VIEW DRAFT MOP

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Glossary of Terms and Acronyms

Acronym	Definition
AAPOR codes	A set of standardized codes used by The American Association for Public Opinion Research (AAPOR) to classify response rate for surveys
BH	Bladder Health
BHI	Bladder Health Instrument
CASI	Computer assisted self-administered instrument (survey)
CLEAR	Clarification of Language, Evaluation And Refinement of questions study
CRF	Case Report Form
EC	Executive Committee
ICF	Informed Consent Form
IRB	Institutional Review Board
LOYOLA	Loyola University Chicago
LUTS	Lower Urinary Tract Symptoms
MOP	Manual of Operating Procedures
NIDDK	National Institute of Diabetes and Digestive and Kidney Diseases
NIH	National Institutes of Health
PAPI	Paper and Pencil Instrument (survey)
PI	Principal Investigator
PID	Participant Identification
PP	Postpartum
PTT	Quantified Standing Paper Towel Test
RC	Research Coordinator
SAE	Serious Adverse Events
SC	Steering Committee (PLUS PIs)
SDCC	Scientific and Data Coordinating Center
UAB	University of Alabama at Birmingham
UCSD	University of California San Diego
UMICH	University of Michigan
UPENN	University of Pennsylvania
VIEW	Validation of Bladder Health Instrument for Evaluation in Women
WASHU	Washington University of St Louis
YALE	Yale University

Glossary of Terms

BHI-The Bladder Health Instrument: This is a large set of survey items bound together into a booklet.
Bladder Diaries: These are a 2-day Bladder Health Symptom diary and 1-day Bladder Health Frequency-Volume diary which are mailed to the woman as part of the kit. They are to be completed prior to in-person clinical evaluation and brought with the participant to the in-person clinical evaluation.
Clinical tests: testing performed as part of Clinical evaluation. Specific assessments include a bladder scan, paper towel test, uroflowmetry, post-void residual (PVR) scan, and dipstick.
BH Rating: This 2-step process is performed by site judges.
(1) The first rating is done during the in-person visit as part of the clinical evaluation, preferably prior to clinical assessment.
(2) The second rating is completed after the in-person visit and is informed by results from the clinical tests and the one day bladder diary These are ratings of the participant's overall bladder health and their bladder health compared to similarly situated women (e.g. women of a similar age or parity). The judge documents their rating on Forms 5 (first rating) and 6 (second rating).
Clinical Evaluation: This refers to the participant' in-person visit to the research site/clinic. The in-person evaluation includes a). written informed consent b). collection and review of legibility of bladder health diaries, c) a judge interview with 2 BH ratings and d) clinical assessment.
Enrolled: Any participant who provides verbal consent to participate in the study and is assigned a study ID number.
Judge: A health care provider who as part of their work/practice are expected to be able to respond to basic questions or statements about the bladder. They will perform the BH Rating.
Kit: Packet of documents and supplies for the completion of the two bladder diaries that is mailed to an enrolled participant after she has completed the BHI.
Randomized: When a participant satisfies all eligibility criteria, provides email and mailing addresses, she will be randomly assigned by the SDCC to a mode of administration of the BHI: PAPI (paper survey) or CASI (computer/online survey).
REDCap: This is the data entry and management system used for the VIEW study.
Screened: Refers to all adult females at least 18 years old who are assessed for eligibility for study participation
Source Document: Documents used to record all original data from participants that support and verify information recorded on the Case Report Form. Information subject to source documentation includes information from screening visits, telephone conversations, screening and study procedures, diagnostic and study related data, and study visits. This includes self-reported items and diaries. If any paper CRF is used as the primary source of information gathering, the paper form should contain information on who completed the form and the date the form was completed (i.e. the person creating the source document).
Survey Packet: The mailed or emailed packet sent by the SDCC to enrolled participants.
The survey packet contains:

a) a cover letter,
b) the BHI including criterion measures,
c) medical history questions,
d) socio-demographic questions, and
e) pre-paid self-addressed return envelope.

