form should be used to track the participant’s clinic visits, and as source documentation for the study data. Any notes made by the RC or PI must be signed by the person writing the note.

VISIT #1 – VISIT #3 CHECKLISTS (VISIT1 – VISIT 3)

Purpose: The Visit #1 – Visit #3 Checklists (**VISIT1 – VISIT3**) list all the forms and outline general administrative procedures to be completed for each visit (**please refer to the Visit Scheduling and Administration section of the MOP for more details**). These forms *must* be completed for every participant, and filed in the participant’s study binder. The checklists *must* also be included in any transmission of CRFs by the Physical Therapist to *either* the clinical center *or* the DCC.

Any forms marked “No” for an item must have an explanation provided in the comment section.

The review and data entry sections *must* be initialed and dated. At Visit 1, the Eligibility Confirmation section must also be initialed and dated.

Who: RC completed.

When: These CRFs are completed when data collection is complete for each visit.

7. MAPP WEB PORTAL ([WWW.MAPPNETWORK.ORG](http://www.mappnetwork.org))

The study’s official website is <http://www.mappnetwork.org>. The website consists of public and private sections.

Multi-Disciplinary Approach to the Study of Chronic Pelvic Pain A A A

[About MAPP](#) | [Discovery Sites](#) | [Core Sites](#) | [Recruiting Sites](#) | [Projects](#) | [MAPP Portal](#) | [Participant Survey](#)

Welcome to the MAPP Research Network Home Page

MAPP News

- Epidemiological Studies
- Urological Phenotyping
- Non-Urological Phenotyping
- Neuroimaging / Neurobiology
- Biomarkers
- Organ Cross-Talk / Pain Pathways
- MAPP Network Data Collection
- MAPP Bibliography
- MAPP Feedback Survey

Sponsor Links

- Department of Health & Human Services (HHS)
- National Institutes of Health (NIH)
- National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)
- USA Gov

Advocacy Links

- Prostatitis Foundation

A New Look at Urological Chronic Pelvic Pain ...

To help better understand the underlying causes of the two most prominent chronic urological pain syndromes—interstitial cystitis/painful bladder syndrome (IC/PBS) and chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS)—the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) of the National Institutes of Health (NIH), has launched a new and novel research study.

The NIDDK’s Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) Research Network embraces a systemic—or whole-body—approach in the study of IC/PBS and CP/CPPS. In addition to moving beyond traditional bladder- and prostate-specific research directions, MAPP Network scientists are investigating potential relationships between these two urological syndromes and other chronic conditions that are sometimes seen in IC/PBS and CP/CPPS patients, such as irritable bowel syndrome, fibromyalgia, and chronic fatigue syndrome.

The multidisciplinary (i.e., scientists employing a variety of research approaches) MAPP Network includes researchers with clinical, epidemiological, and basic research expertise, all working collaboratively:

- Clinical researchers bring experience treating patients
- Epidemiological investigators study the occurrence of, and identify risk factors for, IC/PBS and CP/CPPS
- Basic research scientists examine what’s happening on a cellular level

The MAPP Network includes multiple key focus areas, including:

- Epidemiology of Disease
- Phenotyping of Urological and Non-Urological symptoms
- Neuroimaging / Neurobiology Studies
- Identification of Biomarkers of Disease
- Characterizations of Organ Cross-Talk / Pain Pathways

The MAPP Research Network is comprised of six Discovery Sites that conduct the research studies and two Core Sites that coordinate data collection, analyze tissue samples, and provide technical support.

The MAPP Network also challenges all of the investigators to bring new perspectives to their studies. By promoting novel and innovative research approaches, the MAPP Network aims to discover new and clinically relevant insights that may lead to improved treatment options and better patient care.

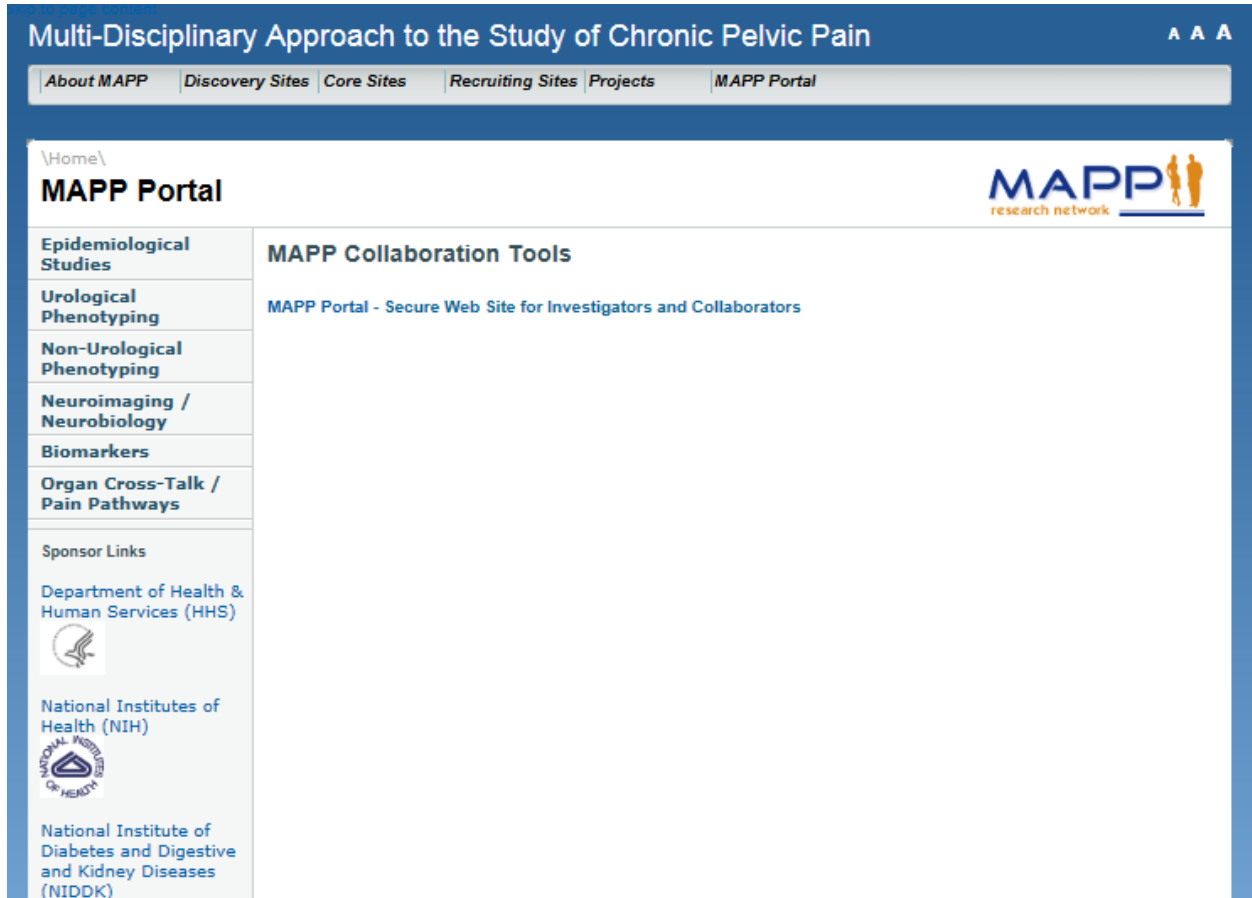
NEW Funding Opportunity for MAPP Network Basic/Translational Science

The **Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) Research Network**, supported by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institutes of Health (NIH), **invites research grant applications to conduct fundamental basic and translational research** focused on urologic chronic pelvic pain syndrome (UCPPS).

The NIDDK has allocated up to \$2 million to the MAPP Network to solicit basic and translational studies **from investigators NEW to the network** that will be conducted in collaboration with the MAPP Network and in support of the network’s goals of informing future clinical investigations and ultimately improving clinical management of UCPPS patients.

- **Public Domain Contents**
 - ❖ MAPP Network and Study Specific public information
 - ❖ General Participant Information
 - ❖ Recruitment Site Contacts

- ❖ Link to Participant Survey
- Private Domain Contents
 - ❖ Data Management System
 - ❖ Research Coordinator Data Entry tools
 - ❖ Study Case Report Forms
 - ❖ Study documents
 - ❖ Participant Web Survey Module



A MAPP web account is necessary to access the private areas of the website. Access is limited to MAPP Study PIs, Investigators, RCs and other MAPP study staff. To inquire about obtaining a MAPP website account, please contact the MAPP Project Management team, (MAPP-PJM@LISTS.UPENN.EDU). Once log-in credentials have been granted, select the “**MAPP Portal – Secure Web Site**” link as shown above.

8. DATA MANAGEMENT SYSTEM USER GUIDE

8.A. Accessing MAPP Data Management System (DMS) Tools

The MAPP Data Management System (DMS) tools are accessible via the private/secure domain of the study’s website, www.MAPPNETWORK.org. You will need to log into the private domain of the study’s website utilizing your MAPP web account to access the study tools and click on the MAPP Portal DMS tab.

