



Multidisciplinary Approach to Pelvic Pain (MAPP)

Trans-MAPP Study of Urologic Chronic Pelvic Pain: Symptom Patterns Study (SPS)

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) Draft Version 1.5

Dated: November 14, 2018

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Targeted ATLAS Therapies						
All Participants	All Participants	All Participants	All Participants	All Participants	All Participants	Males only
Oral opioids (Medication)	Tricyclic antidepressants (Medication)	Pelvic floor physical therapy (Non-Medication)	Elmiron / Oral pentosan polysulfate (Medication)	Neuropathic pain Treatments (Medication)	Cystoscopy with Hydrodistention	Alpha-adrenergic blockers (Medication)
Common Brand Names	Common Brand Names	Common Names	Brand Name	Common Brand Names	Common Names	Common Brand Names
1.Endocet 2.Lortab 3.Oxycontin 4.Percocet 5.Percodan 6.Vicodin 7.Tylenol w/ Codeine	1.Elavil 2.Tofranil 3.Teyzafagit 4.Sensoval	1.Pelvic Physical Therapy 2.Pelvic Floor Physical Therapy 3.Pelvic Floor Dysfunction Therapy 4.Pelvic Floor Myofascial Release 5.Pelvic Floor Rehabilitation	1.Elmiron	1.Lyrica 2.Neurontin	1. Cystoscopy with Hydrodistention	1.Flomax 2.Hytrin 3.Cardura 4.Rapaflo
Common Generic Names	Common Generic Names		Generic Names	Common Generic Names		Common Generic Names
1.Acetaminophen& Oxycodone 2.Acetaminophen& Hydrocodone 3.Oxycodone 4.Acetaminophen& Oxycodone 5.Aspirin& Oxycodone 6.Acetaminophen& Hydrocodone 7.Acetaminophen& Codeine	1.Amitriptyline 2.Imipramine 3.Desipramine 4.Nortriptyline		1.Pentosan Polysulfate Sodium 2.Pentosan Polysulfate Sodium	1.Pregabalin 2.Gabapentin		1.Tamsulosin hydrochloride 2.Terazosin 3.Doxazosin 4.Silodosin

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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 UCPPS, and to identify clinical factors and research measurements to define clinically relevant subgroups of patients with Interstitial Cystitis (IC)/Painful Bladder Syndrome (PBS) in men and women, and Chronic Prostatitis (CP)/Chronic Pelvic Pain Syndrome (CPPS) in men, for future clinical trials, and to inform symptom management.

1.B. Objectives

Building on the findings from the Trans-MAPP Epidemiology and Phenotyping (EP) Study conducted during Phase I of the MAPP Research Network, a second larger and longer prospective observational study of UCPPS patients, the Trans-MAPP Symptom Patterns Study (SPS) was designed. The primary objectives of this study are to:

1. Identify clinical features, participant-reported characteristics, and biological measurements (e.g., biomarkers, CNS structure/function, microbial populations and patterns) assessed at baseline, and during follow-up, that predict, or are strongly associated with, UCPPS symptom patterns (either improvement or worsening) over time.
2. Characterize potential biological changes (e.g., regional versus systemic pain profiles, inflammatory state, function of the central nervous system) associated with changes in symptoms to reveal underlying physiological contributors to improvement or worsening.
3. Further characterize and validate definitions of UCPPS symptom patterns as a clinically significant and patient-valued measure.
4. Establish and validate definitions of phenotypic subgroups of UCPPS patients based on symptom patterns and biological (pathophysiological) features.
5. Develop statistical models for clinical use in predicting differential longitudinal patterns of UCPPS symptoms.

The Trans-MAPP Study of UCPPS Symptom Patterns is designed to correlate clinically important longitudinal symptom patterns with phenotypic characteristics. This study expands previous research conducted by the MAPP Research Network's investigators during the first five years to address clinically important questions of etiology and natural history of UCPPS. Novel features of this study include:

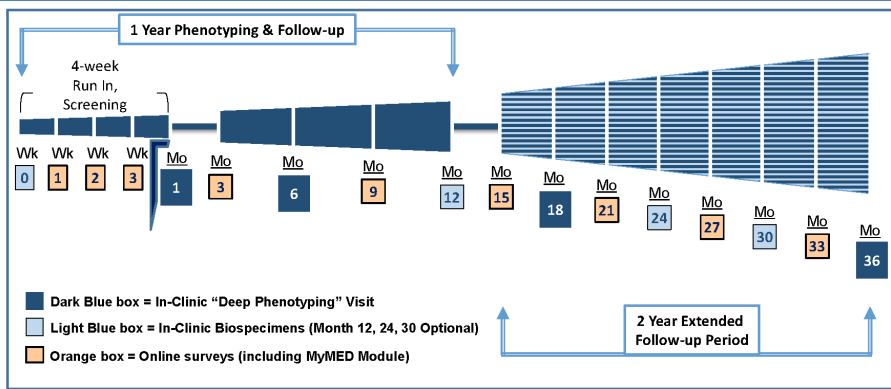
1. A screening visit (week 0) to confirm eligibility, followed by a run-in period of three (3) weekly on-line symptom assessments, in advance of the deep-phenotyping baseline in-clinic visit at week 4, in order to adjust for regression-to-the-mean and confirm subtype classifications for enrichment sampling of target subgroups.
2. Study of the cohort enriched for individuals likely to develop distinct longitudinal symptom patterns (either improvement or worsening) over time.
3. Stratification of study participants at baseline based on candidate predictors (identified in Phase I) of symptom patterns (either improvement or worsening) of symptom progression.

4. Sufficient sample size, resulting from enriched recruitment of targeted subgroups, to provide adequate statistical power to detect baseline and longitudinal phenotypic factors with utility for discriminating patient subgroups with differing symptom patterns.
5. Development and evaluation of a multivariable statistical model based on phenotypic characteristics associated with symptom progression (either improvement or worsening) patterns. The goal is to develop a tool for clinical use that may predict disease course.
6. Application of additional, novel biological measurements (e.g., central nervous system structure/function at baseline and during the follow-up period) to correlate physiological findings with symptom progression profiles.
7. Use of additional novel measures of acute symptom change or flares (e.g., studies of induced flare, new questionnaires to better characterize flares) to complement above assessment (#5).
8. Extended duration of follow-up to permit better characterization of the long-term natural history of these syndromes, including durability of symptom patterns.
9. Expanded assessment of transition from regional pain (i.e., restricted to pelvis) to systemic pain phenotype in UCPPS and relevance to symptom change and presence of co-morbid syndromes.

1.B.1. Description

As summarized in **Figure 1**, the overall design of the Trans-MAPP Symptom Patterns Study (SPS) includes screening and enrollment of eligible UCPPS patients during an initial clinic visit (week 0), followed by a run-in period of 3-weekly internet-based sessions for capture of primary symptom data. These same data are then assessed at a “deep phenotyping” baseline visit at week 4, and then quarterly during an extended follow-up period, until a final in-clinic visit at 36 months. The run-in period is designed to account for regression-to-the mean effects, as well as assessment of variability for selected urologic symptoms and location of pain sites reported on the body map, in order to establish baseline subgroup classifications of each UCPPS participant at the baseline in-clinic visit (month 1), involving a “deep-phenotyping” battery of symptom measures, biospecimen collection, quantitative sensory testing (QST) procedures and neuroimaging scans.

Figure 1. Timeline for MAPP Phase II Symptom Patterns Study



Following the “deep phenotyping” symptom assessment at week 4, each UCPPS participant begins the longitudinal follow-up with internet-based quarterly symptom assessments for a total of 36 months.

Each participant also returns for in-clinic reduced (“lite”) phenotyping data and biospecimen collection every 6 months, as illustrated in **Figure 1**.

Table 1. Schedule of Biologic Specimen Collection

Actual Dist'n: MAPP Phase I						Proposed Dist'n: MAPP Phase II							
BPI Body Map Location	Sex	UCPPS Subtype				Total	BPI Body Map Location	Sex	UCPPS Subtype				Total
		BPS: No		BPS: Yes					BPS: No		BPS: Yes		
		Neither	Painful Filling	Painful Urgency	Both				Neither	Painful Filling	Painful Urgency	Both	
PP Only	Males	14 (24.56)	2 (3.51)	17 (29.82)	24 (42.11)	57	PP Only	Males	60	40	60	160	
	Females	7 (13.73)	4 (7.84)	14 (27.45)	26 (50.98)	51		Females	60	40	60	160	
PP and Beyond	Males	33 (24.63)	14 (10.45)	33 (24.63)	54 (40.30)	134	PP and Beyond	Males	60	40	60	160	
	Females	20 (10.99)	16 (8.79)	34 (18.68)	112 (61.54)	182		Females	60	40	60	160	
Total		74	36	98	216	424	Total	240	160	240	640		

The Trans-MAPP SPS will recruit 640 UCPPS patients meeting the eligibility criteria, recruited from 6 clinical sites.

Approximately one-half of the participants will be male, and one-half will be enriched to meet the body map pain location criteria of pelvic pain (PP) Only, as illustrated in **Figure 2**.

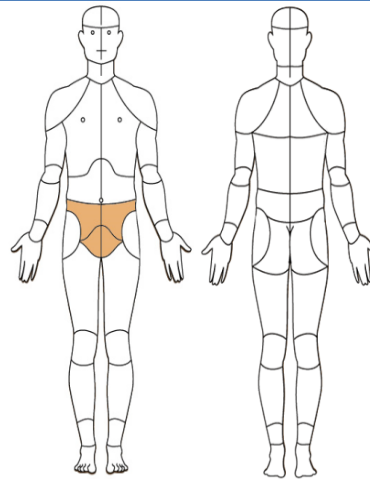
Furthermore, as illustrated in **Table 1** (right-hand panel), these subgroup proportions of 25% (n=160) in each of the four row totals represent enrichment sample size targets,

relative to the subgroup composition recruited within the MAPP Phase I EP Study (left-hand panel). In particular, the MAPP Phase II recruitment strategy will target 50% of males and females within the “PP Only” subgroup.

This “PP Only” localization region will be determined from a body map, in which the participant endorses pain only in one or more of the four highlighted regions on the front view of the Collaborative Health Outcomes Information Registry (CHOIR) (<http://snapl.stanford.edu/choir/>) body map, modified with the abdominal midline to increase the specificity of the PP Only region, as shown in **Figure 2**. To meet these subgroup criteria, participants will need to leave all other body regions blank on the front view, as well as all body regions blank on the back view.

In addition, enrichment recruitment of 240 UCPPS patients (120 males; 120 females) will also be targeted for those who endorse BPS:No. Specifically, these items inquire about the presence of pain that worsens with bladder filling (RICE Q4), and urinary urgency due to pain/pressure/discomfort (RICE Q2/Q3), as shown in **Table 1**. Participants in MAPP Phase I who did not endorse the presence of pain that worsens with bladder filling (RICE Q4), nor urinary urgency due to pain/pressure/discomfort (RICE Q2/Q3), were classified as BPS:No. These enrichment subgroup criteria are based on data-driven results arising from extensive longitudinal symptom patterns analyses of MAPP Phase I data currently underway. These baseline factors appear to be associated with differential likelihoods of being an “Improver”, although the sample sizes are quite limited, as shown in **Table 1** (left-hand panel). However, the sample size requirements are minimized when the key risk factor distributions are 50:50 absent:present. With sample sizes of approximately 320 males and 320 females, this Symptom Patterns

Figure 2. CHOIR Body Map Modified for Regional Specificity of “Pelvic Pain Only”



Study will have 90% power to detect RR=2.0 for these promising risk factors, separately within males and females.

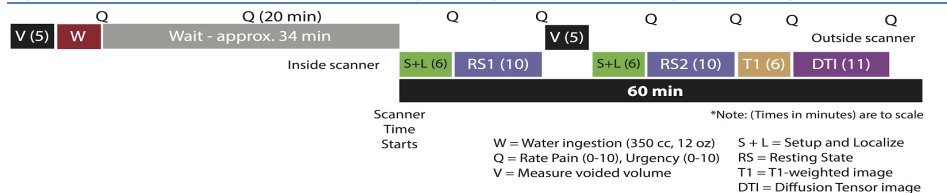
All UCPPS participants from MAPP Phase I will be contacted, and invited to participate in the Symptom Patterns Study, and will be assessed in the identical manner as new participants, as outlined in the eligibility criteria in Section 4.4. These MAPP Phase I re-enrollees into MAPP Phase II will provide even longer-term data regarding symptom progression, although there will be variable length gaps between their 48-week symptom assessment visit and their re-entry into the long-term follow-up study currently underway.

1.B.1.a) Neuroimaging

Based on the Neuroimaging discoveries of MAPP Phase I, The MAPP Phase II Neuroimaging protocol aims to develop a more comprehensive model of the neural representation of UCPPS symptoms and the brain-body interaction that mediates these symptoms in different UCPPS subgroups. To further define the findings of MAPP Phase I, the Phase II Neuroimaging protocol is designed to specifically look at the performance of the bladder filling network longitudinally in a well phenotyped sample of patients with UCPPS.

The Single Session Neuroimaging Protocol will be performed with all MAPP Phase II eligible participants, who are willing to participate in the neuroimaging protocol, at the 1, 6, 18, and 36 months visits as well as at any ATLAS Study 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 3 below. The participant voids before the start of the scanning session, and is then setup in the scanner. The participant is queried (Q) to rate pain (0 -10) and urgency (0 -7) at fixed time points.

Figure 3. Protocol Overview of Bladder Filling Paradigm Based on Resting State Changes



The neuroimaging modalities acquired in the MAPP Phase I study, including structural images of gray matter (T1), white matter (DTI), and fMRI images of brain function in resting state (RS) will be acquired in the MAPP Phase II Single Session Neuroimaging Protocol. However, these data will be collected at multiple time-points in MAPP II participants. Another difference between the MAPP I and MAPP II neuroimaging protocols is the acquisition of an additional RS scan after water ingestion, which when compared to the first RS scan will facilitate the identification of brain networks mediating painful bladder filling in UCPPS patients.

1.B.1.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 in MAPP Phase II. QST will be conducted at the week 4 (baseline) and 6, 18, and 36 month deep phenotyping in-clinic visits, as well as during all ATLAS modules (pre-therapy and post-therapy), on all SPS participants. The MAPP Phase II QST protocol consists of a “core” battery of four methods (Appendix E **QST MOP**) 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).

1.B.1.c) Analysis of Therapies during the Longitudinal Assessment of Symptoms “ATLAS”

Within the SPS is the Analysis of Therapies during the Longitudinal Assessment of Symptoms (ATLAS) protocol. The rationale for the ATLAS protocol is that through exposure of UCPPS patients to pre-defined therapeutic interventions with accompanying phenotyping, a relationship between response (or lack of response) to a given therapy and specific phenotypic profiles may be established. If successful, this would identify sub-sets of UCPPS patients with characteristic phenotypes (i.e., disease marker profiles, degree and patterns of symptoms, influence of symptom flares, presence of co-morbid syndromes, neurological structure/function, etc.) that preferentially respond to specific treatments. This could eventually lead to “personalized analgesia”, by allowing the design of future clinical trials that would specifically test UCPPS therapies restricted to patients with UCPPS “endophenotype” that are expected to respond to a treatment.

1.B.1.d) Trans-MAPP SMARTPHONE APPLICATION To Assess Pelvic Pain: The (M)APP Study

Participants enrolled in the MAPP SPS study will have the option to participate in the (M)APP study following completion of the 6, 18 and 36 month SPS clinic visits. The purpose of this study is to use a mobile smartphone application for assessing pelvic pain variation throughout the day in patients with chronic pelvic pain. The data obtained from the MAPP mobile phone application, (M)APP, will complement, but not replace, the patient-reported questionnaire data obtained from the Symptom Pattern Study (SPS). Data on pain severity, pain location, anxiety, and depression that are collected in the SPS will be examined both cross-sectionally and longitudinally with respect to the (M)APP dataset to ensure that the newly-develop app is a valid assessment. These comparisons will help to inform the hypothesis as outlined below. In addition, there are novel questions in the app that are relevant to chronic pain, but not included in the SPS (e.g., day-to-day stress, alcohol use).

1.C. Study Organization

Participants will be recruited from the following six Discovery Sites as listed in the table below.