Administrative Overview

Purpose/Justification

To facilitate consistency in protocol implementation and data collection across participants and study centers.

Clinical Center Personnel for the VIEW Study

Research Coordinators

The research coordinator(s) will:

- Recruit and screen participants based on inclusion/exclusion criteria
- Enroll participants via REDCap
- Confirm email address and physical address for randomization
- Obtain verbal informed consent
- Record and communicate enrollment status with SDCC via REDCap
- Coordinate scheduling of in-person evaluation and judge interview
- Mail voiding diaries, voiding hats and instructions after completion of BHI survey
- Act as liaison during/conduct the in-person clinical assessment
- Obtain written informed consent
- Collect and review diaries for legibility
- Provide copies of bladder diaries to judge
- Ensure completion of all clinical procedures
- Process participant stipend
- Record and upload CRFs via REDCap data entry
- Depending on center capabilities, either scan bladder diaries to email address provided by SDCC or mail diaries weekly to address provided by SDCC

In addition, the RC will be responsible for maintaining local IRB and regulatory information and providing information to the SDCC for Advarra, the central IRB of record for this study. The RC will also be responsible for notifying the SDCC of any new PLUS personnel requiring certification and/or training and assist with the certification process.

Principal Investigator

The principal investigator (PI) will be responsible for the conduct of the VIEW study performed at their centers. The center PI ensures that appropriate training for personnel has been completed. The center PI is responsible for study implementation and oversight. The center PI may designate a clinical Co-Investigator to oversee the clinical in-person evaluation procedures,and supervise data collection from clinical components of VIEW.

Clinical Evaluator

The clinical evaluator (may be the same individual as the research coordinator, principal investigator, or co-investigator) will be responsible for completing training on the in-person testing procedures and demonstrate competency in bladder scanning, paper towel testing, uroflowmetry, and urine dipstick interpretation. This person will be responsible for completing CRFs during the clinical visit.

Judges

Judges are responsible for completing an interview with the participant according to their standard clinical care. No specific script or training will be required, but all judges will be asked to evaluate a participant's

overall bladder health and their bladder health compared to similarly situated women (based on age, health status, etc.).

Training

Data entry: All personnel who key data or download reports must undergo REDCap training, led by the SDCC.

Research coordinators: Each research coordinator will receive initial and ongoing instruction on screening and enrollment procedures, data entry, consent and shipping procedures as well as instructions on how to evaluate the voiding diaries for legibility. Documentation of review and understanding of the protocol and MOP will be documented on the Staff Training Log.

Clinical Evaluators: Each clinical evaluator will receive online and/or in-person training on the clinical measures collected for the VIEW study. Generally, one or two individuals at each PLUS center will be designated as evaluators. These evaluators are responsible for performing the following measures and either completing CRFs or providing data to the RC for completion of CRFs. Certification forms for each procedure will be signed off by a VIEW implementation team member or a clinically experienced PLUS Consortium member familiar with the test procedures at the research center. Certified evaluators should be indicated on the Staff Training Log located in Box (VIEW Study/Administrative Forms).

1. Bladder scan procedures
2. Paper towel testing
3. Uroflometry
4. Urine dipstick collection and analysis

Judges: A health care provider who as part of their work/practice is expected to be able to respond to basic questions/statements about the bladder. Operationally, this would be any provider (NP, PA, CNM, DNP, MD, DO) in family practice, internal medicine, geriatrics, OB/GYN, and urololgy. The judge will need to complete the Judge Demographics Form (Form 7). Judges at each center will be provided with a Judge ID. This ID will be entered on the Judge Rating Forms (Forms 5 & 6).

Pre Enrollment Processes

1. Recruitment Potential participants from the community will be identified by local research centers, however RCs may also recruit from medical practices/clinics as necessary to capture a range of participants with and without LUTS.