*Please note, as show below, there are two versions of the MAPP data management systems:

1. The Training/Certification Version – Please use this version of the MAPP DMS when completing RC training and certification procedures.
2. The Live Study Version – This version of the DMS may only be used once all RC training and DMS certification procedures have been successfully completed. Please use this version of the MAPP DMS for registering participants and performing data entry.

The screenshot shows the MAPP Portal website. At the top, there is a blue header with the text "Multi-Disciplinary Approach to the Study of Chronic Pelvic Pain" and a "Logout" link. Below the header is a navigation bar with tabs for "Calendar", "Directory", "DMS", "Network Meetings", "Publications", "Phase 2 Concepts", and "Edit Calendar". The "DMS" tab is selected. On the left side, there is a vertical menu with links for "Public Home", "Project Leader", "Research Coordinators", "Trans-MAPP Studies", "Tissue Analysis & Technology Core", "Working Groups", "Site Specific Studies", "Ancillary Committees", "Executive Committee", "Steering Committee", and "Scientific Advisory Committee". The main content area features a "Live Study Version" section with a list of links: "Research Coordinator - Participant Registration Tools", "Trans-MAPP II SPS Data Management System", "Research Coordinator - Generate Visit Schedule", "Research Coordinator - MyMED & Pending Surveys Report", "Research Coordinator - CMSI Report", and "Research Coordinator - FLARE Specimen Collection Report". Below this, there is a "DMS Manual of Procedure" section with links to "Trans-MAPP Epi/Phenotyping OCDMS MOP" (MAPP-OC_DMS_MOP_v1.0.20091113.pdf [5786 KB]), "Cannot_Sign_into_Oracle_Portal_using_IE_browse.pdf" (Cannot_Sign_into_Oracle_Portal_using_IE_browse.pdf [330 KB]), and "Trouble Shooting & FAQs for DMS".

In general, there are 3 main domains for the MAPP Study tools:

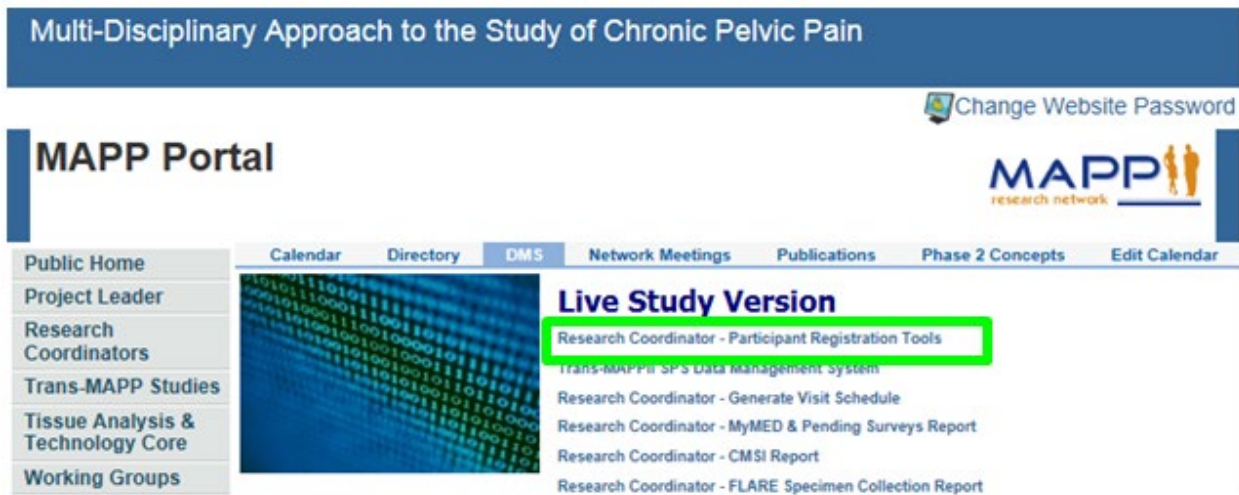
1. Registration, Specimen Collection Management, and Reference Links
 - Research Coordinator – Participant Registration Tools
 - MAPP Participant Registration
 - MAPP Participant/Study Assignment
 - Specimen Collection/Shipment
 - Kit Requests
 - CMED Drug Dictionary

2. Oracle Clinical Data Management System Tools
 - Trans-MAPP Data Management System
 - Oracle Clinical Module – for data entry of RC completed forms (CRFs)
3. Research Coordinator Reports
 - Research Coordinator – CMSI Report
 - CMSI and participant survey completeness report
 - Research Coordinator – Generate Visit Schedule
 - Participant visit schedule report
 - Research Coordinator – Pending Surveys Report
 - 1) Displays pending Participant Surveys once the visit window for a follow-up contact has opened.

The various MAPP study tools will be described in this section except for the Oracle Clinical module, which is described in the Oracle Clinical MOP, Appendix C.

8.B. Research Coordinator – Participant Registration Tools

To access the MAPP Research Coordinator – Participant Registration Tools, log into the private domain of the study’s website with your MAPP web portal account and click the “DMS” tab, then click the “Research Coordinator – Participant Registration Tools” link.

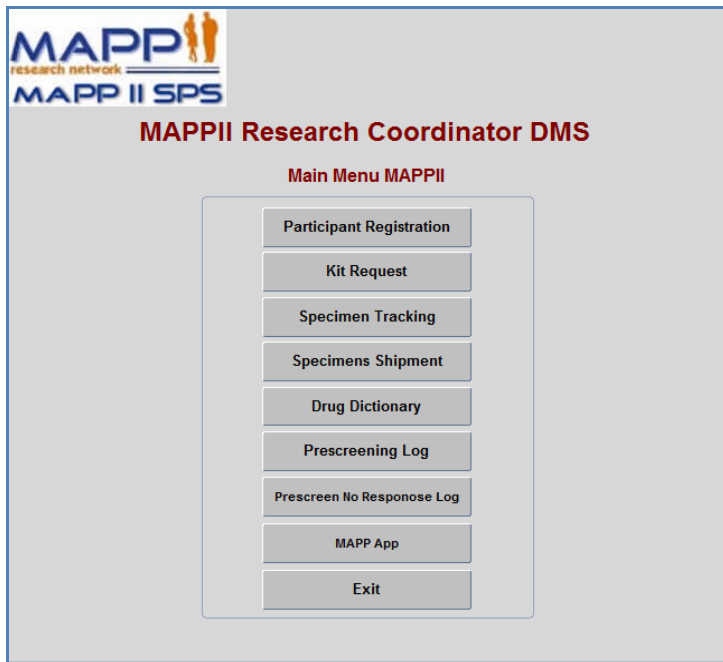


Access to the Research Coordinator – Participant Registration Tools requires a MAPP Research Coordinator DMS user account. Access to this module is limited to MAPP Research Coordinators **ONLY!** To log into the Research Coordinator module, enter your username, password, and the name of the database (OCTRIALP). Note that the username/password you are to use is not the same as the username/password you used to log into the portal.

To inquire about obtaining a MAPP Research Coordinator DMS account, please contact the MAPP DCC Team, MAPP-PJM@lists.upenn.edu.



8.B.1. MAPP Research Coordinator DMS Main Menu



After logging into the database, the MAPP Research Coordinator DMS Main Menu will appear. The main menu consists of buttons that provide access to the various modules within the Research Coordinator – Participant Registration Tools module. Those modules include:

- Participant Registration
- Kit Request
- Specimen Tracking
- Specimens Shipment
- Drug Dictionary
- Prescreening Tools (for SPS participants only)
- MAPP App (for SPS participants only)

8.B.2. Participant Registration Module

To proceed with registering a participant, press the “Participant Registration” button on the MAPP Research Coordinator DMS Main Menu. The Participant Registration Module serves two purposes. First, to assign participants a MAPP Network PID and PIN that will be used for all MAPP Network associated projects. Secondly, to register participants to the Trans MAPP and any other associated MAPP Site Specific studies.

8.B.3. Assigning Participant PID and PIN

To register a new MAPP Network participant, choose your site by clicking on the button next to the “site” field. Then enter the participant’s initials, and press the “tab” key. You will then be prompted to re-enter the initials, and notified if your second entry does not match the first. Then choose the participant’s gender by clicking on the circle next to “M” for male, or “F” for female. Next, enter the

participant’s year of birth in the field labeled “Year of Birth”. Press the “tab” key and you will be prompted to re-enter the year of birth, and notified if your second entry does not match the first. The initials and year of birth are double entered because those two fields are used to create the participant’s pin. Therefore it is very important that these two items are entered accurately. After entering the year of birth twice, press the “save” button located on the upper portion of the data entry screen. This will generate the participants 6 digit participant ID and the participant’s PIN.

The 6 digit participant ID is an automatically generated number that is assigned at the time of registration. The accompanying PIN will consist of the participant's first initial, followed by the last two digits of the participant's birth year, followed by the participant's last initial.