1.C.1. Discovery Sites and Recruitment Centers

LOCATION	NAME
Chicago, IL	Northwestern University Feinberg School of Medicine
Los Angeles, CA	University of California (UCLA)/University of Southern California (USC)

LOCATION	NAME
Iowa City, IA	University of Iowa
Ann Arbor, MI	University of Michigan
Seattle, WA	University of Washington
St. Louis, MO	Washington University

1.C.2. Additional Participating Laboratories and Centers

PRINCIPAL INVESTIGATOR	CENTER
Marsha A. Moses, Ph.D.	Children’s Hospital Boston, Harvard Medical School, Boston MA
J. Richard Landis, Ph.D.	Data Coordinating Core (DCC), University of Pennsylvania, School of Medicine, Philadelphia, PA
M. Scott Lucia, M.D.	Tissue Analysis and Technology Core (TATC), University of Colorado, Denver School of Medicine, Aurora, CO
J. Curtis Nickel, MD, FRCSC	Department of Urology, Queen’s University, Kingston, Ontario, Canada
Garth D. Ehrlich PhD	Professor of Microbiology and Immunology Professor of Otolaryngology-Head, and Neck Surgery Drexel College of Medicine, Philadelphia, PA
Jennifer Anger, MD, MPH Michael Freeman, PhD	Cedars-Sinai Medical Center, Los Angeles, CA

1.C.3. Funding

Funding for the Trans-MAPP EP Study is provided by the National Institute of Diabetes, Digestive and Kidney Diseases (NIDDK), a division of the National Institutes of Health (NIH), Department of Health and Human Services.

1.C.4. Project Cycle

The Trans-MAPP SPS will span five years. It is anticipated that the recruitment phase of the study will occur over a 42-month period beginning in June 2015. After enrollment, participants will then be followed for up to 36 months. Participants enrolled in the study later in the recruitment phase will have less follow-up time. The final months of the project will be dedicated to evaluation and data analysis for publication.

Participants enrolled in the Trans-MAPP SPS will be enrolled during the screening/eligibility visit to both the neuroimaging (if they meet the neuroimaging eligibility criteria) and QST portion of the SPS study. At any time after the participant completes the in-clinic visit at 6 months, and prior to 30 months of follow-up (with sufficient time remaining in follow-up to carry out the data collection), upon notification from the participant of prescribed treatment change to add a pre-specified ATLAS treatment, he/she will be enrolled in the ATLAS module of the SPS. Initiation of specific treatments (ATLAS treatments) will be preceded by an in-clinic assessment of functional/structural neuroanatomy, collection of blood and urine for biomarker and microbiome assessment, trait and state measures, and urologic symptom

profiles using the standard Sym Q data module. Each individual site is responsible to ensure that the appropriate IRB approvals are obtained for all of the SPS modules prior to enrolling participants.

1.D. General Policy

1.D.1. General Protocol Policy

The objectives of the Trans-MAPP SPS 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 MAPP Network Executive Committee approved 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 approval criteria. All changes to the informed consent form must also be approved by the IRB.

2. PARTICIPANT ENROLLMENT

2.A. Participant Population and Recruitment

This study will recruit from 6 clinical sites a maximum total of 640 and minimum total of 600 male and female UCPPS patients meeting the eligibility criteria. Approximately one-half of the participants will be male, and one-half will be enriched to meet the body map pain location criteria of pelvic pain only. In addition, enrichment recruitment of 240 UCPPS patients (120 males; 120 females) will also be targeted for those who endorse BPS:No. Specifically, these items inquire about the presence of pain that worsens with bladder filling (RICE Q4), and urinary urgency due to pain/pressure/discomfort (RICE Q2/Q3).

Each Discovery site is committed to recruiting 107 participants into the Trans-MAPP SPS. Each site will be expected to recruit equal numbers of males and females. Recruitment data will be monitored by the DCC in order to continually assess recruitment rates at each site. Recruitment sources and strategies will vary from center to center, however each clinical center will be responsible for determining how best to recruit participants.

2.B. Identifying Potential Participants

Participant recruitment will be conducted through the urology/urogynecology clinics at most of the designated clinical sites. In some cases, local newspapers and other media will be used to promote the

Commented [TB1]: Updated by Ted B. per Protocol Amendment #6.

Trans-MAPP SPS. Participants may be self-referred or referred through their primary physician (either solicited or unsolicited by the urology/urogynecology clinics). 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 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 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, enter this information into the Prescreening CRF as unable to contact patient, 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 this patient 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 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-NNNN 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 RC placing the call should identify him/herself and inform the potential participant how she/he was selected. The RC should provide information about the study and answer questions. **The RC should NOT give the potential participant information about study-specific inclusion criteria.**

Data for prescreening activity are recorded on Prescreening Logs on a monthly basis. These logs capture efforts of the RC to recruit participants and the flow of potential participants seen at the clinical center. These data are reflected in monthly accrual reports.

2.D. Informed Consent

If the pre-screening contact information indicates that the potential participant is eligible and willing, the RC should schedule a time for the participant to come in to review and complete the informed consent prior to proceeding with the Screening/Eligibility Visit #1.

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

Potentially eligible participants will be contacted either by phone or in person by the RC to determine their interest and eligibility for the study. Once the participant is contacted he/she will be scheduled for a screening/eligibility visit.

- 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.
- 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 CMED2 CRF.

2.D.2. Administration of Informed Consent

Once the person comes into the clinic for the Screening/Eligibility Visit #1, he/she must first be administered the study's informed consent. The consent form describes the Trans-MAPP SPS 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 SPS 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.

Administration of Informed Consent

Prepare Participant ...	Potential participants will be asked to sign the Informed Consent form. The consent form describes the Trans-MAPP SPS 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 SPS as well as consent to genetic testing, each has its own signature requirements. 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...	The informed consent form should be reviewed 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...	The RC will 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 ELIG2 CRF.
Review study tasks	The RC will ask the participant to read a few sentences of the consent form. If the participant cannot read the written material, he/she is ineligible for the study. Responses to this question should be recorded on the ELIG2 CRF.
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 ELIG2 CRF.
Present Optional sections	While it is expected that all participants will agree to participate in all parts of the study, male participants may decide to participate in the Trans-MAPP SPS, but opt out of the prostate massage and accompanying VB3 urine sample as well as the rectal swabs. Female participants may participate but decide to opt out of the vaginal swabs.

Continued followup...	The participant should be made aware of her/his responsibilities throughout the Screening and the Follow-up phases of this study. The importance of continued follow-up is stressed. 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 ELIG2 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. The RC will need to reschedule the Screening/Eligibility Visit and at the subsequent visit, the RC should 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”. A participant should not be asked 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 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...	The RC will 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, the RC will 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 (CRFs).
Sign/date...	<i>Participant must sign and date the informed consent form prior to proceeding with any of the Screening/Baseline procedures.</i>

2.D.3. Participant Confidentiality

HIPAA

At most sites, participants must sign a Health Insurance Portability and Accountability Act (HIPAA) Authorization, in addition to the Informed Consent Form. The HIPAA Authorization may or may not be incorporated into the Trans-MAPP SPS 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 Study

Once consent is obtained, the RC will proceed to register the participant to the Trans-MAPP SPS study to obtain a Trans-MAPP SPS Study Participant ID.

However, if participant is a former Trans-MAPP EP study participant he/she will utilize the same PID assigned to them for the Trans MAPP EP Study. Please access your site’s participant ID log from the MAPP I/Trans-MAPP EP study to assist with matching former participants with the correct study PID to then proceed with registering the participant to the Trans-MAPP SPS.

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

Participants who appear to be eligible following completion of informed consent process will have their name recorded on the Participant ID Log [PTIDLOG] and will be registered into the Trans-MAPP SPS Participant Registration module. New participants, those not formerly enrolled in the MAPP I EP study 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, as well as returning participants from the previous Trans-MAPP EP study, 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 primary recruitment Discovery Sites:

CC	SITE	NAME	LOCATION
01	01	Northwestern University Feinberg School of Medicine	Chicago, IL
02	01	University of California (UCLA)	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 primary recruitment sites there are also several non-recruitment Discovery and Core sites:

CC	SITE	NAME	LOCATION
07	01	University of Pennsylvania (DCC)	Philadelphia, PA
07	02	Harvard Medical School	Boston, MA

CC	SITE	NAME	LOCATION
07	03	Queens 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 minimum 24 hour culture to test for urine pathogens. Eligibility Criteria (as documented on Eligibility Confirmation [ELIG]) are outlined below. Individuals not under the care of a MAPP PI are eligible for the study and should be screened.

2.E.1. Inclusion Criteria

Patients are eligible for the SPS if they meet the following criteria:

1. Participant has signed and dated the appropriate Informed Consent document.
 - Agreed to participate in ALL required Symptoms Patterns Study procedures (including Biospecimen collections, , and Quantitative Sensory Testing)*.
 - Gave permission for use of DNA for genetics studies.
2. Gender recorded in Participant Registration module.
3. Participant is at least 18 years of age.
4. Participant is able to speak, read, and understand English.
5. In the past 3 months participant has had a feeling of pain, pressure, or discomfort in the lower abdomen or pelvic area – that is, the part of the body that is above the participant’s legs and below the belly button. (This criteria does not apply to returning MAPPI participants.)
6. These symptoms have been present for the majority of the time during the most recent 3 months.
7. Participant reports a response of at least 1 on the pain, pressure or discomfort scale (on SYM-Q Screening Q1) for UCPPS symptoms during the past 2 weeks. (This criteria does not apply to returning MAPPI participants)
8. Participant has received a clinical diagnosis of either or both IC/BPS or CP/CPPS (per AUA guidelines) or a clinician familiar with UCPPS criteria confirms participant meets UCPPS evaluation criteria per-protocol. (This criteria does not apply to returning MAPPI participants)

* Please Note: Potential SPS Study participants who are ineligible for the MRI criteria but meet all other study criteria are eligible to participate in the study.

2.E.1.a) Inclusion criteria exceptions for MAPP I participants

MAPPI participants may be enrolled even if they have not had symptoms in the past 3 months and/or score 0 on SYM-Q-Screening Q1.

2.E.2. Exclusion Criteria

Patients meeting any one of the following criteria will not be eligible for enrollment in the Symptom Patterns Study. However, participants who develop any of these exclusion criteria during the follow-up

phase of the study will continue to be followed. It will be recorded in the follow-up data if a participant has developed any of the exclusion criteria.

1. Participant has an on-going symptomatic urethral stricture.
2. Participant has an on-going neurological disease or disorder affecting the bladder or bowel fistula.
3. Participant has a history of cystitis caused by tuberculosis, radiation therapy or Cytoxan/cyclophosphamide therapy.
4. Participant has augmentation cystoplasty or cystectomy.
5. Participant is currently undergoing dose titration or medication adjustments for a poorly controlled autoimmune or infectious disorder (such as Crohn's Disease, Ulcerative Colitis, Lupus, Rheumatoid Arthritis, Multiple Sclerosis, or HIV) which in the opinion of the Investigator could impact bladder symptoms.
6. Participant has a history of any pelvic malignancy (e.g. GI, GU, Gyn)
7. Participant is having ongoing systemic treatment/therapy for any type of cancer.
8. 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.).
9. Participant has severe cardiac, pulmonary, renal, or hepatic disease that in the judgment of the study physician would preclude participation in this study.

Note: If an enrolled participant has a cystoscopy during the course of the study, no changes are made to the visit schedule.

Exclusion Criteria for Males Only

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

2.E.3. Deferral Criteria

Deferral Criterion – Treatment and History

1. If participant has had definitive treatment for acute epididymitis, urethritis, vaginitis, the participant will be deferred for at least 6 months from resolution of symptoms.
2. If participant has history of unevaluated hematuria, this will require the evaluation of a study physician to determine if this has been appropriately evaluated.
3. If participant has had cystoscopy with hydrodistention or kenalog injection, the participant will be deferred for at least 3 months from the date of the procedure.

Deferral Criterion – Prostate related (Males ONLY)

1. If male participant has had a prostate biopsy or transurethral resection of the prostate (TURP) within the last three months, he will be deferred for 3 months following prostate biopsy or TURP.

Deferral Criteria - Urine test results*

A clean-catch midstream urine specimen (VB2) will be obtained from all male and female participants during the initial phase of eligibility confirmation, so that a urine dipstick analysis and urine culture can be done for all participants, and a urine pregnancy test can be conducted for females of child bearing age (excluding post-menopausal and those with a history of hysterectomy).

1. 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 a deferral, participant will be deferred until normal level of nitrites from dipstick urinalysis is confirmed.
2. 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 treated and deferred for at least 6 weeks from the date of positive urine culture result. (Must be documented on Urine Culture Result – UCR form).

* Repeat urine dipstick analysis and urine culture will be performed at all subsequent clinic visits for purposes of data collection and deferral criteria no longer applies.

Deferral Criterion – Pregnancy Test (Females of childbearing potential ONLY)

1. If a female participant has a positive urine pregnancy test she will be deferred until after delivery.

(If a female participant becomes pregnant during the study, she will be withdrawn from the study at the time the pregnancy is identified; data from prior to the pregnancy will be included in the analyses).

Note: If a deferred participant becomes eligible and is re-enrolled, contact the DCC to archive any previously entered data. The DCC will archive the data, add a new ELIG CRF and open the participant survey.

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 Trans-MAPP SPS. 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. Please note, if specimens have been collected for participants who are screening failures, those specimens will be sent to the TATC.

2.G. Participant Withdrawal and Withdrawal Consent

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. Participant data folder is clearly marked to indicate withdrawal and is maintained at the clinical center where the participant was recruited and followed.

2.H. 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 SPS Protocol
- Trans-MAPP SPS Case Report Form (CRF) 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 SPS 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 trial. 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 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

The next section of the manual provides a summary of activities and procedures that occur at each scheduled Trans-MAPP SPS visit and online computer assessment, once a potential participant is consented. The specific directions for completing each Case Report Form [CRF] are found in the “Directions for Completing Case Report Forms” section of this manual.

The Study Visit Schedule, **Appendix A**, describes the types of visits and permissible visit intervals (called visit window) used throughout this manual to describe interaction with study participants. The participant study calendar, which is a tool available in the Data Management System (DMS), will be generated based on the date of the Eligibility CRF completed at the Screening/Eligibility Clinic Visit [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. Online Run-in computer assessments (Week 1, 2, &3) will have a window of 7 days between assessments, 3 days prior and 3 days following the actual target day. The weekly run-in online assessments are not allowed any other time outside of this window. 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.

The visit window for the quarterly online computer assessments is ± 2 weeks. Participants are expected to complete screening, baseline, 6, 18, and 36 month 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 password (PIN) to initiate the survey. If the participant does not finish the survey during the study visit, the participant has until the end of that calendar day (11:59pm) to complete the online questionnaires from home/other location of their choice.

The Months 6, 18, 36 and optional visits (Months 12, 24, 30) visit windows are ± 2 weeks from the target visit dates.

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

The preferred order/administration of assessments during all in clinic visits is as follows:

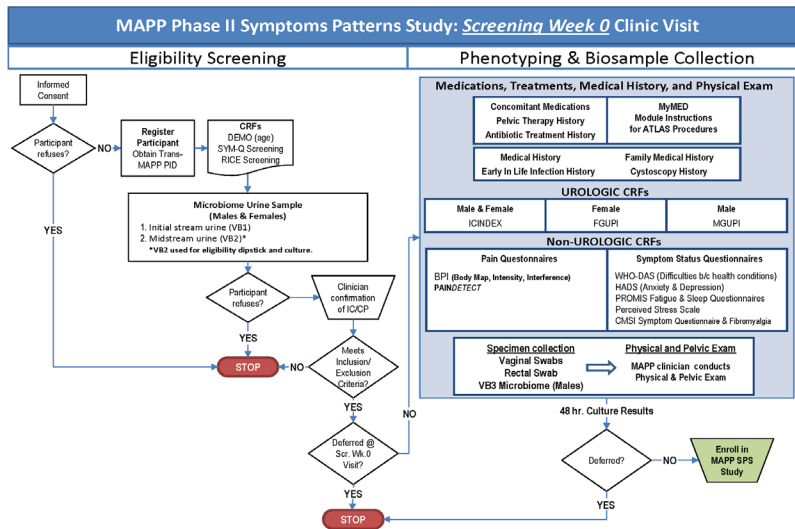
- a. Questionnaires
- b. Blood Draw
- c. Neuroimaging
- d. QST
- e. Physical/Pelvic Exam

Deviations from the above order should be documented on a comment sheet CRF.

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

The screening/eligibility process for this study will require an in-person clinic visit to obtain informed consent for the entire protocol, assess study eligibility, complete a subset of study questionnaires and biospecimen collection, and provide participants with additional information about the study, see Figure 4 below.