Potential participants will be identified through local clinical research center practices, recruitment flyers and community engagement activities using IRB-approved recruitment materials for the clinical and postpartum population (VIEW Study/Recruitment Materials folder). The PLUS research centers may also partner with a family practice clinic, an Obstetrics and Gynecology clinic, community centers, or other centers as deemed helpful. Other recruitment strategies may be proposed and individualized by as needed. The distribution of LUTS within enrolled participants will be monitored by the SDCC and recruitment adjusted as necessary to ensure representation by symptom and age. Recruitment from local specialty clinics may be necessary to fulfill the LUTS categories and will require a partial waiver of consent for pre-screening purposes to identify potential study participants with specific LUTS symptoms/severity.

Each research center will follow the Judge Grid for enrollment numbers. These numbers are site specific based on the number of judges recruited at a particular site and the number of participants each judge will interview. The RC's will follow the tracking/target enrollment minimums (Form 3) for self-report of LUTS categories and symptoms. Once the minimums are met for each site, RC's can then enroll in any category or age group.

Six research centers have unique access to post-partum women due to the nature of the consortium member's practice or recruitment access. These centers will enroll the post-partum population (UAB, UCSD, UMICH, UPENN, WASHU and YALE). Clinical data will be collected from all sample participants.

Recruitment will target 3 groups:

Group 1 – Healthy

Women will be categorized as "healthy" based on self-report of bladder problems in the Screening Level 1 section of the Participant Screening Form (Form 1).

- Therefore, women who are categorized as healthy based on self-report of no bladder problems will not need to be stratified across LUTS categories (rows in Table 1).
- However, "healthy" participants will still be asked to complete screening Level 2 symptom (LUTS) questions.
- To further clarify, if a woman self-reports "healthy" and responds, "yes" to any of the Level 2 LUTS questions, this women will be recognized and counted as "healthy".

The column for Healthy should have a total of twelve participants; it does not matter which, if any, row they fall in.The "healthy" recruitment target is 94 women across all centers. See Table 1.

Group 2 - Self reported LUTS

Each research center will enroll approximately 36 women who meet screening criteria for LUTS.

- During the screening, women will be asked to self-report any LUTS they've experienced and will be placed into categories ranging from mild to severe (represented by columns in Table 1).
- Each center will enroll approximately 12 women in the mild category, 12 in moderate, and 12 women who self report severe symptoms.

- Women will also be asked questions to classify their symptoms into the following LUTS categories: urinary frequency, incontinence, urgency, pain, voiding dysfunction, or frequent UTI (represented by rows in Table 1).
    - Each center will aim to recruit at least 2 participants in each classification of the 6 LUTS categories.
    - Beyond each symptom being present in a minimum of 2 participants, it does not matter how many participants have that LUTS symptom. Each woman can fulfill more than one row/ box in a given column.

Group 1 & 2 Age groups: A minimum of 5 women in each of 4 age groups (18-25; 26-44; 45-64; 65+) should be enrolled and complete all study requirements.

- Age group recruitment requirements can be satisfied independent of self-report of bladder problems.
- The age groups and minimum recruitment targets for each group are specified on the enrollment/tracking form (See Table 1).

Table 1

VIEW Site Specific Target Enrollment Minimums

Self-Report of Bladder Problems					
Healthy Qx=1	***Self-Report of LUTS***	**Mild Qx=2 or 3**	**Moderate Qx=4**	**Severe Qx= 5 or 6**	**Site Total**
12: ☐ ☐	**Row 1 – GA FREQUENCY**	2: ☐ ☐	2: ☐ ☐	2: ☐ ☐	6+
☐ ☐	**Row 2 – GB INCONTINENCE**	2: ☐ ☐	2: ☐ ☐	2: ☐ ☐	6+
☐ ☐	**Row 3 – GC URGENCY**	2: ☐ ☐	2: ☐ ☐	2: ☐ ☐	6+
☐ ☐	**Row 4 – GD PAIN/DISCOMFORT**	2: ☐ ☐	2: ☐ ☐	2: ☐ ☐	6+
☐ ☐	**Row 5 – GE PEEING**	2: ☐ ☐	2: ☐ ☐	2: ☐ ☐	6+
☐ ☐	**Row 6 – GF UTI**	2: ☐ ☐	2: ☐ ☐	2: ☐ ☐	6+
12	**Site Total**	**12**	**12**	**12**	

Qx: Which of the following describes any problems you may have with peeing or your bladder?