Example: PID: 100001
PIN: A72B

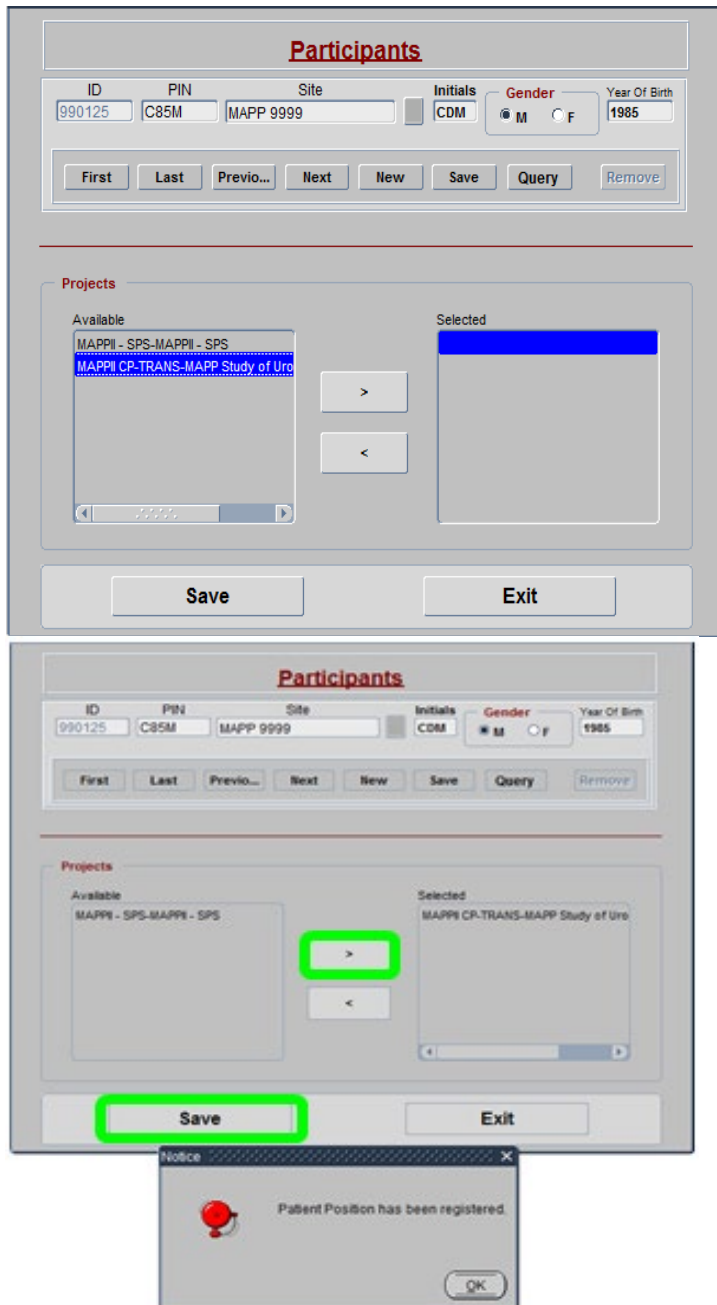
Record all numbers, including leading zeroes, when you record this number on CRFs.

The screenshot shows a software interface for entering participant data. At the top, there is a menu bar with 'Action', 'Edit', 'Query', 'Block', 'Record', 'Field', 'Help', and 'Window'. Below the menu is a toolbar with various icons. The window title bar reads 'MAPP DB: octrialp FORM: PARTICIPANT OPS\$GUEST2 12/10/2009 15:53'. The main content area is titled 'Participants' in red. Below the title, there are several input fields: 'ID', 'PIN', 'Site', 'Initials', 'Gender' (with radio buttons for 'M' and 'F'), and 'Year Of Birth'. Below these fields is a row of buttons: 'First', 'Last', 'Previo...', 'Next', 'New', 'Save', 'Query', and 'Remove'. Below this row is a section titled 'Projects' in red. It contains two list boxes, 'Available' and 'Selected', with arrows between them for moving items. At the bottom of the window are two large buttons: 'Save' and 'Exit'.

8.B.4. Registering Participants to Trans-MAPP Control Study


After a participant has been registered and a PID/PIN combination has been created, the participant must be assigned to a MAPP Network project or projects.

To register a participant to the Trans-MAPP Control Study, please select the study name from the available studies listed in the left box and move it to the box on the right, as shown below. After assigning the participant to a project or projects, press the “save” button at the bottom of the screen.



8.C. Kit Request

To access the kit request module, press the “Kit Request” button on the Main Menu. Pressing the “kit request” button will open the screen below. To request kits, choose the site from the list of sites, then choose the username of the person requesting the kit from the CCCID field and enter the current date in the Request Date field. After that, indicate the number of each type of kit being requested. If additional kits of a particular type are not needed, enter a “0” next to that kit type. In order to submit a kit request, each kit type must have a value entered next to it. Once you’ve indicated the number of each kit type being requested, press the “save” button. This will save the request and generate a kit request ID that will be referenced by the central lab.



DCC Kit Requests

Kit ID	Clinical Site	CCCID	Name	Request Date
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

Urine Specimen Kit (UTRAC2) <input type="text"/>	Vaginal Swab Kit (VSTRAC2) <input type="text"/>	MB Female Urine Kit (UFMBTR2) <input type="text"/>
Plasma Specimen Kit (PTRAC2) <input type="text"/>	Rectal Swab Kit (RSTRAC2) <input type="text"/>	7 Day Salivette Kit (S7TRAC2) <input type="text"/>
3 Day Salivette Kit (S3TRAC2) <input type="text"/>	MB Univ.1 Urine Kit (UUMBTR2) <input type="text"/>	
STIM Tube Kit (STIMTR2) <input type="text"/>	MB Male Urine Kit (UMMBTR2) <input type="text"/>	

First	Last	Previous	Next	New
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Exit	Save
------	------

8.D. Specimen Tracking

To access the specimen tracking module, press the “specimen tracking” button on the main menu. This will open up the specimen tracking module. To create a set of specimen records for a participant, enter the participant’s ID press the “tab” key, and then enter the PIN. If the ID and pin match, the site will be auto-populated. If they do not match, a warning message will appear and you will need to either correct the participant ID or the PIN. After the site field is auto-populated enter the Visit Date in the format MM/DD/YYYY, then select the visit number from the list. Once all of the fields have been entered, press the “proceed” button, and the screen will auto-populate with all of the possible specimens that can be collected at the given visit. For each specimen type, you should then either enter or scan the barcode for each kit, in the appropriate row. Then enter the CRF date, the RCID of the person who filled out the appropriate specimen form, whether or not the specimen was collected, and the date the specimen was collected. The “shipped” and “shippeddt” fields will be auto-populated after the specimens are indicated as shipped via the specimen shipping module. After entering the appropriate data for each specimen type, press the “save” button.

Participant ID:	Pin:
<input type="text"/>	<input type="text"/>
Site:	
<input type="text"/>	
Visit Date:	Visit Number:
<input type="text"/>	<input type="text"/>

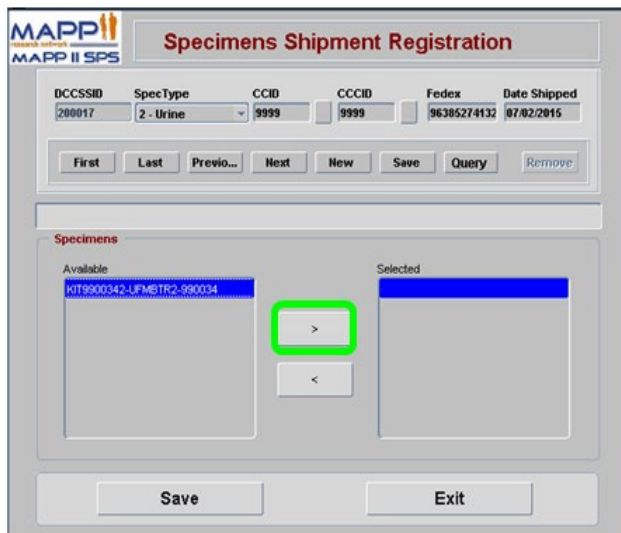
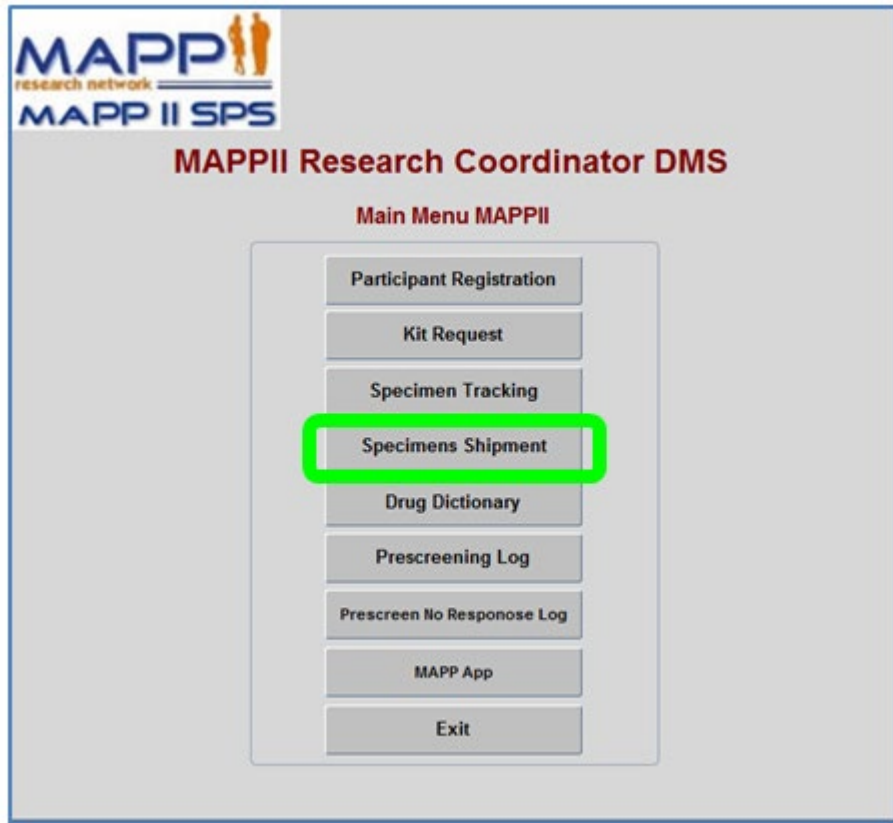
Proceed
Cancel / Exit
SAVE
Defer Specimens