Figure 4. Sequence of MAPP II SPS Screening Visit Data, Physical Exam and Biospecimen Collection



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

- 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-Screening**) – including questions regarding Flares.
Note: If participant reports on the SYM-Q that he/she is currently experiencing a flare during the clinic visit, ask participant to provide a flare VB1 microbiome urine sample.
Note: 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 Screening & Eligibility Confirmation (**RICE Screening**)
- Eligibility Confirmation form (**ELIG2**) – to be completed (Inclusion, Exclusion, Deferral Criteria) prior to participant-entered questionnaire battery.
- Neuroimaging Eligibility Assessment (**ELIG_SCAN2**)
- Microbiome urine specimen (VB1, VB2)
- Urine Culture Result (**UCR**) – confirm negative urine culture from the microbiome VB2 specimen within 48 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 further details in Appendix 2);
 - a urine dipstick test will be performed for the presence of leukocyte esterase, nitrites, and hematuria;
 - If the dipstick is positive for nitrites, the participant will be treated and deferred until urine culture results are available, and deferred for three months from the date of positive urine culture test result.
 - For females of childbearing potential, perform a pregnancy test

All participants should meet with a clinician prior to being enrolled to ensure eligibility requirements are met.

Assuming that the participant meets all eligibility criteria that can be known prior to the results of the 24 hrs (minimum) urine culture (confirmed on ELIG2 form), the participant will begin the Phenotyping, Physical Exam, and additional microbiome specimen collection (VB3).

- Physical and Pelvic Exam (**EXAM2 and PEX**): 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 conducted during the Screening/Eligibility physical exam is required, both the prostate exam/massage and the VB3 urine sample acquired immediately following the prostate massage (males only), as well as 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 (**CYSTO2**)
- Antibiotic Treatment History (**ABHX**)
- Pelvic Therapy History (**PTHX**)
- Documentation of current medications on Concomitant Medications (**CMED2**)

Commented [TB2]: CYSTO form label updated to CYSTO2

The RC will demonstrate and provide each participant with instructions on how to log onto and complete the online participant questionnaires with the participant’s PID and PIN, as well as answer any questions the participant may have. The RC should then escort eligible participants to a quiet comfortable location where he/she can complete the online questionnaire assessments including:

- Interstitial Cystitis Symptom Index (ICSI) and Problem Index (ICPI) (**ICINDEX**)
- Male Genitourinary Pain Index (**MGUPI**)/Female Genitourinary Pain Index (**FGUPI**)
- Early In Life Infection History (**EIL-INF**)
- Pelvic Therapy History (**PTHX**)
- Complex Medical Symptoms Inventory (**CMSI2_Screening**)
- Fibromyalgia symptoms module (**CMSI2_FM2**)
- Brief Pain Inventory: Body Map, Intensity, Interference (**BPI2 Male/Female**)
- PAIN Detect (**PAIN**)
- WHO Disability Assessment Schedule (**WHO-DAS**)
- Hospital Anxiety and Depression Scale (**HADS**)
- PROMIS Fatigue
- PROMIS Sleep
- Perceived Stress Scale (**PSS**)

RCs will use the CMED2 form to track medication changes recorded by the participant via the online “MyMed” module during the course of the study. After the Month 6 visit, RCs will also use the MyMed data to determine if a medication change warrants initiation of an ATLAS Study visit.*

*Please note: Changes in dose of specific medications regarding management of urologic or pelvic pain symptoms is considered and ATLAS eligible event.

If eligible, schedule participant for Neuroimaging scans at Week 4. (See Neuroimaging Protocol - SPS Protocol Appendix 3 - for details)

The entire screening visit is expected to take approximately 2 - 4 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 visit (right-hand panel, **Figure 4**) and corresponding assessments (biospecimen specimen collection, neuroimaging, and QST) are initiated only for participants highly likely to be confirmed eligible after the 24 hrs (minimum) urine culture results are known.

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

- 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)
- The Target window to complete the first, Week 1, online questionnaires
- The date for next in-clinic (Week 4) visit
- Site specific reimbursement for their time and effort
- Copy of signed informed consent
- Site Contact if they have questions

- Introduce and schedule participant for the neuroimaging (if eligible and agreed to participate in the neuroimaging study) and QST procedures that they will have at the Week 4 Baseline in-clinic visit.

Once Participant leaves, RC will need to:

- 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.

Confirming Eligibility

After a 24 hrs (minimum) negative urine culture result is confirmed, the Enrollment Confirmation (**ENROLL**) form will be completed, confirming that all Eligibility Criteria have been met.

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

After baseline enrollment and phenotyping, each participant will be followed quarterly for 36 months, utilizing web-based data collection modules as well as in-clinic visits at 6, 18, and 36 months and optional clinic visits at months 12, 24, and 30.

Upon completing the Screening/Eligibility assessment, the RC should be able to determine if the participant is potentially eligible for the Trans-MAPP SPS. 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, or if the participant should be deferred based on the urine dipstick results.

If the participant does not meet the necessary eligibility criteria, the RC should thank the participant for his/her time and effort, explain to the participant that they did not meet the study eligibility criteria, provide the designated site-specific reimbursement, and discontinue with any additional study measures/visits.

Any candidate failing any of the inclusion or exclusion criteria during the screening/baseline visit will be considered ineligible for the study. 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. Some participants may have their entry into the study deferred to a later time based on consideration of the deferral criteria. A participant previously **excluded**, based on the exclusion criteria, **cannot** be re-screened.

Deferral

If the participant meets the eligibility criteria for the study, but also meets one or more deferral criterion, the RC should explain the specifics of the deferral criterion to the participants, as well as the required follow-up and deferral period prior to re-enrollment into the study, and schedule the participant for a new screening/baseline visit prior to providing the participant with the site designated reimbursement for his/her time and effort.

If a participant is deferred, she/he must begin the screening process again, beginning at Visit #1. When returning to repeat the screening/eligibility visit the Participant will be issued the same Participant ID

and PIN that they were assigned at their initial screening/eligibility visit and will be expected to complete all new screening/eligibility CRFs, provide new biospecimens, as well as repeat all other screening/eligibility procedures including the online participant questionnaire. In the event that a participant is deferred, **do not** discard any of the biospecimens collected, please proceed with shipping all biospecimens collected for deferred participants to the central lab (TATC) in the same manner/time interval which biospecimens for eligible participants are shipped to the lab.

To determine the re-screening date for a participant who has been deferred for more than one criterion, the RC will select one date that allows sufficient time for all deferral criteria to have been resolved. Before re-scheduling Visit #1, the RC should contact the participant by telephone close to the ending date of the deferral period to: review the study with the participant, determine whether the condition is absent or has subsided, and ascertain if the participant is still interested in beginning the screening process again. Please see the Deferral Criteria section 2.E.3 for additional details on deferral requirements and deferral time frames.

In the rare event that a participant is deferred after he/she previously completed the baseline/screening online questionnaire and biospecimen collection, it is the Research Coordinator's responsibility to contact the DCC to inform them that this participant was deferred and to archive the baseline/screening participant survey. Please proceed with sending all biospecimens collected, even for deferred participants, to the central lab (TATC).

If the participant meets all necessary eligibility criteria, the RC should proceed with informing the participant of his/her next visit, provide the participant with his/her follow up calendar, provide information as to what to expect for the Baseline visit, as well as how to log on to the internet for the next three weeks of weekly online internet data capture.

NOTE: The Eligibility CRF must be data entered into the Oracle Clinical Module prior to proceeding with the study visit 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.

3.B. Run In Visits (Week 1-3)

During the run-in period, study participants will complete a brief online module each week for weeks 1, 2 and 3, assessing symptoms, health care utilization, flare status, and quality of life in a weekly time frame via the following questionnaires:

- Symptom, Healthcare Utilization, and Flare Status Questionnaire: (SYM-Q Run-In)
- Global Response Assessment (GRA)
- Interstitial Cystitis Symptom and Problem Index (ICINDEX Run-In)
- RICE Case Definition Questionnaire (RICE_Run-In)
- Female/Male Genitourinary Pain Index (FGUPI/MGUPI)
- Complex Medical Symptoms Inventory (CMSI2_Run-In)
- Fibromyalgia symptoms module (CMSI2_FM2)
- Brief Pain Inventory: Body Map, Intensity, Interference (BPI2 Male/Female)
- PAIN Detect (PAIN Run-In)

- WHO Disability Assessment Schedule (WHO-DAS R.A.)
- Hospital Anxiety and Depression Scale (HADS)
- PROMIS Fatigue
- PROMIS Sleep
- Perceived Stress Scale (PSS_Run-In)

Participants are expected to log on once a week to complete the designated set of questionnaires during the 3 weeks of online data capture as well as the MyMed module. If a participant misses more than one of the three weekly online assessments during the Run-In period, he/she may be removed from the study upon discussion with the site PI regarding participant's ability to commit to the entire study.

3.C. Baseline Visit (Week 4) – Phenotyping, Biospecimen Collection, Neuroimaging, and QST Assessments (Eligible Participants Only)

At week 4, after confirming a negative urine culture from the week 0 specimen, eligible UCPPS patients will undergo a “deep phenotyping” symptom assessment during an extensive in-clinic visit, including biospecimen collection, quantitative sensory testing (QST) procedures and neuroimaging scans (if eligible and agreed to participate in the neuroimaging study).

Note: Participants must complete the Baseline Visit in order to continue participating in the study.

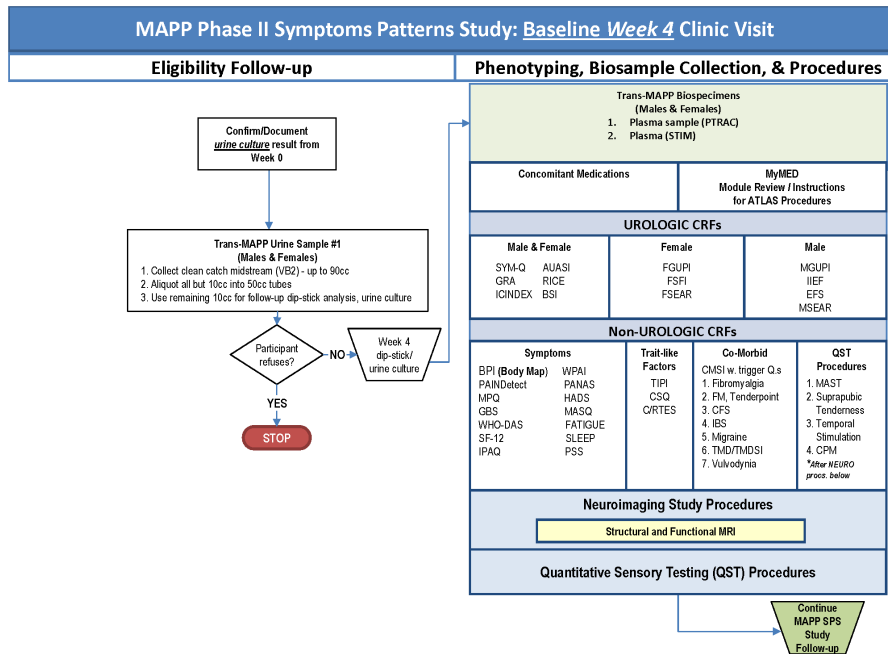
At the Baseline (Week 4) visit, the following sequence of steps will occur (**Figure 5**):

- Biomarker urine specimen (VB2)
 - a clean catch midstream urine (VB2) specimen will be obtained for the urine dipstick test and 24 hrs (minimum) urine culture (see further details in Appendix 2);
 - a urine dipstick test will be performed for the presence of leukocyte esterase, nitrites, and hematuria;
- 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.
- The participant will begin the Deep Phenotyping on-line survey and Biospecimen Sample Collection phase (**Figure 5**) of the Symptoms Patterns Study. If, due to time constraints, participant is not able to complete all of the online assessment, participant may complete the remaining assessments at home. The participant will have until the end of that calendar day (11:59pm) to complete the online questionnaires.
- **Biospecimens:**
 - Blood specimen 10mL ACD plasma vacutainers (Plasma and Buffy Coat DNA)
 - STIM TUBES – Three 1 mL blood samples for stimulated cytokines

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

- Brief clinical diagnostics will also be collected via the **CDX** form including: Height, weight, waist circumference, blood pressure, urine culture results, current flare status/specimen collection, and negative pregnancy test or verbal confirmation based on your site requirements.

Figure 5. Sequence of MAPP Phase II Study Baseline Data and Biospecimen Collection and Procedures



The Deep Phenotyping On-line Survey at the Baseline (Week 4) visit will include the following questionnaires and is expected to take approximately one hour to complete:

Urological Phenotyping Case Report Forms:

- Symptom, Healthcare Utilization, and Flare Status Questionnaire: (SYM-Q_Baseline)
- Interstitial Cystitis Symptom Index (ICSI) and Problem Index (ICPI) form – (ICINDEX)
- Global Response Assessment (GRA)
- AUA Symptom Index (AUASI)
- Rand Interstitial Cystitis Epidemiology (RICE) Study – IC Case Definition Questionnaire
- RICE Bladder Symptom Impact (BSI)
- Concomitant Medications (CMED2) – Documentation of current medications

Female Participants only:

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

Commented [TB3]: CRF label updated to FSFI2

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 (MSEAR) Questionnaire

Participants will be presented with an online log (MyMed) of the medications that they reported taking at the previous visit and will complete online assessments to inform the study if they've stopped taking any of these initial medications or if they've started taking a new medication and if so, the name of the new medication.

Non-Urological Phenotyping CRFs:

Symptoms and Illness Impact

- PAIN Detect (PAIN)
- McGill Pain Questionnaire (MPQ)
- Gracely Box Scales (GBS)
- Brief Pain Inventory (BPI2) + revised body map
- 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)
- Fatigue, and Sleep Questionnaires (PROMIS)
- Multiple Ability Self-Report Questionnaire (MASQ)
- Perceived Stress Scale (PSS)

Traits and 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

- Complex Medical Symptoms Inventory Questionnaire (CMSI)
- CMSI, Fibromyalgia (CMSI2_FM2)
- 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)

During the baseline visit participants will undergo an initial series of Quantitative Sensory Tests (QST) as well as neuroimaging (if eligible) scans. Please see the Neuroimaging protocol ([Appendix 3 in the SPS Protocol](#)) and QST MOP [[Appendix E](#)] for additional details regarding both batteries of tests. 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.

Neuroimaging study CRFs:

- Eligibility Confirmation, Neuroimaging Study (ELIG_SCAN)
- Magnetic Resonance Environment Screening (MR_SCREEN) – Administrative
- Please remember to utilize the study’s standardized pain and urgency scales to display to participants as required during the relevant aspects of the neuroimaging assessments.
- Participants are permitted to take medications for stress/anxiety related to the MRI. However, this should be consistent practice for all follow-up scans.
- Scans must be completed within 48 hours of the in-person Week 4 visit.

QST Assessment CRFs

- QST Screening (QST Screen) – Provides Participants at Screening Week 0 with details and procedures to prepare for at Baseline Week 4.
- Quantitative Sensory Testing CRF (QST) – Captures data collected during administration of the QST procedures and/or confirmation of procedures not conducted and why.

3.C.1. Completing the Baseline Visit

After Participant completes the Baseline procedures and online questionnaires:

- Run Participant CMSI Report from the RC Data Management Tools screen.
- Run Participant Flare report and collect flare urine sample if participant reports a flare at the time of the visit, via the online Sym Q questionnaire.
- 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 form, 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 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.

*Please note, the CMSI, Fibromyalgia Tender Point procedures are not a part of the MAPP II SPS protocol and therefore should not be administered.

- If eligible, transport participant to location where he/she will complete Trans-MAPP Neuroimaging scans (See Neuroimaging Protocol - Appendix 3 of the SPS Protocol - for details)
- Conduct QST Procedures

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

- Assembled saliva collection kit (for at home saliva collections) with completed header information on the linking form for the 3 day post baseline cortisol saliva samples.

RC must pre-record the header information into the DMS prior to providing the kits to the participants. Only participants PID # and PIN should be recorded on the forms in the places as indicated and no other identifying information. See **Appendix B: Biospecimen Collection Manual** - for detailed instructions on assembling and distributing kits.