1= Does not cause me any problems at all
2= Causes me some very minor problems
3= Causes me some minor problems
4=Causes me some moderate problems
5= Causes me some severe problems
6= Causes me some very severe problems

Each cell in columns Mild, Moderate or Severe in the table should have at least two qualified participants. The column for Healthy should have a total of twelve participants; it does not matter which, if any, row they fall in. If they are in the Healthy column and do not fall into any row that is fine.

VIEW Site Specific Target Age Enrollment Minimums

18-25	26-44	45-64	65+
5: ☐ ☐ ☐ ☐ ☐	5: ☐ ☐ ☐ ☐ ☐	5: ☐ ☐ ☐ ☐ ☐	5: ☐ ☐ ☐ ☐ ☐

Each cell in columns 18-25, 26-44, 45-64, and 65+ in the table should have at least 5 qualified participants. It does not matter which, if any, self-report of LUTS the participant has.

Group 3 - Postpartum population

Postpartum recruitment will focus on women who are or will be in the postpartum period within 2 months of recruitment. Women should be at least 6 weeks postpartum during the time of survey completion and must be able to complete the in-person visit by 12 weeks postpartum. This decision will be a site specific determination between research coordinator and participant. If the participant is unable to complete the study requirements in the aloted timeframe (12 weeks post-partum), the RC will move the participant to the clinical population group. If the participant is moved to the clinical group prior to 12 weeks post-partum, the RC will hold releasing the BHI survey to the participant until 13 weeks post-partum. The RC has the option to 1) enter participant information into REDCap at time participant was moved to clinical population but hold randomization or 2) enter participant information for randomization at 13 weeks post-partum.

Recruitment from the obstetric population (pregnant/postpartum) may occur simultaneously with those recruited from community and specialty clinics. Six research centers have unique access to post-partum women. These centers will enroll the post-partum population (UAB, UCSD, UMICH, UPENN, WASHU and YALE). We will use convenience sampling without specific targets for distribution across LUTS or age for recruitment of this population. We are hoping for 26 completed participants per site. Broad demographic representation will be emphasized and tracked.

2. Screening and Enrollment

2. a. Enrollment Criteria: Adult females who are fluent in English and at least 18 years of age may be screened by telephone, online or in person using the Participan Screening Form (Form 1). If the participant meets inclusion/exclusion criteria outlined in the Participant Screening Form, verbal consent should be obtained per center policy.The information from the Participant Screening Form should be entered in REDCap.

Inclusion criteria:

- Community dwelling
- Age ≥18 years old
- Female sex assigned at birth
- Fluent in written and spoken English
- Able to read and provide informed consent
- Stand independently without human assist (e.g. cane/walker okay) for up to 3 minutes
- Get to bathroom and use toilet on own-without help from another person
- Willing to complete BHI validation survey and 2-day Bladder Health Symptom diary and 1-day Bladder Health Frequency-Volume diary prior to in-person clinical evaluation
- Available and willing to commit to an in-person evaluation within 6 weeks of completing BHI

Additional inclusion criteria for Postpartum Group:

- Pregnant in 3rd trimester or recently post-partum
- Available and willing to visit a site clinic to complete an in-person evaluation within 6-12 weeks postpartum (may be enrolled prior to delivery)

Exclusion criteria

- Physical or mental condition that would prohibit self-administration of questionnaire either electronically or using paper and pencil (e.g. dementia/cognitive impairment/blindness/severe arthritis)

- Institutional living arrangement (e.g. skilled nursing, long term care or rehabilitation center)
- Pregnant at the time of data collection
- Diagnosis or history of bladder cancer, kidney transplant, pelvic radiation, or currently getting dialysis
- Unable to stand and toilet independently
- Current participation in a research study about bladder
- Past participation in SHARE or CLEAR BHI CI.