Barcode	Spec Type	Crf Date	Rcid	Collected	Collectdt	Shipped	Shippeddt
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
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<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

8.E. Specimens Shipment

To access the specimens shipment module, press the “specimens shipment” button on the main menu. This will open the “Specimens Shipment Registration” screen. To create a shipment, select the shipment type, then choose the ID of the person creating the shipment, indicate the FedEx tracking number and the ship date. After entering those items, press the “save” button, which will create a shipping ID. After

saving the shipment information, the lower portion of the screen will show the specimens available for shipping from your site. Choose the specimens you want to include in the shipment, and move them to the box on the right hand side. Then press the “save” button.



8.F. Drug Dictionary

To access the drug dictionary, press the “Drug Dictionary” button on the main menu. Doing so will open the drug dictionary tool (medication reference tool) which will allow for searching of drug brand names and generic names and corresponding drug codes. To perform a search, enter the search term in the

Brand Name or Generic Name field, then press the “execute query” button. All of the drugs that contain the entered Brand Name or Generic Name will be returned in the “Drug Names and Codes” table, along with associated drug codes. Choose the appropriate code for the drug you are searching for, and write the drug code on the case report form.

The screenshot displays the Oracle Developer Forms Runtime - Web interface for a medication reference search. The window title is "Oracle Developer Forms Runtime - Web" and the Oracle logo is visible in the top right corner. The menu bar includes "Action", "Edit", "Query", "Block", "Record", "Field", "Help", and "Window". The status bar shows "MEDICATION REFERENCE" and "OPS\$GUEST1 12/10/2009 16:07 US Eastern Time".

The form is divided into three main sections:

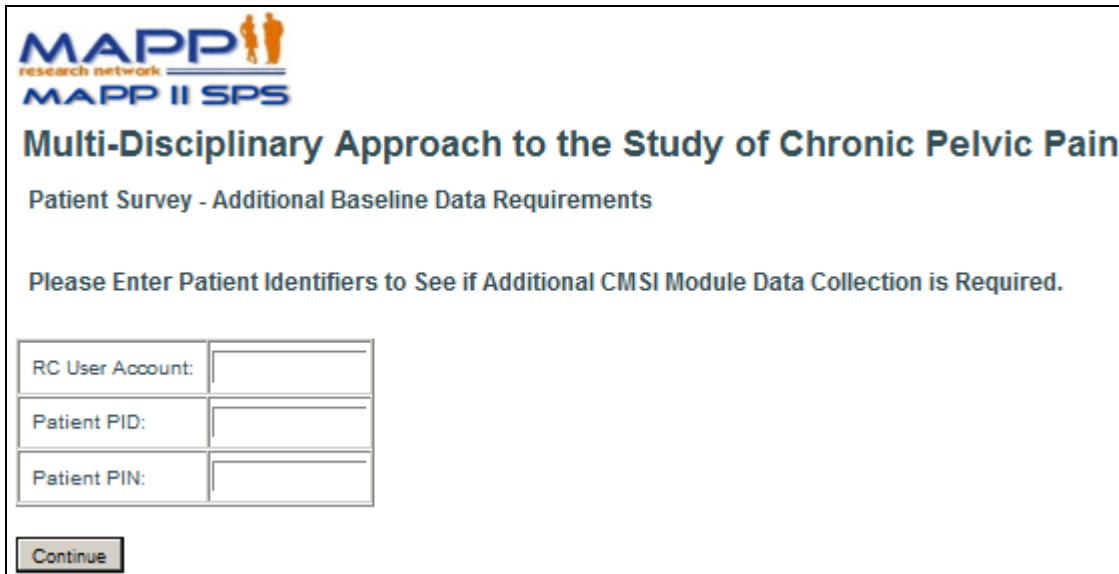
- Enter Query Criteria:** Contains three radio buttons and text input fields: "Brand Name : ...", "Generic Name ...", and "Drug Code: ...".
- Sort Criteria:** Contains three radio buttons: "Drug Code", "Brand Name", and "Generic Name".
- Drug Names and Codes:** A table with three columns: "Drug Code", "Brand Name", and "Generic Name". The table is currently empty and has a vertical scrollbar on the right side.

At the bottom of the form, there are two buttons: "Execute Query" and "Cancel".

The status bar at the bottom left shows "Record: 1/1".

8.G. Participant CMSI and Completion Report Module

To access the Participant CMSI and Completion Report, choose the “Research Coordinator – CMSI” link from the DMS tab of the MAPP network Portal. Doing so will take you to the CMSI module screen. Once there, enter your DMS username the participant’s ID and the Participant’s PIN, then press the “continue” button. This will open up the CMSI and Survey Completion report for the indicated participant.



The screenshot shows a web page with the MAPP research network logo at the top left. The main heading is "MAPP II SPS Multi-Disciplinary Approach to the Study of Chronic Pelvic Pain". Below this is the sub-heading "Patient Survey - Additional Baseline Data Requirements". A instruction reads "Please Enter Patient Identifiers to See if Additional CMSI Module Data Collection is Required." There are three input fields: "RC User Account:", "Patient PID:", and "Patient PIN:". A "Continue" button is located at the bottom left of the form area.

RC User Account:	<input type="text"/>
Patient PID:	<input type="text"/>
Patient PIN:	<input type="text"/>

8.H. Participant Calendar Module

To access the Participant study visit calendar, choose the “Research Coordinator – Generate Visit Schedule” link from the DMS tab of the MAPP network Portal. Doing so will take you to the Participant Visit Schedule Report screen. Once there, enter your DMS username the participant’s ID and the Participant’s PIN, then press the “continue” button. This will open up the Participant Visit Schedule report for the indicated participant.



Multi-Disciplinary Approach to the Study of Chronic Pelvic Pain

Participant Visit Schedule Report

Please Enter Identifiers to Generate Participant Visit Schedule.

RC User Account:	<input type="text"/>
Patient PID:	<input type="text"/>
Patient PIN:	<input type="text"/>

8.I. Pending Surveys Report

This tool may be used by the RC to monitor the progress of Participants as they complete the Month 3 surveys. If a visit window appears to be close to closing and a Participant has not yet completed the follow-up Participant Survey, contact the Participant with a reminder to complete the pending Participant Survey.

8.J. Oracle Clinical DMS Module

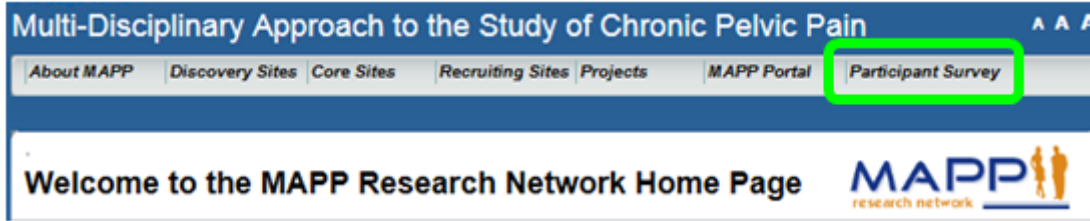
9. PARTICIPANT FOLLOW-UP INTERNET ASSESSMENTS

9.A. Participant Follow- Up

The participant survey is accessible via the study’s website, www.MAPPNETWORK.ORG. Participants will be required to log on to the website and enter their PID and PIN to gain access to their quarterly online questionnaires. It is expected that the Month 3 questionnaires will take participants approximately 30 - 45 minutes to complete; while the clinic visit online questionnaires will take about 45 - 60 minutes to complete.