- Instruction sheet for accessing and completing the online Participant questionnaire
- Instruction sheet regarding monthly internet medication questionnaires (MyMed)
- A reminder of their study PID# and PIN (this can be included on the Contact Completion Calendar or separate site specific format)
- The date for next in-clinic (6-month) visit
- Introduce and schedule participant for neuroimaging (if eligible and willing to participate in the neuroimaging study) and QST studies for the 6 month visit (if possible)
- Site specific reimbursement for their time and effort
- Site Contact if they have questions

Once Participant leaves, RC will need to:

- 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. Baseline Cortisol Salivary Sample Collection

Following the baseline visit Salivary cortisol will be measured twice daily (morning (4-9am) and bedtime (8pm-12am)). To establish a baseline measure, saliva specimens will be collected at home by the participant during the 3 day period following the week-4 Baseline Deep-Phenotyping 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.

3.E. Monthly Internet Medication Questionnaires Data Capture

Throughout the course of the 36 month study, starting at the Week 0 (Screening/Eligibility) visit, participants will provide information regarding current medications and targeted non-medication treatments. This information will be utilized to track medication and non-medication treatment changes. After the Screening/Eligibility visit, participants will provide information on a monthly basis about medication and non-medication treatment changes via the MyMed internet questionnaires. Participants will be presented with an online log of the medications that they reported taking at the previous clinic visit and asked to complete online questionnaires to inform the RCs if they have stopped taking any of the initial medications or started taking a new medication and if so, the system will prompt the participant to enter the name of the new medication.

Encourage participants to notify study personnel if they begin taking an ATLAS targeted therapy. The MyMed module does not automatically alert sites if a participant reports starting an ATLAS therapy. If a participant is prescribed an ATLAS targeted therapy for non-UCPPS purposes, prior to enrolling into ATLAS, please contact the DCC for guidance regarding enrollment eligibility.

3.F. Quarterly Assessments

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

- Urologic Questionnaires**
 - Symptom and Health Care Utilization Questionnaire (SYM-Q_Follow-up)
 - Global Response Assessment (GRA)
 - Interstitial Cystitis Symptom Index and Problem Index (ICINDEX)
 - RICE Case Definition Questionnaire (RICE_Follow-up)
- Female Participants only:**
 - Female Genitourinary Pain Index (FGUPI)
- Male Participants only:**
 - Male Genitourinary Pain Index (MGUPI)
- Non-Urologic Questionnaires:**
 - Complex Medical Symptoms Inventory (CMSI2_Follow-up)
 - Fibromyalgia symptoms module (CMSI2_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)

Commented [TB4]: CRF label updated to BPI2

3.G. Deep Phenotyping In-clinic Visits at 6, 18 and 36 Months

Participants will come into the clinic at months 6, 18, and 36. During these visits biospecimens will be collected (see Table 2 in MOP Section 4 for details) including 2 separate voids for biomarker and microbiome samples. QST and Neuroimaging (if eligible) assessments will be done. Neuroimaging scans must be completed within 48 hours of the in-clinic visits. 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. The MAPP App [(M)APP] protocol should also be discussed with each participant at each visit. Participants have the option to participate in (M)APP at each of the 6, 18 or 36 month visits. See **Appendix F - (M)APP Procedures** - for instructions on how to register a participant.

Use participants' non-dominant arms, if possible, when drawing blood. See **Appendix B: Biospecimen Collection Manual**.

Men and women will have pelvic exams the **Month 18 Visit** only. QST procedures should occur prior to pelvic exam, if possible. (If not possible, record this on the CRF. Ideally, plan the pelvic exam in the afternoon after QST and neuroimaging.)

A brief set of clinical and diagnostic procedures and forms will also be administered at months 6, 18, and 36 including:

- **CDX** form procedures: Height, weight, waist circumference, blood pressure, urine culture results, current flare status/specimen collection, and negative pregnancy test confirmation.
- Pelvic Therapy History (PTHX)
- Antibiotic Treatment History (ABHX)
- Concomitant Medications (CMED2) – Documentation of current medications
- Cystoscopy History (CYSTO2) will be collected at the **18 and 36 month clinic visits only**.

In addition, a more extensive set of questionnaires is administered at these visits, as compared to the limited subset administered for the quarterly non-clinic visits. This assessment will also be administered via the internet.

This set of questionnaires includes all of the CRFs from the quarterly assessments, plus the additional CRFs listed subsequently:

- Urological Phenotyping CRFs:**
 - AUA Symptom Index (AUASI)
 - RICE Bladder Symptom Impact (BSI)
- Female Participants only:**
 - Female Sexual Function Index (FSFI)
 - Female Self-Esteem and Relationship Questionnaire (FSEAR)
- Male Participants only:**
 - International Index of Erectile Function (IIEF)
 - University of Washington Ejaculatory Function Scale (EFS)
 - Male Self-Esteem and Relationship Questionnaire (MSEAR)
- Non-Urological Phenotyping CRFs:**
 - Complex Medical Symptoms Inventory (CMSI2_Follow-up)
 - Fibromyalgia symptoms module (CMSI2_FM2)
 - Brief Pain Inventory (BPI2) plus Revised Body Map
 - 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)
 - Anger, Fatigue, and Sleep Questionnaires (PROMIS)
 - Multiple Ability Self-Report Questionnaire (MASQ)
 - Perceived Stress Scale (PSS)
 - Catastrophizing Sub-scale (CSQ)
 - Recent Traumatic Events (RTES)

At the conclusion of the 6 and 18 Month visits, provide participants with collection and shipping materials for the 7 day “at home” Cortisol saliva collection. Participants will be asked to collect 2 samples a day for 7 days according to the salivette instructions on the back of the “7 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. If, at the 36 Month visit, one or both of the previous scheduled collections were missed, provide participant with the collection and shipping materials for the 7 day cortisol collection.

If the participant agrees to participate in the (M)APP Protocol, register the participant in the DMS (M)APP module and upload the (M)APP on the participant’s phone. Provide the participant with information about the 4 daily prompts. See **Appendix F** -(M)APP Procedures – for detailed information.

Ad Hoc Deep Phenotyping In-clinic visit “substitution” for 6, 18 and 36 Month visits

Participants who miss a deep phenotyping visit may complete an ad hoc deep phenotyping clinic visit prior to the next deep phenotyping visit. The Ad-Hoc Deep Phenotyping Visit Initiation [DP-INIT] CRF is entered into the DMS to record this visit. Note that the visit numbers are different for each visit. The Ad-Hoc Deep Phenotyping visits correspond to the clinical Deep Phenotyping visits as follows:

Ad Hoc Deep Phenotyping Visit Number	Deep Phenotyping Clinic Visit Number and Type
81	10 6-month visit
82	22 18-month visit
83	40 36-month visit

The [DP-INIT] CRF must be entered on the day of the Deep Phenotyping visit with the CRF date of the Ad-Hoc Deep Phenotyping Visit in the header of the CRF. Once the [DP-INIT] CRF is entered, the Participant Survey will be available for online completion. The RC Log-In Code (14921012) will need to be entered to initiate the surveys.

All Participant Survey, Clinical CRF, QST, and Neuroimaging data collection procedures for the Ad-Hoc Deep Phenotyping visit are designed and proceed in the same way as they do for a regularly scheduled Deep Phenotyping clinic visit.

Once the Participant Survey has been entered and all data collection for the Ad-Hoc Deep Phenotyping visit has concluded, the Ad-Hoc Deep Phenotyping Visit Stop [DP-STOP] CRF must be entered. The [DP-STOP] CRF serves as an indicator for the Participant Survey software that the visit has concluded and the regular SPS time line for follow-up visits resumes.

Optional Clinic Visits at 12, 24 and 30 Months

Participants will complete a series of online questionnaires, as well as have the option of including an in-clinic visit at months 12, 24, and 30 months, primarily for biospecimen collection. QST and Neuroimaging scans are not done at these visits. This set of questionnaires includes:

- Urologic Questionnaires**
 - Symptom and Health Care Utilization Questionnaire (SYM-Q_Follow-up)
 - Global Response Assessment (GRA)
 - Interstitial Cystitis Symptom Index and Problem Index (ICINDEX)
 - RICE Case Definition Questionnaire (RICE)
- Female Participants only:**
 - Female Genitourinary Pain Index (FGUPI)
- Male Participants only:**
 - Male Genitourinary Pain Index (MGUPI)

- Non-Urologic Questionnaires:**
- Complex Medical Symptoms Inventory (CMSI2_Follow-up)
 - Fibromyalgia symptoms module (CMSI2_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)

- Non-Urological Phenotyping CRFs:**
- Medical Outcomes Health Survey (SF-12)
 - International Physical Activity Questionnaire (IPAQ)
 - Work Productivity & Activity Impairment Questionnaire (WPAI)
 - Feelings and Emotions Questionnaire (PANAS)
 - Multiple Ability Self-Report Questionnaire (MASQ)
 - Catastrophizing Sub-scale (CSQ)
 - PTHX

4. BIOLOGICAL SPECIMENS

Biologic specimens collected during the course of the study include urine, blood, saliva, and rectal and vaginal swabs. The schedule of these collections is summarized below.

Please see the Biospecimen collection CRFs and **Appendix B: Biospecimen Collection Manual** for additional details regarding collection, storage, and shipment of the biospecimens.

Table 2: Schedule of Biologic Specimen Collection

Blood Collection	Blood specimen 10mL ACD plasma vacutainers (Plasma and Buffy Coat DNA)	4 weeks, 6, 12, 18, 24, 30, 36 months and ATLAS 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 4 weeks, 6, 18, 36 months and ATLAS visits
Biomarker Urine	Spot urine specimen Biomarker/VB2 (up to 90mL)	4 weeks, 6, 12, 18, 24, 30, 36 months and ATLAS Visits
Saliva	Salivary cortisol samples	2 times a day, waking and bedtime <ul style="list-style-type: none"> • 3 day period after week 4 visit • 7 day period after 6 and 18 Month visits • 7 day period after 36 Month visit IF one or more scheduled collections were missed
Microbiome	Urine (VB1 ~20 mL, VB2 and VB3 ¹ ~30-40mL each)	Female: 0 weeks and 18 months: VB1 and VB2 6, 12, 24, 30, 36 months, and ATLAS visits: VB2 At flare during any clinic visit: VB1 and VB2 Male¹: 0 weeks and 18 months: VB1, VB2, and VB3 6, 12, 24, 30, 36 months, ATLAS: VB2 At flare during any clinic visit: VB1, VB2, and VB3
	Rectal Swabs ²	Female/Male: 0 weeks, 18 months
	Vaginal Swabs ³	Female: 0 weeks, 18 months

¹VB3 Urine collection in males following prostate massage is optional

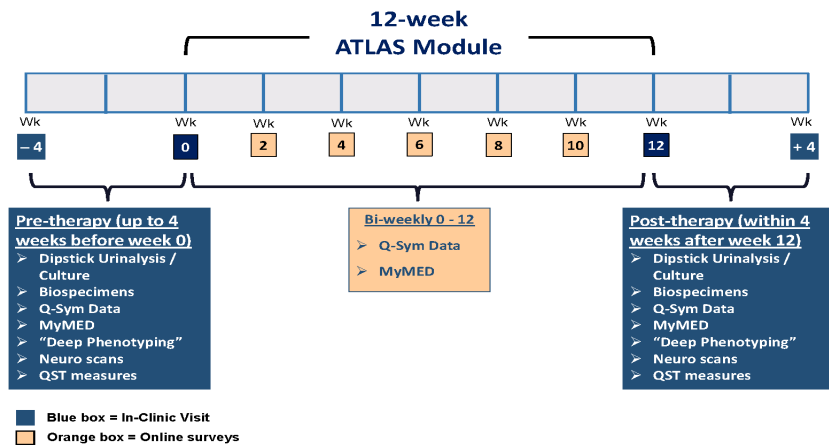
³Collection of vaginal swabs is optional at visits that include physical exam - 12, 24, 30 months visits are optional.

²Collection of rectal swabs is optional at visits that include physical exam

5. ANALYSIS OF THERAPIES DURING THE LONGITUDINAL ASSESSMENT OF SYMPTOMS (ATLAS)

Upon completion of the 6-month in-clinic visit, each MAPP SPS participant will be asked to notify the study coordinators at the time of any planned treatment change to targeted ATLAS therapies (Figure 7). This notification of intent to seek treatment change to add a pre-specified ATLAS treatment of interest will trigger a phenotyping battery of tests, as summarized below, to be conducted within 8 weeks before and up to 8 weeks after a 12-week more intensive bi-weekly internet-based symptom data capture. Taken together, the ‘pre-treatment’ ATLAS phenotyping, biweekly ATLAS symptom assessments, and ‘post-treatment’ ATLAS phenotyping are referred to as an ‘ATLAS module’. If a participant is prescribed an ATLAS targeted therapy for non-UCPPS purposes, prior to enrolling into ATLAS, please contact the DCC for guidance regarding enrollment eligibility.

Figure 6. Timeline for MAPP Phase II Symptom Patterns Study: ATLAS Module



The ATLAS module will be initiated either upon notification from the participant of a prescribed treatment change to add a pre-specified ATLAS treatment or increase a current ATLAS treatment dose; or if the RC identifies ATLAS treatment initiation/change via MyMed report, within the longitudinal follow-up period of the Symptom Patterns Study. This longitudinal follow-up period will begin at any time after the participant completes the in-clinic visit at 6 months, and prior to 30 months of follow-up (with sufficient time remaining in follow-up to carry out the data collection noted in above figure). All medications and all UCPPS therapies (medications, procedures, and nontraditional therapies) will be tracked prospectively on a monthly basis throughout the 36-month SPS. As summarized in Table 6, initiation of specific ATLAS treatments will be preceded by an in-clinic assessment of functional/structural neuroanatomy, collection of blood and urine for biomarker and microbiome assessment, trait and state measures, and urologic symptom profiles using the standard Q-Sym data module. In an effort to reduce participant burden, if ATLAS module occurs within 8 weeks before or after a core MAPP in-clinic visit (for Month 6, only 8 weeks after), the MAPP core visit will count as the ATLAS pre-treatment in-clinic visit.

If a participant is unable to come to the clinic for a pre-treatment ATLAS visit, he/she may still be enrolled in ATLAS and complete the online ATLAS questionnaires. Notify participants as soon as possible after the ATLAS initiation CRF [ATLAS-INIT] is entered in the DMS to complete the online questionnaires within 24 hours. The same procedures apply for a participant who has already begun an ATLAS therapy.

5.A. Eligibility of Time Intervals for ATLAS Modules

The eligible time interval to initiate an ATLAS module during longitudinal follow-up within the SPS was designed to not impact the ongoing usual clinical care for UCPPS symptom management, but to maximize the potentially relevant phenotypic measurements, prior to initiating a treatment change, during the new therapy period, and again at 12 weeks post-therapy change. A maximum of two ATLAS modules may be implemented for each SPS participant, subject to the following criteria:

- 1st ATLAS module may begin only after the Month 6 in-clinic visit is completed. However, if participants begin an ATLAS treatment within 7 days prior to the Month 6 visit, the Month 6 SPS visit may serve as the ATLAS pre-treatment phenotyping visit.
- If a participant begins a new ATLAS treatment, the site will have up to 7 days after initiation of that new treatment to initiate an ATLAS module.
- Any ATLAS module may not begin later than month 30, and must be completed by month 35
- No minimum time period between 1st and 2nd ATLAS module, but if the start of the 2nd module is within 2 months of the end of the 1st module, then the post-therapy measurements from the 1st module are permitted to serve as pre-therapy measurements for the 2nd module
- 36-month final in-clinic visit must occur regardless of timing of last ATLAS module
- If an ATLAS module overlaps with scheduled SPS data collection (e.g., on-line quarterly symptom assessments, scheduled deep phenotyping visits), ATLAS data collection will supersede SPS data collection.
- On-line quarterly data collection increases to bi-weekly frequency during the 12-week ATLAS therapy period
- Entire time-span for ATLAS therapy module includes 4-week window pre-therapy change and 4-week post-therapy for data collection from participants, procedures and testing

5.B. Pre-specified ATLAS Therapies

The rationale for this study is that through exposure of UCPPS patients to therapeutic interventions with accompanying phenotyping, a relationship between response (or lack of response) to a given therapy and specific phenotypic profiles may be established. If successful, this would identify subgroups of UCPPS patients with characteristic phenotypes (i.e., disease marker profiles, degree and patterns of symptoms, influence of symptom flares, presence of co-morbid syndromes, neurological structure/function, etc.) that preferentially respond to specific treatments. This could eventually lead to “personalized analgesia”, by allowing us to subsequently design future clinical trials that would specifically test UCPPS therapies in just the UCPPS “endophenotype” that we expect to respond to a treatment with a certain mechanism.