9.B. Accessing Participant Follow Up Survey

To access the online questionnaires, participants will need to log onto the MAPP Study website (www.MAPPNETWORK.ORG) from any internet browser, for example Internet Explorer, Firefox, or Safari, and click on the “Participant Survey” tab at the top of the screen.



After clicking on the “Participant Survey” tab, a new screen will appear that will require the participant to enter his/her MAPP Study Participant ID (PID) and PIN to gain access to your questionnaires.

A screenshot of the MAPP II SPS login screen. The page title is "MAPPII - Multi-Disciplinary Approach to the Study of Chronic Pelvic Pain". The MAPP research network logo is at the top left. Below the logo, the text "Please enter:" is displayed. There are two input fields: "PID:" and "PIN:". A "Submit" button is located at the bottom left of the form.

9.C. Completing Participant Internet Survey

Once the participant enters his/her MAPP PID and PIN they will then see the following introduction screen:



Multi-Disciplinary Approach to the Study of Chronic Pelvic Pain

Introduction

Welcome and thank you for participating in the MAPP study.

The following questions are designed to provide details about your urological symptoms, non-urological pain, sexual function, your health, anxiety, depression, anger, fatigue, sleep, perceived stress, and complex medical symptoms. Please answer all questions to the best of your ability. For any questions which you can not or prefer not to answer, please click the "Continue" button and you will be taken to the next question. As you continue through the survey a progress indicator at the bottom of the screen will let you know how much of the survey has been completed. Also, for your reference, the name of the questionnaire will appear at the top of each screen.

If you encounter any difficulties using the MAPP Participant survey, please immediately contact the Research Coordinator at the Clinical Center where you enrolled in the MAPP study.

Progress:



By pressing the 'Continue' button, the survey will start. Once the survey starts, participants will have the ability to move backward and forward within the survey. In addition, participants will be able to stop and return at a later time to complete the questionnaires, if necessary. Hitting the browser "back" button on their computer screen will allow them to go back within the survey to review questions that they previously answered.

Please note that while going back, if they change any of their previous answers, they will be required to answer all of the questions from that point forward. If at anytime a participant needs to end his/her session prior to completing all of the questions, simply inform them to exit out of their internet browser and the session will end.

All of their answers/responses up to the point that they exited the survey will be saved. Once they log back on to complete the survey, the system will start at the very next question following the last question that was completed prior to stopping.

Remind participants to log onto the system within the scheduled target window to complete the questionnaires as specified at the Week 0 clinic visit.

9.D. Missed Surveys

The calendar that the RC provides to the participant at the Week 0 clinic visit will include the target date that the participant is expected to log onto the website to complete each online survey.

9.E. Help Completing Surveys

Participants should be instructed to contact the clinical center for any problems/issues completing their online assessments or if they lost their PID and PIN and require the information again. If necessary, **the RC can contact the DCC Help Desk to provide technical support related to problems and issues that may arise when working with the web based Data Management System.**

10. PARTICIPANT SAFETY

10.A. Risks and Benefits

10.A.1. Risks

Before giving consent to participate in this study, the Research Coordinator must inform the participant of all potential risks related to participation in this study, as outlined in the protocol and informed consent form.

10.A.2. Benefits

There may be no direct benefit to the participant by participating in this study. Participants will be contributing to scientific knowledge and possibly helping other patients with Urologic Pelvic Pain Syndromes.

11. Human Subject Considerations

11.A. Trans-MAPP Participant Considerations

11.A.1. Participant Follow-up

Participants who enroll in the study and complete a Screening/Eligibility Week 0 visit will be followed through internet questionnaires completion at Month 3, as well as an in-person clinic visit 6 months after their initial Screening/Eligibility visit. A complete list of protocol elements to be collected at the Screening/Eligibility and follow-up visits is provided in **Appendix A: MAPP Phase II Control Protocol Visit Schedule.**

During the study, participants will be contacted by the Discovery Site Research Coordinators with email reminders to log on for their Month 3 assessment, as well as to facilitate scheduling of the Month 6 follow-up visit. Participants who do not complete their scheduled Month 3 assessment will be contacted by phone for further prompting or discussion of any issues with study participation.

11.A.2. Participant Retention

Retention of participants is central to internal validity of the study and will be an extraordinarily high priority of the investigators and staff. A key element is a pleasant, attentive and responsive staff that provides a reasonably flexible schedule. Other clinical center features that promote high retention rates include local tracking systems and frequent staff meetings.

11.A.3. Participant Withdrawal

Participants are free to withdraw (or be withdrawn) from the study at any time. There are many reasons a participant may want to do so. They include:

- Unanticipated events unrelated to the study
- Significant concurrent illness
- Protocol noncompliance
- Investigator’s discretion
- Withdrawn informed consent
- Relocation
- Dissatisfaction with study
- Loss of interest in the study
- Lost to follow-up
- Reason(s) for withdrawal will be documented on case report forms and entered in the DMS.

The RC will complete the Study Stop [**SSTOP**] form selecting the most representative reason for withdrawal. Every effort should be made to encourage participants to continue with study visits.

The withdrawal request can be made in person or during a phone contact. The Participant data folder should be clearly marked to indicate withdrawal and is maintained at the clinical center where the participant was recruited and followed.

11.A.4. Participant Reimbursement

As compensation for their time and effort, subject reimbursement (provided by each site) should be provided. Appropriate amounts and actual schedule of reimbursements should be determined by each site.

11.B. Ethical Issues

11.B.1. Potential Risks to Participants

The protocol includes in addition to questionnaires, a physical examination, pelvic exams, urine specimen collection, blood draws, Neuroimaging studies, and Quantitative Sensory Testing (QST).

Minimal physical risk to discomfort to participants arises from the physical and pelvic exam, however, the Pelvic Muscle examination could increase pain during exam and transiently after the exam.

Any risks or discomfort from either procedure is temporary. The risks associated with other study procedures are as outlined below.

11.B.1.a) Risk Associated with Collection of the Biomarker Urine and Blood Specimens

Urine specimens are collected at all in clinic study visits. Urine specimen collection is routine patient care and should not present a burden to participants. Blood collection is also routine patient care but participants will have blood drawn for research purposes only. The volume of blood obtained poses no physiological risk. There is minimal risk of temporary mild pain, discoloration, bruising or infection at the place where the needle is inserted. The risks also include possible fainting. These risks are minimized by the use of trained personnel to draw blood.

11.B.1.b) Risk Associated with Collection of the Optional Rectal, and Vaginal Swabs

Optional rectal and vaginal swabs will be collected at week 0 and Month 6 study visits. While it may pose temporary discomfort, there are no known risks associated with the collection of the rectal and vaginal swabs.

11.B.1.c) Risk Associated with Neuro Imaging Assessments

Neuroimaging studies are conducted at week 0 and Month 6 clinic visits. The specific risks of the Neuroimaging procedures relate to the site specific protocols, but in general, the physical risks associated with this study are those associated with MRI scanners. Functional Magnetic Resonance Imaging Scan does not involve injections or any radioactive tracers. Some people experience dizziness or a metallic taste in their mouth if they move their head rapidly in the magnet. However, this is only a temporary effect and is not experienced if the head is kept still. The scanner produces loud sounds at times and insulated earphones will be provided to reduce the noise you hear. Although the long-term risk of exposure to magnetic fields and radiofrequencies associated with MRI is not known. The possibility of any long-term risk is extremely low in view of the information accumulated over the past twenty years. If unrestrained iron or steel objects are accidentally brought near the MRI magnet, they can be pulled very quickly toward the magnet and can strike people in or near the magnet. Such an event is very unlikely because precautions are taken to prevent such objects from being brought near the magnet. Participants are screened for iron or steel implants or clips from surgery, or metallic objects such as shrapnel or metal slivers in their bodies and are excluded from study if present. Dental fillings do not present a hazard.

11.B.1.d) Risk Associated with Quantitative Sensory Testing (QST)

Quantitative Sensory Tests (QST) are conducted at week 0 and Month 6 clinic visits. The QST procedures may cause minor but temporary physical discomfort. Study personnel will be trained by the investigators to be sensitive to participant discomfort and concerns. Research Coordinator will stop the QST anytime that the participant indicates that pain or unpleasantness of the task becomes unbearable.

Specifically, MAST testing may cause some temporary physical discomfort on the thumbnail. The MAST device incorporates a number of mechanical, electrical, and software safety features to prevent injury in the event of user error or device failure, including a safety pin that the participant can turn to immediately remove the pressure from the thumb.

The pressure algometer and pointed skin probe are commonly used in QST studies and will not cause tissue injury at the maximum forces applied in this study (8 kg/cm² and 256 mN, respectively). However,

both instruments may cause minor physical discomfort in the areas of testing (forearm, shoulder, and pelvic region) that is expected to resolve within minutes of test completion. These instruments may also cause small skin indentations and/or skin reddening that is expected to resolve within a couple hours. These tests will be halted automatically if the participant reports a pain rating of 100.

The heated water used in the CPM test will also cause some temporary discomfort of the foot and lower leg. The maximum temperature of the water (46.5°C) and the duration of immersion (1 minute) are below the recommended standards of the U.S. Consumer Product Safety Commission (Publication 5098) to prevent scalding injury in adults. The researcher who is conducting the test will stop any procedure immediately if the participant finds it too discomforting. Towels will be provided for drying the participant's feet after testing.

11.B.2. Risk/Benefit Assessment

This is a study to investigate the relationship between UCPPS and other chronic pain conditions to better understand the pathophysiology of these often disabling syndromes. Although there will not be any direct benefits to the participants, the information obtained from this study has considerable potential benefit to future patients and to society as a whole by providing new information about the pathophysiology of these conditions. This study may well lead to the discovery of common risk factors, symptoms, or potential biomarkers related to these complex disorders, and may, therefore, lead to improved management and treatment.

11.B.3. Gender and Minority Inclusion

This is a multi-center study recruiting a clinical population from numerous institutions across the United States. We estimate the racial/ethnic composition of participants to be approximately 85% White/Caucasian, 10% African American, and 5% Latino/Hispanic, Asian/Pacific Islander, and Other. We plan to enroll equal numbers of men and women.

11.C. Participant Confidentiality

Procedures to assure confidentiality will be strictly observed. All identifiable personal health information data should be (1) kept in confidential locked files; (2) identified by subject number only; and (3) kept separately from identifying information used for subject tracking and follow-up contacts. Identifying information will be kept in separate locked files. No identifying information will be disclosed in reports, publications or presentations.

A log of the participant names, participant ID numbers, and pertinent registration information (e.g., home address, telephone number, and emergency contact information) should be maintained in a locked area at each clinical site. Only the participant ID number and initials are utilized when communicating with the DCC staff or entering data into the study database. Any communication between DCC and clinical sites regarding participant data will occur via the participant ID number. Any forms or documents sent to DCC, IRB or other regulatory authorities should have all personal information removed.

12. STUDY ORGANIZATION AND OVERSIGHT

12.A. Discovery Sites

Six (6) Discovery Sites participating in the Trans-MAPP Control Study will have primary responsibility for developing the study protocol, recruiting a sufficient number of study participants, maintaining high rates of follow-up and data collection, obtaining data of high quality, and interpreting, presenting, and publishing findings from the study. The 6 Discovery Sites, with Principal Investigators, are as follows:

1. University of California, Los Angeles (UCLA)/ University of Southern California (USC),
Los Angeles, CA
Principal Investigators: ***Emeran A. Mayer, M.D.*** ***Larissa V. Rodriguez, M.D.***
Professor and Executive Director Professor
Center for Neurobiology of Stress Department of Urology
2. Northwestern University, Chicago, IL
Principal Investigators: ***David J. Klumpp, Ph.D.*** ***Anthony J. Schaeffer, M.D.***
Associate Professor Herman L. Kretschmer Professor & Chairman
Department of Urology Department of Urology
3. Washington University, St. Louis, St. Louis, MO
Principal Investigators: ***Gerald L. Andriole, M.D.*** ***H. Henry Lai, M.D.***
Professor of Surgery Assistant Professor of Surgery
Chair, Division of Urologic Surgery Division of Urologic Surgery
Director, Prostate Study Center,
Barnes-Jewish Hospital
4. University of Iowa, Iowa City, IA
Principal Investigator: ***Karl J. Kreder, M.D., M.B.A.***
Professor and Clinical Chair
Director, Urodynamics and Reconstructive Urology
5. University of Washington, Seattle, WA
Principal Investigator: ***Dedra Buchwald, M.D.***
Professor, Epidemiology and Medicine
6. University of Michigan, Ann Arbor, MI
Principal Investigators: ***Daniel J. Clauw, M.D.*** ***J. Quentin Clemens, M.D., M.S.C.I.,***
Professor of Anesthesiology & Professor of Urology, Director,
Medicine Division of Neurology & Pelvic
Rheumatology, Director, Reconstructive Surgery
Chronic Pain & Fatigue Research
Center.

In addition to these Discovery Sites, the following individuals were funded to provide expertise in particular scientific and translational areas related to MAPP goals:

1. Harvard Medical School, Boston, MA
Marsha A. Moses, PhD
Julia Dyckman Andrus Professor, Harvard Medical School
Director, Vascular Biology Program Boston Children’s Hospital
Department of Surgery Harvard Medical School and Boston Children’s Hospital
Richard S. Lee, MD
Assistant Professor of Surgery (Urology), Harvard Medical School
Director, Urologic Oncology, Co-Director, Urologic Trauma Boston Children’s Hospital
2. Queen’s University, Kingston Ontario
J. Curtis Nickel, MD, FRCSC
CIHR Tier 1 Canada Research Chair in Urologic Pain and Inflammation
Professor of Urology
Dean A. Tripp, PhD
Associate Professor
Garth D. Ehrlich, PhD
Professor of Microbiology and Immunology
Professor of Otolaryngology-Head and Neck Surgery,
Drexel College of Medicine, Philadelphia, PA
3. Cedars-Sinai Medical Center, Los Angeles, CA
Jennifer Anger, MD, MPH
Associate Professor of Urology
Associate Director of Urological Research
Michael Freeman, PhD
Professor in the CSMC Departments of Surgery, Medicine and Biomedical Sciences
Jayoung Kim, PhD
Associate Professor of Surgery and Biomedical Sciences

12.B. Data Coordinating Core (DCC)

The Data Coordinating Core (DCC) for the MAPP Research Network is located at the University of Pennsylvania School of Medicine, Philadelphia, PA.

- Principal Investigator:** J. Richard Landis, Ph.D.,
Professor of Biostatistics, University of Pennsylvania
- Co- Investigator:** Alisa Stephens, Ph.D.,
Assistant Professor of Biostatistics, University of Pennsylvania
- Co-Investigator (IC/BPS):** Robert M. Moldwin, MD,
Professor, Department of Urology
Hofstra North Shore-Long Island Jewish School of Medicine
- Co-Investigator (CP/CPPS):** Michel Pontari, MD,
Vice-Chairperson and Professor, Department of Urology,
Temple University

The DCC is responsible for the following:

- Set-up and maintenance of the MAPP longitudinal data collection website for patient- reported outcomes
- Providing biostatistical expertise in research design, outcome measures and analytic strategies for translational and clinical investigations of UCPPS
- Guiding and implementing statistical analyses, interpretation of findings, and supporting presentations and publication of results
- Facilitating the conduct of multi-disciplinary basic and translational research, by providing scientific leadership in the design and implementation of research projects across the MAPP Research Network
- Promoting network-wide quality assurance standards, practices and tools, including a comprehensive, secure www-based data management system (DMS) for collection and centralized storage of all multi-site study data
- Collaborating with the TATC Laboratory on best practices for data collection, specimen tracking and storage, as well as support technical processes between the DCC and TATC
- Providing comprehensive Data Coordinating Core administrative support for the MAPP Research Network, promoting effective communications, coordinating meetings, working groups, document development and management, and distribution of study proceedings
- Supporting the MAPP Research Network Ancillary Projects, assisting in their design, as well as implementing a process for the submission, review, and development of ancillary studies

12.C. Tissue Analysis and Technology Core (TATC)

The Tissue Analysis and Technology Core (TATC) is located at the University of Colorado, Denver School of Medicine, Department of Pathology, Aurora, CO

Principal Investigator: ***M. Scott Lucia, M.D.***, Associate Professor of Pathology,
University of Colorado, Denver

Co-Investigator: ***Adrie van Bokhoven, Ph.D.***, Assistant Professor of Pathology,
University of Colorado, Denver

The TATC will be responsible for the following:

- Providing specimen collection, banking, annotation/blinding, distribution services across the MAPP Research Network
- Providing genomic and proteomic analyses and generate assay platforms for multi-site efforts and individual site efforts as needed
- Coordinating procedures for coding, shipping, processing, receipt and storage of biosamples at the TATC site and future transfer of the biorepository to the NIDDK Biorepository

12.D. NIDDK Program Staff

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) will be responsible for oversight and administration of the scientific conduct of this research. Representatives from the NIDDK will work with the DCC and TATC to develop and implement the study.