Network investigators identified 6 treatments in men and 5 treatments in women that will be the focus of ATLAS study investigations. These choices were based on the treatment patterns observed in MAPP Phase I as well as the desire to examine treatments which may improve symptoms through ‘centrally-

acting’ and ‘peripherally-acting’ mechanisms, recognizing that this categorization scheme dichotomizes the presumed mechanisms of these interventions based on our interpretation of available information. Feasibility concerns were also taken into account. For instance, NSAIDs were commonly taken by MAPP Phase I study participants; however, investigators felt that this likely represented patient self-medication for a wide range of medical conditions rather than for UCPPS. Similarly, bladder instillations were a commonly reported therapy, but these are frequently used as ‘rescue’ therapy for flares at the time of clinic visits, which would not permit sufficient time to conduct pre-therapy ATLAS assessments. The treatments that will initiate more in-depth assessment (Figure 7) are:

- 1) **Oral opioids.** This will be categorized as a centrally-acting therapy, and will be examined in both men and women. While these agents may be utilized intermittently by patients, MAPP network investigators feel that the more common practice pattern at MAPP sites is to provide prescriptions to be used on a regular (e.g. daily) basis as opposed to very intermittent use.
- 2) **Tricyclic antidepressants.** This will be categorized as a centrally-acting therapy, and will be examined in both men and women.
- 3) **Pelvic floor physical therapy.** This will be categorized as a peripherally-acting therapy, and will be examined in both men and women. Please note:
 - Physical therapy Pelvic Focused - Includes therapies (behavioral and manual) dedicated to relaxation of the pelvic floor musculature. Although external work is performed (myofascial release, tissue rolling, stretching), *much of the therapy is conducted transvaginally and/or transrectally.* Biofeedback devices may be used. Patients are often taught stretching techniques and methods to perform their own myofascial release, often through the use of varied dilators.
 - Generalized: As employed in patients with pelvic pain, this form of care centers upon external work, i.e., tissue rolling, external myofascial release, and stretching. *No management to the pelvic floor musculature is performed through a transvaginal or transrectal approach.*
 - Self Therapy: Pelvic Floor Rehab Techniques, often taught by physical therapists or experienced medical personnel, that often include tissue rolling, stretching, exercises, biofeedback, and the use of internal and external myofascial release.
- 4) **Alpha-adrenergic blockers.** This will be categorized as a peripherally-acting therapy, and will be examined in men only.
- 5) **Oral pentosan polysulfate (PPS).** This will be categorized as a peripherally-acting therapy, and will be examined in both men and women
- 6) **Neuropathic pain medications.** This will be categorized as a centrally-acting therapy, and will be examined in both men and women.
- 7) **Cystoscopy with Hydrodistention.** This will be categorized as a peripherally-acting therapy, and will be examined in ATLAS studies in both men and women.

Figure 7. Examples of Common Targeted Therapies for ATLAS Monitoring

Example Targeted ATLAS Therapies by Treatment Type Updated

*PLEASE NOTE: For these examples each number matches the corresponding brand name and generic name for medications.
An extended list of Brand & Generic Names will be provided to Participants for reference in case of ATLAS med. additions.

Targeted ATLAS Therapies						
All Participants	All Participants	All Participants	All Participants	All Participants	All Participants	Males only
Oral opioids (Medication)	Tricyclic antidepressants (Medication)	Pelvic floor physical therapy (Non-Medication)	Elmiron / Oral pentosan polysulfate (Medication)	Neuropathic pain Treatments (Medication)	Cystoscopy with Hydrodistention	Alpha-adrenergic blockers (Medication)
Common Brand Names	Common Brand Names	Common Names	Brand Name	Common Brand Names	Common Names	Common Brand Names
1.Endocet 2.Lortab 3.Oxycontin 4.Percocet 5.Percodan 6.Vicodin 7.Tylenol w/ Codeine	1.Elavil 2.Tofranil 3.Trezyfagit 4.Sensoval	1.Pelvic Physical Therapy 2.Pelvic Floor Physical Therapy 3.Pelvic Floor Dysfunction Therapy 4.Pelvic Floor Myofascial Release	1.Elmiron	1.Lyrica 2.Neurontin	1. Cystoscopy with Hydrodistention	1.Flomax 2.Hytrin 3.Cardura 4.Rapaflo
Common Generic Names	Common Generic Names	Common Names	Generic Names	Common Generic Names	Common Names	Common Generic Names
1.Acetaminophen& Oxycodone 2.Acetaminophen& Hydrocodone 3.Oxycodone 4.Acetaminophen& Oxycodone 5.Aspirin& Oxycodone 6.Acetaminophen& Hydrocodone 7.Acetaminophen& Codeine	1.Amitriptyline 2.Imipramine 3.Desipramine 4.Nortriptyline	5.Pelvic Floor Rehabilitation	1.Pentosan Pentosan Polysulfate Pentosan Polysulfate Sodium	1.Pregabalin 2.Gabapentin		1.Tamsulosin hydrochloride 2.Terazosin 3.Doxazosin 4.Silodosin

5.C.

Notification Procedures for ATLAS Modules

Upon completion of the 6-month in-clinic visit, each MAPP participant will be requested to notify the MAPP research coordinators immediately when they intend to change their UCPPS treatment regimen, including prescription medications, nonprescription agents, procedures, therapies, and ‘nontraditional’ treatments. This notification will be done either via telephone to a dedicated MAPP telephone number, or via an on-line notification form. Any change, including starting a new UCPPS therapy, increasing dosage of an existing ATLAS medication, or stopping an existing UCPPS therapy will be recorded. Participants will be educated and reminded about the therapies that are of specific interest to MAPP for ATLAS modules.

When a new ATLAS therapy is identified, participants will have the option to participate by completing the bi-weekly online ATLAS questionnaires only or in addition to the online questionnaires, undergo a battery of ‘pre-treatment’ and ‘post-treatment’ phenotyping tests, conducted in person at the clinic. It is ideal that this testing be conducted before the new ATLAS treatment is initiated. A 8-week window will be allowed to complete the ‘pre-treatment’ ATLAS studies prior to starting the ATLAS therapy.

However, if the RC identifies an ATLAS treatment initiation/change via MyMed report; or the participant notifies RC they’ve already begun a new ATLAS treatment; if it’s within 7 days from the start of the medication initiation or change, do the following:

- ask participant to come in for an ATLAS DP visit if it can be scheduled within 4 weeks [Note: SPS visit scheduling takes priority]; enter ATLAS-INIT in the DMS as soon as possible and ask participant to complete the questionnaires within 24 hours. Questionnaires will not be repeated at the ATLAS DP visit.
- if participant declines, ask participant to complete baseline ATLAS online questionnaires within 24 hours and continue module for 12 weeks

If an ATLAS DP visit can be scheduled, but a scanner is not available, proceed with the DP visit without the scans. This only applies to ATLAS DP visits.

During the ATLAS therapy, biweekly on-line symptom assessments will be completed by participants for 12 weeks. After 12 weeks of ATLAS therapy, an additional set of ‘post-treatment’ phenotyping tests will be conducted. A 4-week window will be allowed to complete the ‘post-treatment’ phenotyping after the 12 weeks of ATLAS therapy. Schedule this visit whether or not the participant had a “pre-treatment” ATLAS deep phenotyping visit.

The pre-treatment and post-treatment ATLAS visits include the following:

- All deep phenotyping CRFs and participant questionnaires
- Complete QST battery
- Neuroimaging (if participant agree to participate in the neuroimaging protocol)
- Biomarker specimen collection

During the pre and post ATLAS clinic visits, the Research Coordinator will enter the participant’s ID and PIN to initiate the participant online 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.

Biweekly on-line assessments during ATLAS therapy will include MyMed and the quarterly symptoms questionnaires:

- | | |
|-------------------|-----------------|
| • SYM-Q_Follow-up | • GUPI |
| • GRA | • ICSI and ICPI |
| • RICE_Follow-up | • WHO_DAS |
| • CMSI2_Follow-up | • HADS |
| • CMSI2_FM2 | • FATIGUE |
| • BPI2 | • SLEEP |
| • PAIN | • PSS |

Once the post treatment ATLAS phenotyping visit is complete, participants will resume the SPS online/clinic schedule.

5.D. ATLAS Data Collection

The intent is that all MAPP participants who begin an ATLAS therapy will complete the entire ATLAS module. However, the MAPP investigators acknowledge that this is probably not realistic. For instance, some MAPP participants may be unable to complete the entire 12 weeks of therapy due to side effects, lack of efficacy or other reasons. However, it is expected that a post treatment ATLAS visit will be completed for all ATLAS initiated modules, even if the treatment was terminated prior to the end of the 12 week ATLAS module. For participants undergoing *Cystoscopy with Hydrodistention*, the entire 12 week ATLAS module should be administered and the Post ATLAS visit offered at the end of the 12 weeks.

5.E. ATLAS Tracking of Concomitant Medications and Treatments

At all in-person SPS protocol visits (baseline, 6 months, 18 months, 36 months, pre-treatment and post-treatment ATLAS visits) a comprehensive assessment of current UCPPS therapies (medication and non-medication, prescription and nonprescription) will be performed using standardized CRFs. Other medications (for non-UCPPS indications) will also be tabulated at these times. Throughout the 36 months of the SPS, participants will be requested to submit an update to these medications and therapies on a monthly basis via MyMed. Research Coordinators will regularly monitor the CMED2 data for ATLAS type medication changes of interest as well as contact participants on a monthly basis to remind them to complete the MyMed module. This will serve as a reminder for participants to report new UCPPS therapies (especially ATLAS therapies) and will also collect ongoing data about concomitant non-UCPPS medication use which could potentially confound data interpretation for ATLAS studies. This monthly data collection for medications and treatments will occur throughout the study, irrespective of ATLAS data collection efforts.

5.F. Coordination of ATLAS Activities with Scheduled SPS Data Collection

From baseline to 6 months, no ATLAS events will be conducted in order to provide a period of uninterrupted data collection for the SPS and to allow researchers and participants to become acclimated to the study procedures (including the deep phenotyping visits at baseline and month 6). The maximum number of deep phenotyping assessments that any MAPP participant would experience is 8. Each participant may complete no more than two ATLAS modules during the 36-month SPS study period. This limit was put in place to reduce complexity and individual study participant burden.

The first ATLAS module may begin only after the 6 month in-clinic visit is completed. However, if a participant begins an ATLAS treatment within 7 days prior to the Month 6 visit, the Month 6 SPS visit may serve as the ATLAS pre-treatment phenotyping visit.

Following completion of the Month 6 visit, to avoid participant burden, if a participant reports an ATLAS treatment change up to 8 weeks post completion of their 6 month visit, the 6 month visit may serve as the ATLAS pre-treatment phenotyping visit.

In addition, after the Month 6 Clinic Visit there will be an 8 week 'window' after each scheduled SPS deep phenotyping visit that may serve as the ATLAS "pre-treatment" visit. This 'window' means that for any ATLAS therapy that occurs within 8 weeks of a regularly scheduled SPS deep phenotyping visit, the data from the

deep phenotyping visit will be used as the 'pre-treatment' ATLAS phenotyping battery. If at the time of the 12 week visit, the participant is due for a SPS deep phenotyping visit, the ATLAS visit will count as the SPS visit.

If a participant begins a new ATLAS treatment, the site will have up to 7 days after initiation or start of that new treatment to initiate an ATLAS module.

6. 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 be notified by the DCC to 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 easy link to participants's own data collection page. A follow up email 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

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

7.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 baseline visit, forms collecting eligibility criteria and symptom questionnaires should be completed prior to the administration of physical exams or other study procedures.

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 to ensure that you are using the correct form versions.

7.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 of ALL PAGES of 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.

Commented [NR5]: Ted Please update according to Amend #6 and any other changes not incorporated. Thanks .

Commented [TB6]: CRF section updated with Amendment #6 and other applicable changes.

- 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 should always verify the forms in a packet against the corresponding Visit Checklist and the Visit Schedule (**SCHEDULE**) 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 when they each record data. 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.

7.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, the RC ID will be recorded 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.

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

Each Principal Investigator (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.

7.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.

7.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.

7.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 Clinical Center. It is a six-digit number that is unique to the Clinical Center 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 01-40 for SPS Visits, 61-67 for ATLAS Module 1 Visits, and 71-77

for ATLAS Module 2 Visits. ***Please Note:** The Data Management System also has “Visit 0” which is exclusively as a unique data collection module for collection of **Concomitant Medications** across **ALL VISITS**.

CRF Date: This is the date of the case report form is completed, in most cases, the date of the visit/contact.

RC and PI ID: Each Research Coordinator and Principal Investigator 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.

7.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
CRFs completed by Research Coordinator:	
Pre-screening – Epidemiology and Phenotyping Study Pt.s	PRESCR2
Screening/Eligibility forms:	
Demographics	DEMO
Symptom, Health Care Utilization & Flare Questionnaire - Screening	SYM-Q_Screening
Rice Case Definition Questionnaire- Screening	RICE_Screening
Eligibility – Epidemiology and Phenotyping Study Pt.s	ELIG2
Eligibility – Control Participants	ELIG_Scan2
Urine Culture Result	UCR
Enrollment	ENROLL
Medical History, Treatment, and Physical Exam:	
Medical History	MEDHX2
Family Medical History	FAMHX
Concomitant Medications	CMED2
Antibiotics Treatment History	ABHX
Pelvic Therapy History	PTHX
Cystoscopy History	CYSTO2
Physical Exam	EXAM2
Pelvic Exam (Female & Male)	PEX_Female/PEX_Male
Brief Clinical Diagnostics for Baseline & Follow-up	CDX
Co-morbid Diagnostic Modules completed per answers given on Complex Medical Symptom Inventory:	
Fibromyalgia – Tender Point Exam	CMSI2-FM2-TP
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)	UUMBTRAC
Microbiome Urine Specimen Tracking (Female/Male)	UFMBTRAC UMMBTRAC
Rectal Swab Specimen Tracking	RSTRAC2
Vaginal Swab Specimen Tracking	VSTRAC2
Home Saliva Collection, 3 day	S3TRAC2

Case Report Forms – Data Entry Forms	
Form Name	Form Code
Neuroimaging CRFs	
Neuroimaging Day of Scan MRI Screening Procedures (Administrative)	NEURO-MR_SCREEN
Neuroimaging Day of Scan Data & Procedures Status Confirmation	NEURO_SCAN2
Neuroimaging Data Collection CRF	NEURO_CRF
Quantitative Sensory Testing Procedures	
Quantitative Sensory Testing Screening	QST Screen
Quantitative Sensory Testing CRF	QST
ATLAS Module CRFs	
ATLAS Module Initiation	ATLAS-INIT
ATLAS Module Stop	ATLAS-STOP
PRN forms (filled out as-needed):	
Study Stop	SSTOP
Consent Withdrawal	CONWITHDR
Consent Change	CONSENT_CHG
Reinstatement of Consent	RECON
Procedural or Unanticipated Problems	PUP
Ad-Hoc Deep Phenotyping Visit Initiation	DP-INIT
Ad-Hoc Deep Phenotyping Visit Stop	DP-STOP

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 & Flare Questionnaires for Run-In, Baseline, Follow-up, and ATLAS Contacts	SYM-Q Run-In SYM-Q Baseline SYM-Q Follow-Up SYM-Q ATLAS
Global Response Assessment	GRA; GRA_ATLAS
Interstitial Cystitis Symptom Index Interstitial Cystitis Problem Index	ICINDEX ICINDEX Run-In ICINDEX ATLAS
AUA Symptom Index	AUASI
RICE Case Definition Questionnaire	RICE Run-In RICE Follow-up RICE ATLAS
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	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_Run-In CMSI2_Baseline CMSI2_Follow-Up CMSI2_ATLAS
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

Case Report Forms – Data Entry Forms	
Form Name	Form Name
PAIN Detect	PAIN PAIN Run-In PAIN ATLAS
McGill Pain Questionnaire	MPQ
Gracely Box Scales	GBS
WHO Disability Assessment Schedule	WHO-DAS; WHO-DAS_R.A.
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 PSS_Run-In PSS_ATLAS
Ten-Item Personality Inventory	TIPI
Thoughts About Symptoms	CSQ
Childhood/Recent Traumatic Events Scale	CTES RTES

7.D. CRFs completed by Research Coordinator:

[PRESCR2] PRE-SCREENING

- Purpose:** To collect information regarding the prescreening process for participants to be recruited:
- This data will be used to generate monthly accrual reports. In particular, the total reported for Question #2 must be a sum of the values recorded for Question #s 3, 4, 5, and 6 for reporting purposes. Please refer to the instructions on the forms regarding how to be sure the totals for Question #s 3, 4, 5, and 6 reflect the total reported in Question #2 each month. Special consideration must be taken for participants whose decision to participate is pending from one month to the next. Please see the instructions in the margin next to Question #s 3, 4, 5, and 6 on the forms about how to account for participants whose decision is “pending”.
- Who:** Research Coordinator completes
- When:** Once a month (This form should be entered in the DMS no later than the 5th of every month for reporting purposes.)

7.E. 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:** Screening Week 0

General Directions

- Question #7 Record annual family income in US dollars.
- Question #11 A partner can be someone of the same sex.

[SYM-Q SCREENING] SYMPTOM, HEALTHCARE UTILIZATION, & FLARE STATUS QUESTIONNAIRE

- Purpose:** To collect eligibility information at Visit #1 (Q.#1) and 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. This form also collects information about current flares and flares in the past 3 months. This form also asks if the Participant uses a flare management plan.
- Who:** Participant completes **SYM-Q_Screening** and RC enters in the DMS at the Screening Week 0 visit.
- When:** Screening Week 0

[RICE_SCREENING] RICE CASE DEFINITION QUESTIONNAIRE, SCREENING

- Purpose:** To collect eligibility information at Visit #1 (Q.#1) and 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:** Research Coordinator
- When:** Screening Week 0

[ELIG2] ELIGIBILITY CONFIRMATION – FOR SYMPTOMS PATTERNS STUDY PARTICIPANTS

- Purpose:** To determine and ensure the participant’s eligibility for entry into the SPS.
- Who:** Research Coordinator
- When:** Screening Week 0 Visit

General Directions:

Note: Participants must consent to provide DNA specimens (blood and cheek swab) as detailed on the Eligibility form in order to be eligible for the study. Participants must also consent to provide biomarker specimens for biomarker studies in order to be eligible. Participants must also agree to participate in ALL Symptoms Patterns Study procedures and Quantitative Sensory Testing. Please note: consent to participate in the neuroimaging protocol is no longer an eligibility requirement for SPS study participation; however, it is still an eligibility requirement for Control Study participants.

Deferral criteria require that a urine specimen be collected for dipstick, urinalysis, and (for female Participants) pregnancy test. Results of the urine culture must be documented on the Urine Culture Result – Deferral Criterion for Eligibility Confirmation **[UCR]** form.

Transgender individuals are not excluded. However, record their biological sex and self-identified gender on the **COMMENTS** CRF.

Data entry instructions:

Inclusion Criteria Q6-8: MAPPI EP participants can answer “No” to these questions and still be eligible to participate. All Exclusion Criteria Q11-18 must be “No” for both MAPPI EP participants and new individuals to be eligible.

Q10: This question must be answered and initialed if Q9 is “No prior clinical diagnosis of IC/BPS or CP/PPS available.”

For ALL Symptoms Patterns Study Participants, the **ELIG2** form must be the first form entered in the DMS. If a Participant must be *deferred* please enter ONLY the ELIG2 form and no other baseline visit CRFs. If a Participant is found to be *ineligible* also please enter ONLY the ELIG2 form and no other baseline visit CRFs.

[ELIG_SCAN] ELIGIBILITY CONFIRMATION, NEUROIMAGING STUDY*

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

Who: Research Coordinator

When: Screening Week 0

[CONT_SCAN] NEUROIMAGING SCREENING AND ENROLLMENT CONFIRMATION FOR CONTROL PARTICIPANTS

Purpose: To determine and ensure the Control participant’s eligibility for entry into the Neuroimaging procedures of the study. Control Participants must have no pelvic pain, pressure, or discomfort. All Inclusion Criteria responses must be “Yes” to be eligible for enrollment.

Who: Research Coordinator

When: Screening Week 0 Visit

General Directions:

Once Control Participants have been confirmed for participation in Neuroimaging Procedures, they will complete only the Neuroimaging scan and procedures. The only data recorded for Control Participants will be via the NEURO_SCAN and NEURO_CRF. No other questionnaires or CRFs will be completed for Controls.

[UCR] URINE CULTURE RESULT – DEFERRAL CRITERION FOR ELIGIBILITY CONFIRMATION

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 must be treated and deferred.

Who: Research Coordinator

When: Screening Week 0 Visit

[ENROLL] 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. Please note, Q.#2 includes an answer option to confirm if a participant has been deferred.

Who: Research Coordinator

When: Screening Week 0 Visit

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.

7.F. Medical History, Treatment, and Physical Exam:

[MEDHX2] MEDICAL HISTORY

- Purpose:** To obtain information about the participant’s history of Interstitial Cystitis (IC)/Painful Bladder Syndrome (PBS) and/or Chronic Pelvic Pain Syndrome (CPPS)/Chronic Prostatitis (CP) as well as general medical history.
- Who:** Research Coordinator completes CRF with information obtained from participant interview
- When:** Screening Week 0 Visit

General Directions

- Q #1: This refers to when the participant’s symptoms **first appeared**. This scenario is not necessarily the same as when the participant’s symptoms were **first diagnosed** by a physician.
- Q. #s 1a, 2a, and 3a: If the participant does not recall the exact age, ask the participant to make a best guess.

Responses on MEDHX will be verified with participant’s medical records at the Clinical Center or another treatment facility.

Please also note that if a participant has been diagnosed with any of the conditions/disorders in questions 9 - 17 and/or has had any of the procedures listed in questions 18 - 20, by answering “1-Yes” to any of those questions all checkboxes for the corresponding sub-sets of conditions/disorders/procedures specified must be answered “1-Yes, 0-No, or 88-Unknown”. Please do not leave any sub-sets of checkboxes blank if any of the answers for questions 9 – 17 and/or 18 - 20 are “1-Yes”.

[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:** Screening Week 0

General Directions

Please be sure 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”, please be sure the Participant completes, to the best of his or her ability, the table on page 2 of the FAMHX form.

[CMED2] CONCOMITANT MEDICATIONS AND [MYMED] TREATMENT TRACKING MODULE

CMED2

- 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.
- To monitor the use of medications which are for urologic or pelvic pain symptoms.

To track medication changes in conjunction with the monthly MyMED treatment tracking feature of the Participant Survey which may initiate an ATLAS treatment tracking module.

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 Screening Week 0, Baseline Week 4, ALL Follow-up Clinic Visits and PRN Monthly if medication changes are reported by the Participant via the MyMED monthly treatment tracking procedures.

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.

If participant is using CBD, use the category “herbal medications – other.”

If participant is taking 1 medication in 2 different ways (for example, orally and an instillation), only add to CMED2 one time (as 1 record).

Additional CMED2 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, 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.

***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** tool in the Data Management System application.
- Drug Name:** This is the generic name for the medication/treatment, generated from the **Medication Reference** tool.
- Medication Start Date:** The date the participant began taking the medication in the current time period.
- Medication Stopped?:** This checkbox confirms the continuation or discontinuation of medications. If “Medication Stopped?” is checked “O-No” the medication will be included in the MyMED monthly medication tracking module for the Participant to confirm as continuing or discontinued. If a Participant confirms a medication is discontinued via MyMED a report will confirm the medication is stopped and the RC will record that the medication has been stopped on the CMED2 form. **For Urologic or Pelvic Pain Symptoms:** Confirm with the Participant if each medication was taken due to any urologic or pelvic pain symptoms. These symptoms may be associated with any of the conditions (IC/PBS or CP/CPPS) related to this study. Please clarify in the space provided in the comments section at the bottom of the CMED2 form any reason a medication is taken for urologic or pelvic pain symptoms which are not related to the

conditions associated with this study (for example, if a medication is being taken to treat symptoms associated with a kidney stone).

ATLAS Medication: Check “Yes” if the medication is an ATLAS targeted medications. Record this answer even if participant is taking this medication prior to the Month 6 visit (e.g. at screening).

MyMED – Please note, medications recorded as stopped or newly started on the MyMED module Participant Survey form are also updated/entered as needed on the Concomitant Medications [CMED2] form

Purpose: To collect information from the Participant via the Participant Survey in order to record all stopped or newly started concomitant medications/treatments for urologic or pelvic pain symptoms currently taken by the participant, while in the study.

Please note, medications which the participant records as stopped or newly started must be updated/added as needed to the Concomitant Medications [CMED2] form along with the date the medications were stopped or started.

A report in the DMS Tools section of the study website will summarize stopped and newly started medications per participant.

As of the month-6 visit and through the month-30 visit, new medications/treatments taken for urologic or pelvic pain symptoms will be monitored by the RC via the report summarizing these medications/treatments per-participant. If any medications/treatments qualify as ATLAS treatments, the participant will be invited to participate in up to two 12-week ATLAS treatment monitoring modules.

Who: Participant completes via online survey, Research Coordinator updates the CMED2 form with stopped and newly started medications as needed.

When: All Visits

[ABHX] ANTIBIOTICS TREATMENT HISTORY

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

Who: Research Coordinator

When: Screening Week 0, Months 6, 18, and 36 Clinic Visits. Also at optional Month 12, 24, and 30 Clinic Visits

[PTHX] PELVIC THERAPY HISTORY

Purpose: To record non-medication pelvic therapies received and/or utilized by the Participant. Of particular interest will be pelvic physical therapy since it is a targeted ATLAS treatment.

Who: Research Coordinator and Participant Completed

When: RC completes at Screening Week 0, Baseline Week 4, Months 6, 18, and 36 Clinic Visits. Also at optional Month 12, 24, and 30 Clinic Visits.

The Participant completes monthly via the MyMED treatment tracking module in the Participant Survey.

[CYSTO2] CYSTOSCOPY HISTORY

- Purpose:** To record whether or not participant has had a cystoscopy. If available, images from the cystoscopy should be provided in digital format to the DCC.
- Who:** Research Coordinator
- When:** Entered at Screening Visit only for documentation of available cystoscopy and Hunners lesion history data. Data collection can be completed at any time during follow-up but the CRF is entered only at the Screening visit, Visit #1.

Review available electronic medical records back to 2000, if available. Do not request medical records outside of your site health system or review paper medical records. If the participant has had more than 1 cysto in the past (or past 18 months at Month 18 and 36), report the most recent cystoscopy finding.

[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 reviews this form for completeness.
- When:** Screening Visit

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.

Question #11 (Males only): Collection of the VB3 specimen is encouraged of all male Participants, but, as with any study procedures, this procedure may be skipped at the Participant’s request. Record an answer of “0-No” if a male Participant declines to give a VB3 specimen.

[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:** Screening Week 0 and Month 18 Clinic Visit

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 Pelvic Exam Procedures forms for further instructions.

[CDX] CLINICAL DIAGNOSTICS FOR BASELINE AND FOLLOW-UP

- Purpose:** To capture clinical diagnostic details during Follow-up including height, weight, umbilical circumference, blood pressure, urine culture results, symptom flare, and confirmation that female Participants are not currently pregnant.
- Who:** Research Coordinator
- When:** Baseline Week 4 and **ALL** In-Clinic Follow-up visits including Optional Clinic Visits.

General Directions

Please note that if a female participant confirms she is pregnant during follow-up she must be withdrawn from the study.

7.G. 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:** Baseline Week 4 and Months 6, 18, and 36 Clinic Visits

[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:** Baseline Week 4 and Months 6, 18, and 36 Clinic Visits

[CMSI2_VDYN2] COMPLEX MEDICAL SYMPTOMS INVENTORY - VULVODYNIA

- Purpose:** To capture data about the Participant’s symptoms related to Vulvodynia, if reported per the CMSI Questionnaire
- Who:** Research Coordinator
- When:** Baseline Week 4 and Months 6, 18, and 36 Clinic Visits

[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:** Baseline Week 4 and Months 6, 18, and 36 Clinic Visits

[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: Baseline Week 4 and Months 6, 18, and 36 Clinic Visits

[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: Baseline Week 4 and Months 6, 18, and 36 Clinic Visits

7.H. Specimen Tracking CRFs:

[PTRAC] 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: Baseline Week 4 and Months 6, 18, & 36 Clinic Visits as well as Months 12, 24, & 30 Optional Clinic Visits.

[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: Baseline Week 4 and Months 6, 18, & 36 Clinic Visits

[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: Baseline Week 4 and Months 6, 18, & 36 Clinic Visits as well as Months 12, 24, & 30 Optional Clinic Visits.

[UUMBTRAC] MICROBIOME UNIVERSAL URINE SPECIMEN TRACKING (VB2)

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. 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 Months 6, 18, and/or 36 Clinic Visits if supply of these kits runs low.

Who: Research Coordinator

When: Screening Week 0 and Months 6, 18, & 36 Clinic Visits as well as Months 12, 24, & 30 Clinic Visits

[UFMBTRAC, UMMBTRAC] 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. 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 Months 6, 18, and/or 36 Clinic Visits if supply of these kits runs low.
- Who:** Research Coordinator
- When:** Screening Week 0 and Months 6, 18, & 36 Clinic Visits as well as Months 12, 24, & 30 Clinic Visits

[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 and Month 18 Clinic Visit

[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 and Month 18 Clinic Visit

[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 at Screening Week 0 when distributed to the Participant. Participant completes shipping procedures from home.
- When:** Following Baseline Week 4

[S7TRAC2] HOME SALIVA COLLECTION, 7 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 at Month 6 when distributed to the Participant. Participant completes shipping procedures from home.
- When:** Following Month 6, 18 and 36 visits. Only completed for Month 36 if Months 6 and/or 18 collections were missed.

[MR_SCREEN] NEUROIMAGING DAY OF SCAN MRI SCREENING PROCEDURES (ADMINISTRATIVE)

- Purpose:** This CRF is completed as a follow-up check to the ELIG_SCAN form in order to confirm that a Participant is a suitable candidate for the MAPP SPS Neuroimaging procedures, and to provide the Participant with some guidelines about what to expect during the day of the Neuroimaging study MRI scan.
- Who:** Research Coordinator
- When:** Baseline Week 4 and as a follow-up review of MRI procedures at Months 6, 18, & 36 Clinic Visits as well for ATLAS modules at ATLAS Weeks 0 & 12.
- *Note:** *This CRF is completed ONLY if participant is participating in Trans-MAPP Neuroimaging Study.*

[NEURO_SCAN2] 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:** Baseline Week 4 and Months 6, 18, & 36 Clinic Visits as well as for ATLAS modules at ATLAS Weeks 0 & 12.
- 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:** Baseline Week 4 and Months 6, 18, & 36 Clinic Visits as well as for ATLAS modules at ATLAS Weeks 0 & 12.
- Use **Q47** to record deviations or comments about the scans.

[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:** Screening Week 0

[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:** Baseline Week 4 and Months 6, 18, & 36 Clinic Visits as well as for ATLAS modules at ATLAS Weeks 0 & 12.

[ATLAS-INIT] ATLAS MODULE INITIATION

- Purpose:** To record the initiation date of an ATLAS treatment tracking module and details regarding the targeted ATLAS treatment to be monitored for the subsequent 12 weeks.
- Who:** Research Coordinator
- When:** ATLAS Week 0
- Note:** If a participant is prescribed an ATLAS targeted therapy for non-UCPPS purposes, prior to enrolling into ATLAS, please contact the DCC for guidance regarding enrollment eligibility.
- Q2:** This question is to record the timeframe in which an ATLAS visit occurred. Months 6 and 18 visits may be used as ATLAS baseline visits. Months 12, 24, and 30 may not be used as ATLAS baseline visits. If an ATLAS baseline visit did not occur within a core visit timeframe, mark "ATLAS Baseline visit" only. The same applies to Q10 for the final ATLAS clinic visit timeframe.

[ATLAS-STOP] ATLAS MODULE STOP

- Purpose:** To record the stop date of an ATLAS treatment tracking module and details regarding the targeted ATLAS treatment followed during the ATLAS module.
- Who:** Research Coordinator
- When:** ATLAS Week 12

7.1. PRN CRFs

[SSTOP] STUDY STOP POINT

- Purpose:** To record the date the participant completed the trial or the date and the primary reason for a participant's termination from the follow-up phase of the study.
- Who:** Research Coordinator and Principal Investigator
- When:** 36-month visit, or at time of early study withdrawal.