NIDDK Program Staff: *Christopher Mullins, Ph.D.*, Director,
Basic Cell Biology Programs in Urologic & Kidney Disease
John W. Kusek, Ph.D., Director,
Kidney & Urological Clinical Trials

12.E. MAPP Steering Committees and Subcommittees

The primary governing body of the study is the Steering Committee, which is comprised of each of the Directors/Co-Directors at the Discovery Sites, DCC, TATC, and the NIDDK Project Scientists. Dr. J. Quentin Clemens from the University of Michigan is the Chair of the Steering Committee. The Steering Committee develops policies for the study pertaining to access to patient data and specimens, ancillary studies, performance standards, publications and presentations. They develop the study protocols and meet to discuss the progress of the study and resolve problems that arise.

A subset of the Steering Committee membership makes up the Executive Committee. This includes NIDDK MAPP Program staff, together with the Chair (Dr. Clemens) and Co-Chairs (Dr. R Moldwin and Dr. M. Pontari) of the Steering Committee, the DCC PI and co-investigators, and the TATC PI. The Executive Committee has frequent (typically weekly) teleconferences and makes the day-to-day decisions of the MAPP, consulting the larger Steering Committee or specific members where necessary.

In addition to the Steering and Executive Committees, subcommittees may be established on such areas as recruitment and quality control, publications, and ancillary studies. Small working groups may be established to prepare manuscripts and presentations. The following subcommittees have been established to address specific study issues:

- Biomarkers Working Group
- Microbiome Working Group
- Epidemiological Study Working Group
- Neuro-Imaging Working Group
- Organ Crosstalk Working Group
- Quantitative Sensory Testing Working Group
- Phenotyping Working Groups: Urological and Non-urological
- Study Design/Forms Review Subcommittee
- Quality Control Committee
- Publication Committee
- Patient Report Outcomes

12.F. External Experts Panel

An External Experts Panel (EEP) for the MAPP Research Network was appointed to review protocols and advises the NIDDK Program staff in the overall conduct of the MAPP Research Network. An independent group of experts in areas such as Urology, Rheumatology, Epidemiology, Ethics, Health Economics, and Biostatistics who are not otherwise involved in the study have been recruited by the NIDDK to evaluate the proposed protocol and periodically review the progress of the study.

13. STUDY MANAGEMENT

13.A. Discovery Site Responsibilities

13.A.1. Discovery Site Director and Investigators

Conduct of particular aspects of the study may be delegated to qualified personnel; however, it is the responsibility of each Discovery Site Director to oversee the overall study management. The Discovery Site staff must be trained in all study procedures.

Each Discovery/Recruitment Site is responsible to screen, recruit, enroll and retain a designated number of study participants. It is the responsibility of the Discovery/Recruitment Site study staff to assess their accrual, ensure participant confidentiality, maintain appropriate study documentation, enter and transfer data in a timely manner, and participate in the MAPP study meetings and conference calls.

Each Discovery/Recruitment site is responsible for staffing at least one RC to coordinate all activities at the site level. If an RC leaves the study, however, the on-site investigator is responsible for hiring a replacement immediately to ensure overlap among the relevant individuals. The departing RC is responsible for training the replacement RC on issues concerning the study specific to the clinical site.

The success of the study depends heavily on the ability of the clinical sites to retain enrolled participants throughout their follow-up visits. The onus of keeping participants interested in the study, therefore, resides in the hands of the clinical site staff. Potential ways of accomplishing this are:

- Emphasizing the advantage of having a dedicated RC and/or PI available to answer calls.
- Making a dedicated phone line with voice mail available to study participants.

It is expected that each site will manage the study with integrity, professionalism, and confidentiality and will adhere to all applicable federal regulations and Good Clinical Practice Guidelines. The RC is expected to provide the most complete and accurate data possible.

The responsibilities of each Discovery/Recruitment Site RC include:

- Recruiting, screening, enrolling, and following participants throughout the course of the study.
- Confirming eligibility of each participant based on the study criteria identified in the Protocol.
- Data entry of Research Coordinated CRFs will be performed at the clinical sites.
- Adhering to study Protocol and the MOP in the implementation of procedures and the acquisition of data.
- Responding to inquiries regarding study information and reporting from the DCC in a timely fashion.
- In-servicing staff at clinical site to the study Protocol.

- Enlisting aid of staff at Discovery/Recruitment sites to assist with identification of potential participants.
- Maintaining approval from regulatory affairs board for study site.
- Completing and submitting annual/final reports to regulatory affairs board for study site.
- Serving as liaison with study site co-investigators.
- Submitting information regarding Procedural or Unanticipated Problems according to study/site policy.
- Maintaining a study follow-up schedule which will plot out the course of visits that the Participant must complete on-line surveys and in-clinic contacts.

13.A.2. Institutional Review Board

It is the responsibility of each Discovery Site to conduct the study according to the protocol, and to adhere to all applicable regulatory guidelines, and to provide the appropriate IRB with all pertinent material including a copy of the informed consent. Approval of the protocol and the informed consent form must be obtained, and forwarded to the DCC and TATC, prior to screening or enrolling participants. The Investigator also maintains the responsibility of initiating protocol re-approval, notification of protocol and/or consent form changes, notification of unanticipated events, and termination of the study according to the appropriate IRB requirements.

The PI/RC must maintain documentation of appropriate licensure or accreditation for all clinical laboratory facilities used for study samples analysis.

13.A.3. Record Retention

Investigators maintain study documents on-site and in an orderly fashion for a minimum of 6 years, and make available to the sponsor or the sponsor's representative: the signed study protocol, amendments, informed consent documents, and approval letters from the IRB, CRFs, all primary source documentation, and all letters of correspondence. The DCC maintains all study records for a period in accordance with their internal SOPs and applicable regulations.

13.B. Data Coordinating Core responsibilities

13.B.1. Quality Assurance

The DCC has developed written standard operating procedures (SOPs) to ensure that all aspects of the study are conducted in a standard and uniform manner. These procedures are organized into a Manual of Procedures (MOP), which complies with the protocol, Good Clinical Practice (GCP), and applicable regulatory requirements. The DCC will include a comprehensive Quality Assurance (QA) Plan in the MOP that will consist of the following activities:

Personnel Training and Certification: Prior to this Trans-MAPP EP Study initiating patient enrollment, a comprehensive training session will be conducted with all study personnel that will encompass all aspects of the study, including communication, principles of GCP, study implementation and procedures, data entry and verification, test and specimen collection and transfer.

Clinical Protocol, MOP Adherence and Auditing Activities: The DCC will request and verify specific information from clinical centers, to ensure the application of study procedures as they apply to participant safety, required intervals for timely conduct of procedures, appropriate documentation of data and specimens, and compliance with SOPs. This information will take the form of a written report, and may be acquired during clinical site monitoring visits.

Database Auditing: A comparison of a certain percentage of data written on CRFs to that entered into the electronic database provides information that describes and quantifies the accuracy of the data entry process and use of the data management system by personnel at each Discovery Site. This information will take the form of a written report.

Database Administration and Network Security: The DCC has SOPs established for authorizing and documenting secure access to the study website, study documents and the electronic Data Management System (DMS). These procedures ensure that only authorized personnel are able to view, access, and modify study data.

Data Reporting: A set of standard reports will be developed to describe study activities that include accrual, study progress, and data quality. These reports will be developed using Oracle Reports and provided to investigators, NIDDK and designated committees as appropriate.

Preparation and Integrity of Analysis Datasets: The DCC Database Administrator will create a set of standard data access descriptor/view files, which will be used in the generation of SAS analysis datasets. As datasets are extracted from the main study database, they can be utilized separately from direct database processing, thereby, safeguarding the integrity of the data.

Data Management: The DCC provides overall coordination, logistical support, and implementation for all aspects of the study protocol including data collection, data processing, tracking of participant recruitment, tracking of specimens, training, quality assurance, and statistical analysis. The Clinical Research Computing Unit (RCU), through its clinical data management, project management, and software systems developments, places into the field and maintains a state-of-the-art www-based data system that accommodates all scientific study data, and permits tracking and coordination of all Trans-MAPP Research Network activities within the framework of multidisciplinary project teams.

13.B.2. Clinical Site Monitoring

The MAPP Research Network is a cooperative agreement study in which all investigators and the NIDDK have a shared responsibility for the overall quantity and quality of the data collection.

It will be the responsibility of the DCC to monitor the quantity and quality of data being collected throughout the course of the study. However, at the present time, there are no plans for site monitoring.

13.B.3. Website Enhancements

The DCC has developed a MAPP Network website (<http://www.mappnetwork.org/>) for study-wide communication management, data and document management, and activity management and coordination. The website provides general information to the public, single-point restricted access to tools and information for investigators and clinical center study personnel including study resources, communication

tools as well as data entry and management tools. It also provides an additional level of restricted access for DCC study personnel.

During the in-clinic Week 0 phenotyping visit at the Discovery Site, after eligibility confirmation, each participant will be authenticated by the RC into a specialized module of the DMS deployed for participants to enter questionnaire data directly via a web browser.

Using a password-protected identity management module, this DMS will also be accessible to enrolled participants via a web browser for reporting their Month 3 assessments.

13.B.4. Data Security

The research computing environment for the MAPP DCC is supported by a Biomedical Research Computing (BRC) group within the Clinical Research Computing Unit (CRCU) of the Center for Clinical Epidemiology and Biostatistics (CCEB) at the University of Pennsylvania School of Medicine. The BRC group is responsible to provide an integrated research computing and storage environment in a manner that supports the required confidentiality, integrity, and access of a common set of research data through all stages of its use, operated in a FISMA-compliant/FDA sensitive manner. The MAPP project is maintained within this compliant environment.

The CCEB General System Security Plan (CCEB-GSSP) is available on request to provide a quick read into the security within the CRCU, listing several of the security attributes most requested. Also available on request is a memo from Penn’s Chief Scientific Officer affirming Penn’s continuing commitment to meeting and maintaining its FISMA compliance. The CCEB/CRCU has performed a security and risk assessment using outside auditors to perform a gap analysis on its security measures against the FISMA recommended NIST SP800-18 and SP800-53 controls documents. The results of this assessment provided Penn Medicine’s Chief Scientific Officer with the confidence to support and write a memo that is the AMC’s equivalence of a federal “Authority to Operate (ATO) certification, as required for Federal agencies.”

The CRCU database environment for MAPP utilizes Oracle’s Advanced Security Option (ASO) with two primary foci: 1.) Strong encryption of the database transmissions to protect data traversing the data networks to and from the CRCU databases; and 2.) Internal database encryption of individual sensitive data elements, thus protecting ePHI data within the database. Both of these features are in use with the MAPP protocols and databases. The CRCU further utilizes a database monitoring tool that maintains an audit of all user session activities that occur against the protected MAPP databases. This tool is able to then recreate requested past user sessions to track all changes that occurred to data in the databases.

13.B.5. CRCU Software Systems Help Desk

Sponsored Project Help Desk (SPHD)

The SPHD provides technical support to all study personnel using DMS software developed and distributed by the DCC. This includes all DMS web links available on the study web page, Web Portal, and concerns with DCC-provided hardware. The Help Desk will answer questions concerning the operation of the DMS and will assist in resolving any issues that hinder the effective use of the software.

Technical Support

The Help Desk will provide technical support related to problems and issues that may arise when working with the application provided by the CRCU.

The Help Desk will not be responsible for providing technical support for hardware and/or software that was not provided by the CRCU (e.g. Operating systems, networking/collaborative software, word processors, spreadsheets, modems, printers, and hardware) and has direct local institutional support.

13.B.6. Assignment of DMS Accounts

A DMS account consists of a username and password that uniquely identifies a user. DMS accounts are required for a user to gain access to the data entry area, and are the primary means for ensuring data security and confidentiality. Therefore, it is critically important that all DMS accounts are kept secure and confidential and are not shared with anyone.

NOTE: The username and password used to individually access your project Web site (www.mappnetwork.org) is **not** your DMS username and password. Access to the project Web site infers no access to the project DMS. You may reach the project DMS through a link from within the project Web site but will then be prompted for a specific DMS account username and password.

In addition to providing data security and confidentiality, DMS accounts provide a means to trace all database activities to individual user accounts.

To obtain DMS accounts, a Clinical Center or Site representative should notify the CRCU project manager of the requested user's name and provide a general idea of what functions the user will be performing in the DMS. The CRCU Project Manager will in turn notify the Sponsored Project Help Desk of the new user request.

*****Important*****

When a DMS account has been created, the Sponsored Project Help Desk or the CRCU project manager will contact the user with his/her account information.

When personnel leave the project, a representative from the Clinical Center or Site should contact the SDCC Project Manager immediately. The Sponsored Project Help Desk will then take the necessary actions to deactivate that user's database account.

13.B.7. Procedures for Obtaining Help Desk Support

Study personnel can contact the Sponsored Project Help Desk by e-mail or telephone.

E-mail Support

The Sponsored Project Help Desk can be e-mailed at:

crcuhelp@mail.med.upenn.edu

When sending e-mail, the following information must be provided:

- Name (User Name)
- Study Name – (Project Name)
- Clinical Center Name / Location

- Phone number
- Detail description of the problem and level of urgency (low, medium, high)

Telephone Support:

- The Sponsored Project Help Desk can be contacted at (215) 573-4623.
- The caller will be forwarded to voicemail. When leaving a voicemail message, the caller **must** provide the following information:
 - Name (User Name)
 - Study Name – (Project Name)
 - Clinical Center Name / Location
 - Phone number (where the user can be reached)
 - Detail description of the problem and level of urgency (low, medium, high)

Help Desk Expected Response Time:

Every effort will be made to respond to voicemail and/or e-mail messages as soon as possible. To facilitate a timely response, help desk personnel are equipped with pagers and will be paged when there is a new voicemail message. Whenever possible, the Sponsored Project Help Desk will attempt to resolve the issue during the initial call. Occasionally, a problem may occur that requires additional interaction between the caller, the Help Desk and the CRCU personnel. Client patience and cooperation is always appreciated during such periods. Our goal is to restore normal operations as quickly as possible.

Help Desk Availability:

The Sponsored Project Help Desk is available during normal business hours (Monday-Friday 0800 – 1700 U.S. Eastern Standard Time).

13.C. Tissue Analysis and Technology Core Responsibilities

13.C.1. Personnel Training

TATC along with the DCC will conduct a personnel training session and a certification session for staff who will perform clinical procedures before initiation of the protocol. This comprehensive training session includes all aspects of the protocol and MOP implementation such as specimen collection, handling, processing, and shipping. Periodic conference calls and training sessions will be conducted to uphold standard application of procedures.

13.C.2. Specimen Kit Distribution, Banking, Annotation/Blinding

TATC will generate and provide MAPP-specific collection kits for use by Discovery Sites as needed. Requests for kits will be done through an online ordering mechanism located on the MAPP Portal direct from TATC. The collection kits and components are bar-coded and will be linked with the participant at the time of registration of the participant with the DCC. Collected specimens will then be shipped to TATC for inventory into the biorepository.

The collection and handling procedures will follow the guidelines established by the NIH Best Practices Policies for biorepositories (www.biospecimens.cancer.gov). No patient identifiers will be used on the collection tubes and tracking forms. As specimens are received from sites, they will be scanned into the biorepository database, and archived in the appropriate freezer/storage unit until needed. Specimen tracking information will be entered into the database by TATC personnel.

13.C.3. Biorepository Collection, Management and Distribution

The TATC will act as a central repository for all body fluid and tissue specimens generated by the MAPP, its member Discovery Sites and other research entities as approved by the Network. To provide the highest quality non-biased patient samples, uniformly prepared and analyzed and to meet the needs of individual research teams, TATC will provide guidance and personnel training to collection sites on protocol development and specimen collection and handling. The TATC will develop and distribute specialized specimen collection kits, and coordinate specimen collection, processing, annotation, bar-coding, shipping, banking, and distribution. The TATC will identify and implement best information technology architecture for the MAPP research network and provided access to its services through the MAPP Research Network portal hosted by the DCC. The biorepository will meet all NIH standards, and will provide specimens to researchers according to IRB, HIPAA and NIH procedures that protect the confidentiality of all consented patients whose tissue and blood are archived. The TATC will also work with the NIDDK Biorepository to coordinate procedures for collection, coding, storage and eventual transfer as directed by the NIDDK.

13.C.4. Specialized Assay Platforms

The TATC will generate and provide specialized assay platforms for specimen analysis such as protein and/or tissue arrays, DNA extractions and purifications as needed for individual Discovery Site efforts or ancillary/pilot projects.

Proteomics, Metabolomics, Transcriptomics: The TATC will provide centralized mass spectrometry services to assist the MAPP Research Network with proper collection and handling of specimens, consultative assistance for proteomics, metabolomics, and transcriptomics studies, and performance of a wide variety of assays, including chromatography-based proteome profiling, protein arrays, cytokine arrays, multiplexed ELISA, mass spectrometry and NMR-based targeted and mass spectrometry analyses (nanoLC ion trap and nanoLC hybrid quadrupole-linear ion trap).

Genomics, Genotyping: The TATC will provide consultative assistance and genomics services to assist the MAPP Research Network with advanced genotyping techniques. Methods for analysis of single nucleotide polymorphisms (SNPs) include single base extension assays with detection of incorporated base by fluorescence polarization, Taqman single SNP assays on 96- or 384-well real-time instruments or Taqman analysis of 32 or 64 SNPs on a nanoscale. Access to Sequenom and Illumina platforms are also available for larger scale studies.

APPENDIX A: STUDY VISIT SCHEDULE

APPENDIX B: BIOSPECIMEN COLLECTION MANUAL

APPENDIX C: ORACLE CLINICAL MOP

(See Separate Document)

APPENDIX D: CASE REPORT FORMS

(See Separate Document)

APPENDIX E: QUANTITATIVE SENSORY TESTING MOP