General Directions

The Study Stop Point [sstop] form is completed at the time of withdrawal, if a participant opts to withdraw from the study early. Otherwise, the form is completed at the end of the 36-Month Visit (Visit #40), the last study contact. 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.

[CONWITHDR] 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.

[CONSENT_CHG] CONSENT CHANGE

Purpose: To document the change of consent for a Participant’s biospecimen(s) and or data/information to be used for the purposes of this study and/or other studies. Changes in consent for participation in study procedures are also documented on this form for such procedures as QST, the MAPP smart phone app, and contact for future studies.

Who: Research Coordinator

When: Visit at which the Participant informs the study staff of the wish to change consent for any biospecimen(s), data, or procedures.

General Directions:

If a Participant wishes to change 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.

[RECON] 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.

[PUP2] 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:** RC 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. Record UTIs on this form.**

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:** 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** Principal Investigator (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.

[DP-INIT] AD-HOC DEEP PHENOTYPING VISIT INITIATION

Purpose: To record details for an ad-hoc Deep Phenotyping clinic visit if a regularly scheduled Deep Phenotyping clinic visit was missed

Who: Research Coordinator

When: At the start of an ad hoc clinic visit

General Directions

The date of the ad-hoc Deep Phenotyping clinic visit as recorded in the CRF Date on this form serves as the initiation date for Participant Survey data collection at this ad-hoc Deep Phenotyping clinic visit.

[DP-STOP] AD-HOC DEEP PHENOTYPING VISIT STOP

Purpose: To record details for an ad-hoc Deep Phenotyping clinic visit if a regularly scheduled Deep Phenotyping clinic visit was missed

Who: Research Coordinator

When: At the completion of an ad hoc clinic visit

General Directions

The CRF Date on this form serves as the stop date for the ad-hoc Deep Phenotyping clinic visit.

Once this CRF is saved in the DMS, the original MAPPII SPS visit schedule will apply for all subsequent visits from this CRF Date.

7.J. CRFs completed by Participant via online survey:

[SYM-Q] SYMPTOM ASSESSMENT QUESTIONNAIRE (FOR RUN-IN, BASELINE, FOLLOW-UP, AND ATLAS CONTACTS)

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. This form also collects information about current flares and triggers the FLARE Questionnaire, when applicable.

Who: Participant
When: Run-In, Baseline Week 4, and ALL Follow-up and ATLAS Contacts

[GRA] GLOBAL RESPONSE ASSESSMENT

Purpose: To record current symptom status and change in symptoms over the course of the study.
Who: Participant
When: Run-In, Baseline Week 4, and ALL Follow-up and ATLAS Contacts

[ICINDEX] IC SYMPTOM & PROBLEM INDEX

Purpose: To collect information on the participant's assessment of IC/PBD symptoms and problems related to these symptoms.
Who: Participant
When: All Visits

[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: Baseline Week 4 and 6, 18, & 36 Month Deep Phenotyping Clinic Contacts as well at ATLAS Weeks 0 & 12 Contacts.

[RICE] 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: All Visits

[BSI] RICE BLADDER SYMPTOM IMPACT

Purpose: To capture how the severity of symptoms impact quality of life.
Who: Participant
When: Baseline Week 4 and 6, 18, & 36 Month Deep Phenotyping Clinic Contacts as well at ATLAS Weeks 0 & 12 Contacts.

[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: Screening Week 0

7.K. 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: All Visits

[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: Baseline Week 4 and 6, 18, & 36 Month Deep Phenotyping Clinic Contacts as well at ATLAS Weeks 0 & 12 Contacts.

[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: Baseline Week 4 and 6, 18, & 36 Month Deep Phenotyping Clinic Contacts as well at ATLAS Weeks 0 & 12 Contacts.

7.L. 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: All Visits

[IIEF] INTERNATIONAL INDEX OF ERECTILE FUNCTION

Purpose: To capture data about male sexual function.

Who: Male Participant

When: Baseline Week 4 and 6, 18, & 36 Month Deep Phenotyping Clinic Contacts as well at ATLAS Weeks 0 & 12 Contacts.

[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: Baseline Week 4 and 6, 18, & 36 Month Deep Phenotyping Clinic Contacts as well at ATLAS Weeks 0 & 12 Contacts.

[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:** Baseline Week 4 and 6, 18, & 36 Month Deep Phenotyping Clinic Contacts as well at ATLAS Weeks 0 & 12 Contacts.

7.M. Non-urologic CRFs

[CMSI2] COMPLEX MEDICAL SYMPTOMS INVENTORY QUESTIONNAIRE

- Purpose:** For the Participant 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:** All Visits

[CMSI2_FM2] COMPLEX MEDICAL SYMPTOMS INVENTORY - FIBROMYALGIA

- Purpose:** To capture data about the Participant’s symptoms related to Fibromyalgia, if reported per the CMSI Questionnaire
- Who:** Research Coordinator
- When:** All Visits

[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:** All Visits

[PAIN] PAIN DETECT

- Purpose:** To record general pain symptom details and ratings for types of pain experienced around the body.
- Who:** Participant
- When:** All Visits

[MPQ] MCGILL PAIN QUESTIONNAIRE

- Purpose:** To capture pain ratings for the intensity of general types of pain.
- Who:** Participant
- When:** Baseline Week 4 and 6, 18, & 36 Month Deep Phenotyping Clinic Contacts as well at ATLAS Weeks 0 & 12 Contacts.

[GBS] GRACELY BOX SCALES

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

When: Baseline Week 4 and 6, 18, & 36 Month Deep Phenotyping Clinic Contacts as well as ATLAS Weeks 0 & 12 Contacts.

[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: WHO-DAS is completed at screening, week 4, quarterly, and Months 6, 18, and 36 and optional visits at Months 12, 24, and 30. **WHO-DAS R.A.** CRF is completed at run-in weeks 1, 2, 3.

[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: Baseline Week 4; 6, 18, & 36 Month Deep Phenotyping Clinic Contacts; 12, 24, & 30 Month Optional Clinic Contacts as well as ATLAS Weeks 0 & 12 Contacts.

[IPAQ] INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE

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

Who: Participant

When: Baseline Week 4; 6, 18, & 36 Month Deep Phenotyping Clinic Contacts; 12, 24, & 30 Month Optional Clinic Contacts as well as ATLAS Weeks 0 & 12 Contacts.

[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: Baseline Week 4 and 6, 18, & 36 Month Deep Phenotyping Clinic Contacts; 12, 24, & 30 Month Optional Clinic Contacts as well as ATLAS Weeks 0 & 12 Contacts.

[PANAS] PANAS

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

Who: Participant

When: Baseline Week 4; 6, 18, & 36 Month Deep Phenotyping Clinic Contacts; 12, 24, & 30 Month Optional Clinic Contacts as well as ATLAS Weeks 0 & 12 Contacts.

[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: All Visits

[MASQ] MULTIPLE ABILITY SELF-REPORT QUESTIONNAIRE

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

Who: Participant

When: Baseline Week 4; 6, 18, & 36 Month Deep Phenotyping Clinic Contacts; 12, 24, & 30 Month Optional Clinic Contacts as well as ATLAS Weeks 0 & 12 Contacts.

[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: All Visits

[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: All Visits

[PSS] PERCEIVED STRESS SCALE

Purpose: For the Participant to indicate feelings and thoughts during the past month.

Who: Participant

When: All Visits

[TIPI] TEN ITEM PERSONALITY INVENTORY

Purpose: For the Participant to rate personality traits per the scale provided.

Who: Participant

When: Baseline Week 4

[CSQ] THOUGHTS ABOUT SYMPTOMS

Purpose: To capture data about mechanisms the Participant uses to cope or deal with symptoms.
Who: Participant
When: Baseline Week 4; 6, 18, & 36 Month Deep Phenotyping Clinic Contacts; 12, 24, & 30 Month Optional Clinic Contacts as well at ATLAS Weeks 0 & 12 Contacts.

[CTES/RTES] CHILDHOOD/RECENT TRAUMATIC EVENTS SCALE

Purpose: To capture data about traumatic events in the Participant’s past.
Who: Participant
When: **RTES** completed at Baseline Week 4 and the 6, 18, & 36 Month Deep Phenotyping Clinic Contacts as well at ATLAS Weeks 0 & 12 Contacts. **CTES** is completed only at Baseline Week 4. NOTE: In the CRF packet, RTES for week 4 is not a standalone CRF and is included after CTES CRF.

7.N. 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
VISIT1 - 40	Visit #1 - 25 Checklists

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

Binder: Clinic Regulatory Binder

All personnel working on the TRANS-MAPP SPS 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: This CRF records 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 ID’s 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 #25 CHECKLISTS (VISIT1 – VISIT 40)

Purpose: The Visit #1 – Visit #40 Checklists (VISIT1 – VISIT40) forms 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: Research Coordinator

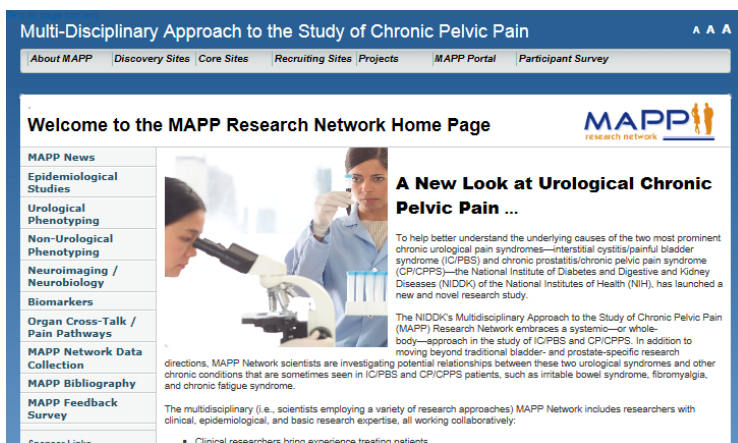
When: These CRFs are completed when data collection is complete for each visit.

8. 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.

• **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).

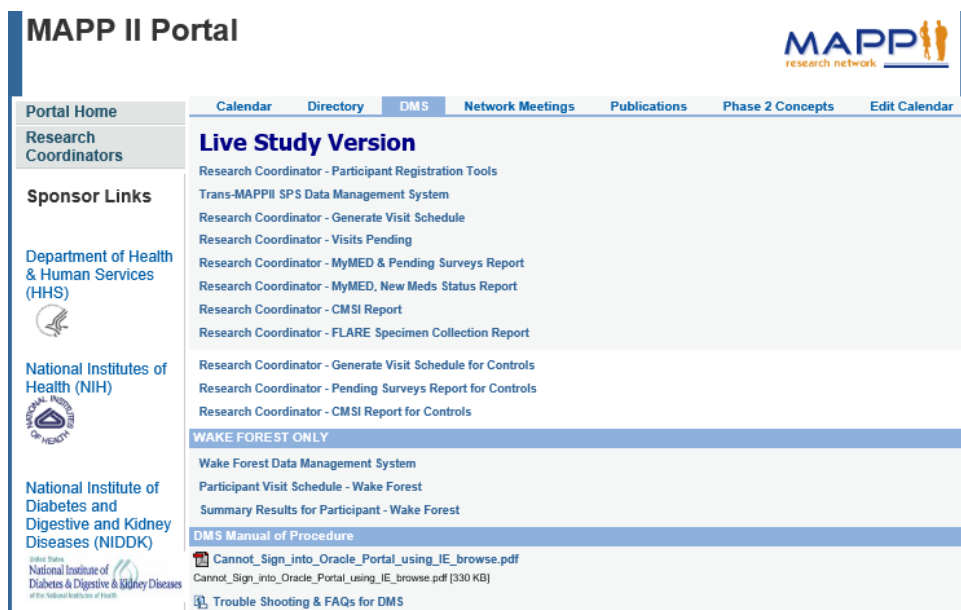
9. DATA MANAGEMENT SYSTEM USER GUIDE

9.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.



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

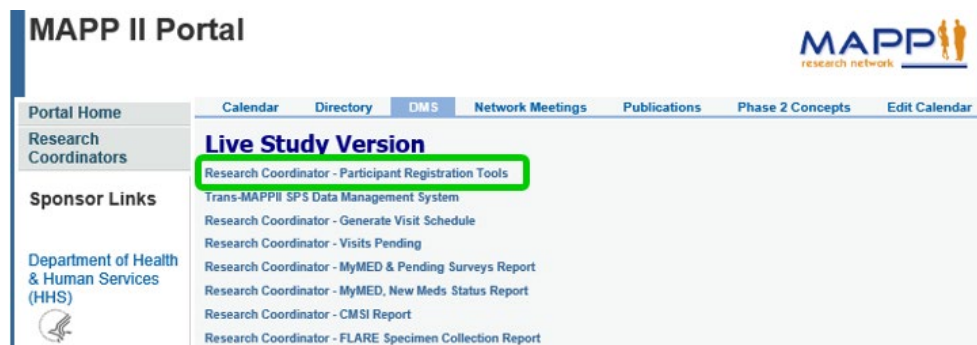
1. Registration, Specimen Collection Management, and Reference Links
 - Research Coordinator – Participant Registration Tools
 - MAPP Participant Registration
 - MAPP Participant/Study Assignment
 - Specimen Collection/Shipment
 - Kit Requests
 - CMED Drug Dictionary

- 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.

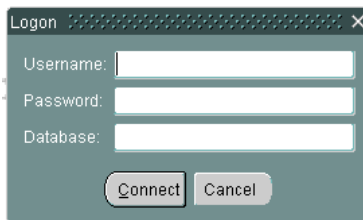
9.B. Research Coordinator – Participant Registration Tools

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.

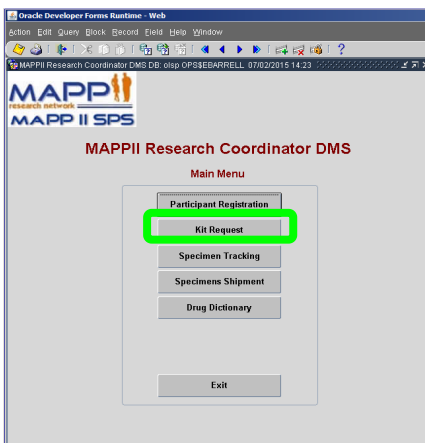


9.B.1. MAPP Research Coordinator DMS Main Menu

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
- Pre-screening



9.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.

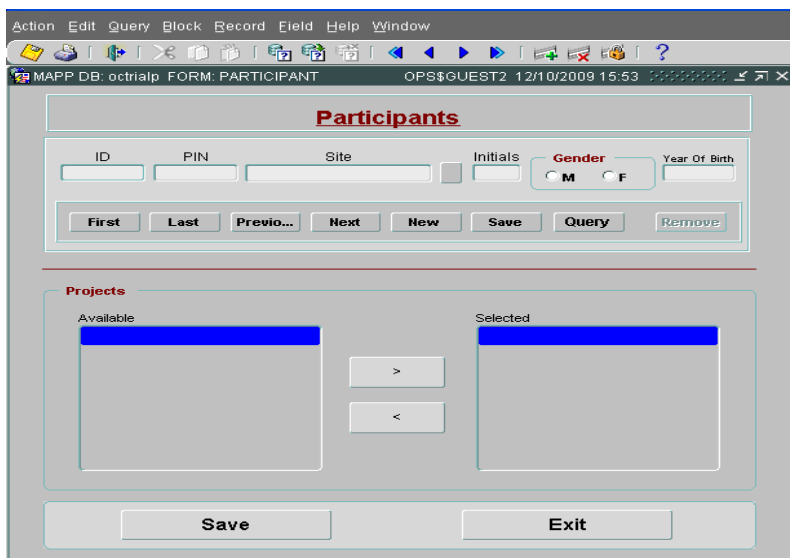
9.B.3. Assigning Participant PID and PIN

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

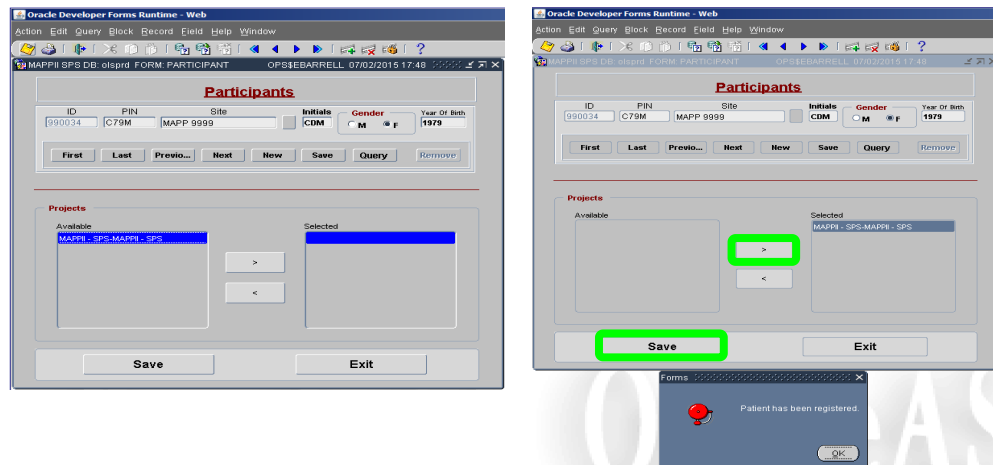
Record all numbers, including leading zeroes, when you record this number on CRFs.



9.B.4. Registering Participants to Trans-MAPP SPS 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 SPS, 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.



9.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.

MAPP
research network
MAPP II SPS

DCC Kit Requests

Kit ID Clinical Site CCCID Name Request Date

Urine Specimen Kit (UTRAC2) Vaginal Swab Kit (VSTRAC2) MB Female Urine Kit (UFMBTR2)

Plasma Specimen Kit (PTRAC2) Rectal Swab Kit (RSTRAC2)

3 Day Salivette Kit (S3TRAC2) MB Univ.J Urine Kit (UUMBTR2)

STIM Tube Kit (STIMTR2) MB Male Urine Kit (UMMBTR2)

First Last Previous Next New

Exit Save

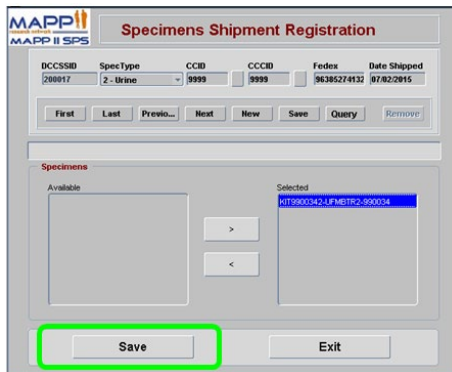
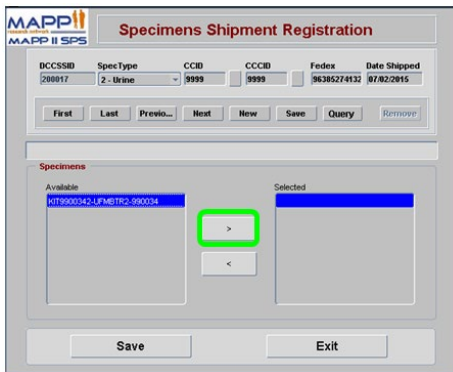
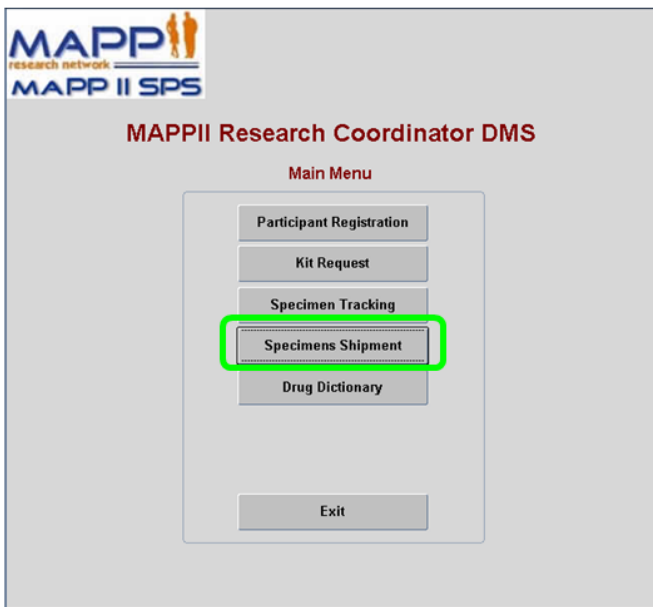
9.D. Specimen Tracking

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.

Barcode	Spec Type	Crf Date	Rcid	Collected	Collectdt	Shipped	Shippeddt

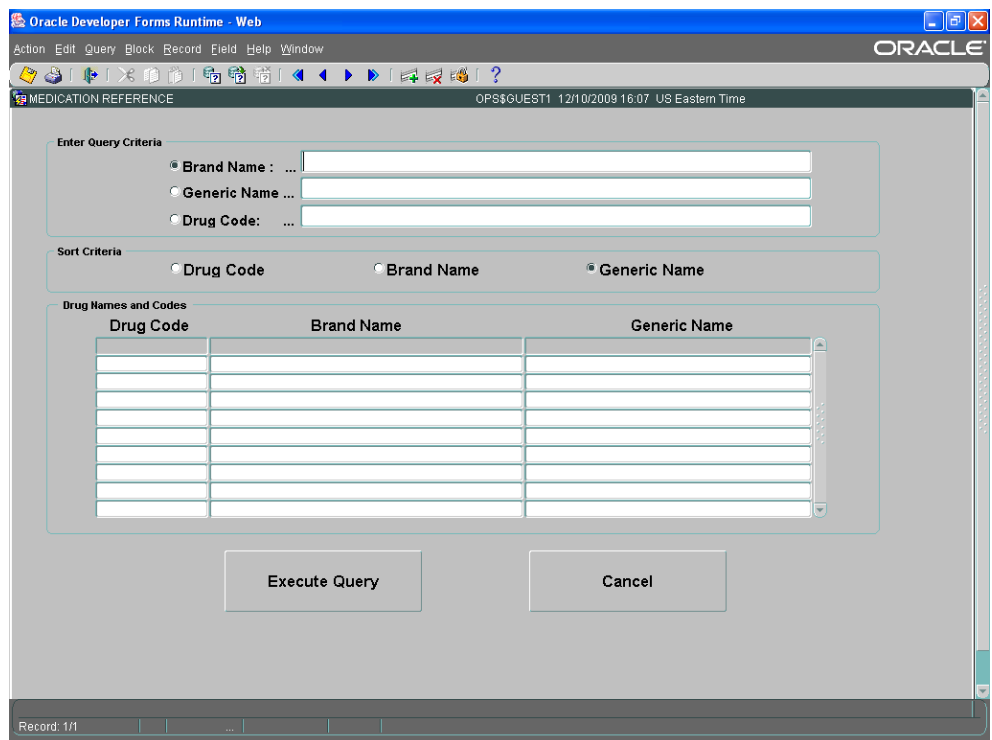
9.E. Specimens Shipment

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.



9.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 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.



9.G. Pre-screening

To access the Pre-screening modules select the “Pre-screening Menu” button on the Main Menu. The Pre-screening modules are used to record the monthly Pre-screening data for each of the three different types of potential study participants contacted. In order to access the Pre-screening modules, enter your site number and the study for which you will be entering data.

***Please note:** Pre-screening data entry is due by the 5th of each month for the preceding month. For example, the Pre-screening data for April would be due by the 5th of May.

As shown below, the Pre-screening data entry modules appear and collect data in the same fashion as the Pre-screening CRFs.

Pre-screening Summary for Epidemiology and Phenotyping Study

1. Month of Report: /

2. Number of subjects with initial contact this month:

a. Number who were contacted in person:

b. Number who were contacted by phone:

c. Number who were contacted in other ways:

Status of subjects currently in the pre-screening process:

3. Number of subjects no longer considered for participation (“Pre-screening failures”):

a. Number of subjects no longer considered due to no internet access, or refusal to use internet for Participant survey:

4. Number of subjects with decision for participation or scheduled consent pending:

5. Number of subjects consented:

6. Number of subjects who declined to consider participation:

a. Number of subjects who are not interested in participating following protocol:

b. Number of subjects who did not consider this study beneficial:

c. Number of subjects who have concerns about the research processes:

d. Number of subjects who have medical condition(s) unrelated to chronic pain that may interfere with participation:

e. Number of subjects who prefer (additional) compensation:

f. Number of subjects who have concerns about data privacy/ protection of personal medical information:

g. Number of subjects who are not bothered enough by the symptoms to justify participation:

h. Number of subjects who refused to provide biomarker specimens (including blood, cheek swab specimen, and/or urine specimen):

7. Number of subjects who learned about this study through:

a. Physician for this study:

b. Other physicians:

c. Central database:

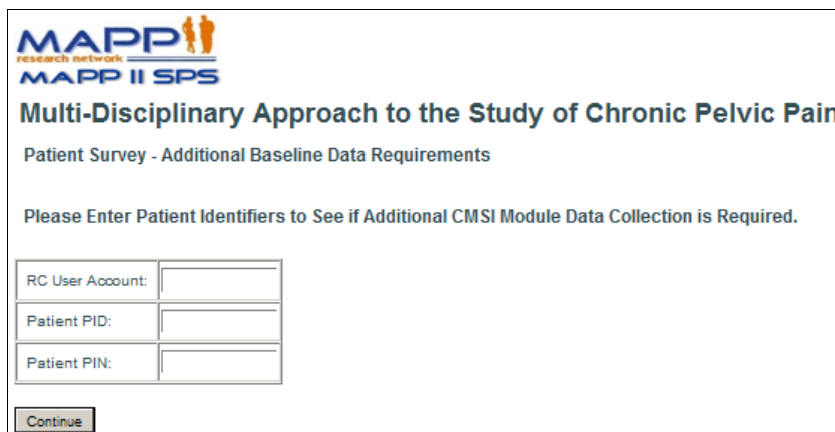
d. Newspaper:

e. Internet:

f. Other:

9.H. 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 interface for the MAPP research network. At the top left is the MAPP logo with the text "research network" and "MAPP II SPS" below it. The main heading is "Multi-Disciplinary Approach to the Study of Chronic Pelvic Pain". Below this is the subtitle "Patient Survey - Additional Baseline Data Requirements". A message 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.

9.I. 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"/>

9.J. Pending Surveys Report

This tool may be used by the RC to monitor the progress of Participants as they complete the weekly Run-in and quarterly 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.

9.K. Oracle Clinical DMS Module – See APPENDIX E – Oracle Clinical MOP

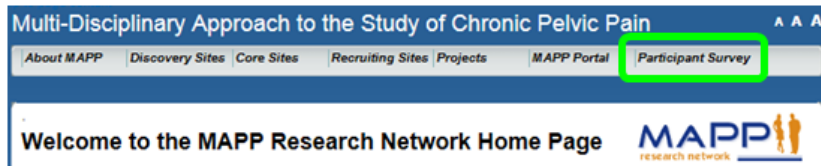
10. PARTICIPANT FOLLOW-UP INTERNET ASSESSMENTS

10.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 quarterly questionnaires will take participants approximately 30 - 45 minutes to complete; while the clinic visit online questionnaires will take about 45 - 60 minutes to complete.

10.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 the questionnaires.

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

10.C. Completing Participant Internet Survey

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



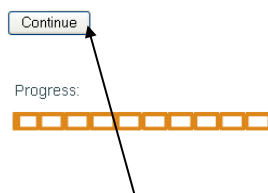
Multi-Disciplinary Approach to the Study of Chronic Pelvic Pain

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.



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 back onto the system within the scheduled target window to complete the questionnaires as specified on the participant calendar provided to them at the baseline clinic visit.

10.D. Missed Surveys

The calendar that the RC provides to the participant at the baseline clinic visit will include the target date that the participant is expected to log onto the website to complete each biweekly or bimonthly survey.

Participants are allowed 3 days before and 3 days after the actual scheduled date to log onto the system to complete the Run-in and ATLAS necessary questionnaires. Participants are allowed 7 days before and 7 days after the actual scheduled date to log onto the system to complete the quarterly online questionnaires. Once this period ends, they will not be able to complete another survey until the contact window opens for the next scheduled online survey, as indicated on the participant’s study calendar.

10.E. Help Completing Surveys

Instruct Participants 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.**

11. PARTICIPANT SAFETY

11.A. Risks and Benefits

11.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.

11.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.

12. HUMAN SUBJECT CONSIDERATIONS

12.A. Trans-MAPP Participant Considerations

12.A.1. Participant Follow-up

Participants who enroll in the study and complete a screening/eligibility visit will be followed up with quarterly internet questionnaires, as well as in-person clinic visits at 6, 18, and 36 months with optional clinic visits at 12, 24, and 30 months in addition to the online data capture at those time points in the study. A complete listing of protocol elements to be collected at the baseline/screening and follow-up visits is provided in **Appendix A: Study Visit Schedule.**

During the course of the study, participants will be contacted by the Discovery Site Research Coordinators with email reminders to log on for their quarterly assessments, as well as to facilitate scheduling of the 6, 18, and 36-month follow-up visits. Participants who do not complete their scheduled quarterly internet contact assessments will be contacted by phone for further prompting or discussion of any issues with study participation.

12.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.

12.A.3. Participant Withdrawal

It is anticipated that over the course of the 36-month follow-up period, participants may withdraw from the study. This may occur officially by formal notification from the participants to the investigator, or unofficially when a participant cannot be reached via the usual methods of contact. Every effort will be made to acquire complete data on all participants. However, a participant may withdraw consent for use of his or her data at any time.

Participants who relocate to an area from which it is no longer feasible to travel to the center for the follow up in-clinic visits will be asked to continue participation in the study by completing the quarterly online assessments.

12.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.

12.B. Ethical Issues

12.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.

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

Urine specimens are collected at all in clinic and ATLAS 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 several more tubes than usually obtained in the evaluation of UCPPS will be requested. However, the number of actual needle sticks will not be significantly increased over routine care, and 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 your blood.

12.B.1.b) Risk Associated with Collection of the Optional Microbiome VB3 Urine Sample, Rectal, and Vaginal Swabs

Optional VB3 urine samples (male only), rectal, and vaginal swabs will be collected at week 0, 18 months and ATLAS study visits. While it may pose temporary discomfort, there are no known risks associated with the

collection of the rectal and vaginal swabs. Male participants will be asked to collect VB3 specimens that require a prostate massage. Risk associated with a prostate massage includes temporary discomfort.

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

Neuroimaging studies are conducted at week 4 (baseline), 6, 18, and 36 month clinic visits as well as any ATLAS Study 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.

There is a risk that the water ingestion protocol will generate pain, including a possible pain flare-up. The neuroimaging session contingency plan shows how this risk will be minimized so that the acquiring this data will not cause undue urgency in the participant.

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

Quantitative Sensory Tests (QST) are conducted at week 4 (baseline), 6, 18, and 36 month clinic visits as well as any ATLAS Study 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. The participant should inform the Research Coordinator to stop the QST anytime that the 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.

12.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.

12.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.

12.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.

13. STUDY ORGANIZATION AND OVERSIGHT

13.A. Discovery Sites

Six (6) Discovery Sites participating in the Trans-MAPP SPS 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 Department of Urology
Center for Neurobiology of Stress

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

13.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,**
Associate Professor, Department of Urology
Hofstra North Shore-Long Island Jewish School of Medicine
- Co-Investigator (CP/CPSPS):** **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

13.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

13.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

13.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 (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

13.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.

14. STUDY MANAGEMENT

14.A. Discovery Site Responsibilities

14.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.

14.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.

14.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.

14.B. Data Coordinating Core responsibilities

14.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 (CRCU), 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.

14.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.

14.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 baseline phenotyping visit at the Discovery Site, after eligibility confirmation, each patient will be authenticated by the RC into a specialized module of the DMS deployed for patients to enter questionnaire data directly via a web browser.

Using a password-protected identity management module, this DMS will also be accessible to enrolled patients via a web browser for reporting their bi-weekly and bi-monthly contact assessments.

14.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.

14.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.

14.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.

14.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).

14.C. Tissue Analysis and Technology Core Responsibilities

14.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.

14.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.

14.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.

14.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.

- 15. APPENDIX A: STUDY VISIT SCHEDULE (See bookmark panel on left)
- 16. APPENDIX B : BIOSPECIMEN COLLECTION MANUAL (See bookmark panel on left)
- 17. APPENDIX C: ORACLE CLINICAL MOP (See Separate Document)
- 18. APPENDIX D: CASE REPORT FORMS (See Separate Document)
- 19. APPENDIX E: QUANTITATIVE SENSORY TESTING (QST) MOP (See bookmark panel on left)
- 20. APPENDIX F: (M)APP PROCEDURES (See bookmark panel on left)