- Women who are self catherizing by self report for neurogenic bladders are considered excluded as not being able to toilet independently.

Each research center will follow the target enrollment minimums outlined on page 7 of the MOP. During the screening process, if a participant is excluded and becomes a screen failure, the RC should still enter the screen form into REDCap and include reason for exclusion.If the RC learns during the screening process a participant has qualified for a LUTS category that is already full, the RC should communicate to the participant the specific category is fulll; however we may call her in the future if needed. The screening process does not have to be fully completed, but must be entered into REDCap with the information collected and randomization held.If anyone is assigned a study ID#, that screen form should be entered into REDCap and appropriate fields completed.

2.b. Online Screening Survey

Each center will have access to a link for an online screening survey in REDCap. This survey will contain a subset of the questions from the paper screening form to assess LUTS symptoms and severity. RCs will be able to access results from the survey and identify any potential participants. If a potential participant is identified and contacted, the RC will use a paper screening form to assign them a study ID and complete the screening process.

For participants that completed the online screening form, RCs should check the box "Check here if participant completed online screening" and enter the Online Screening ID (the ID number the participant was assigned in the online screening survey). The RC should skip to the "Screening Level 2 Summary Table" and enter the sections the participant qualified for based on their online screening form. The RC will then need to contact the participant and start with Part 4: Eligibility. The RC may also choose to complete the entire screening form again with the participant if they think it is necessary.

2.c. Study IDs

Creation of study ID is determined by SDCC with a different format for the Clinical Population and Postpartum Population. The Clinical Population IDs will have the following format: CENTER_C001 – CENTER_C100 (100 PIDs per site). The Postpartum Population IDs will have the following format: CENTER_P01 – CENTER_P50 (50 PIDs per site). These are assigned to anyone who completes a participant screening form, regardless of whether they are enrolled or are a screen failure. If a center needs more PIDs generated, SDCC should be contacted and more PIDs will be added to REDCap.

2.d. CENTER PID names:

Loyola: LUC
Washington University in St. Louis: WASHU
Yale University: YALE
University of California San Diego: UCSD
University of Alabama at Birmingham:UAB

2.e. Enrollment and Scheduling Considerations:

Each site has autonomy which scheduling strategy works best for them. Consider your site's specific constraints and work with your clinic staff as much as possible to accommodate participants'needs. For instance, take into account the schedules with limited evening/weekend availability; judges who only see participants from a certain age; or LUTS categories.

Post Enrollment Processes

1. Randomization

Clinical Population

A participant must provide an email and mailing address prior to randomization to mode of administration by the SDCC (PAPI or CASI).

During enrollment, participants without an email address will be offered participation in the mailed administration only (PAPI). Those who only provide an email address (are homeless or don't have an address or reliable US mail at their address to send the kit) may still participate by CASI if they can travel to a research center to pick up the kit.

Once screening is complete for a participant, the RC will enter screening data into REDCap which will notify SDCC for randomization to either PAPI or CASI mode. The SDCC will send out the BHI to be completed. All materials sent to the participants will contain logos and contact information for the research center RC. Those completing the electronic BHI will also be provided contact information for the local center personnel. The RC will be copied on the email sent to the participant for those completing the electronic BHI.

Postpartum Population

Enrollment will proceed in a fashion similar to the community sample. These participants may be recruited prior to delivery and may select their mode of BHI administration. If they do not choose a mode of BHI administration, they will be randomized by the SDCC. They will be mailed/emailed the survey packet to complete no earlier than 6 weeks post-partum. After participant completion of the BHI, the in person clinical evaluation will be scheduled to take place by (up to and including) 12 weeks post-partum. The remainder of the procedures for the study are the same as the community clinical population sample. If the participant has already delivered at the time of screening, the delivery date should be entered in the due date section part 3, # 4 of the screening form .

2. BHI Completion

A. If the BHI is not complete: If a participant does not return the BHI (within 15 days for the PAPI group; within 7 days for the CASI group), the RC will be notified via email to call the participant.

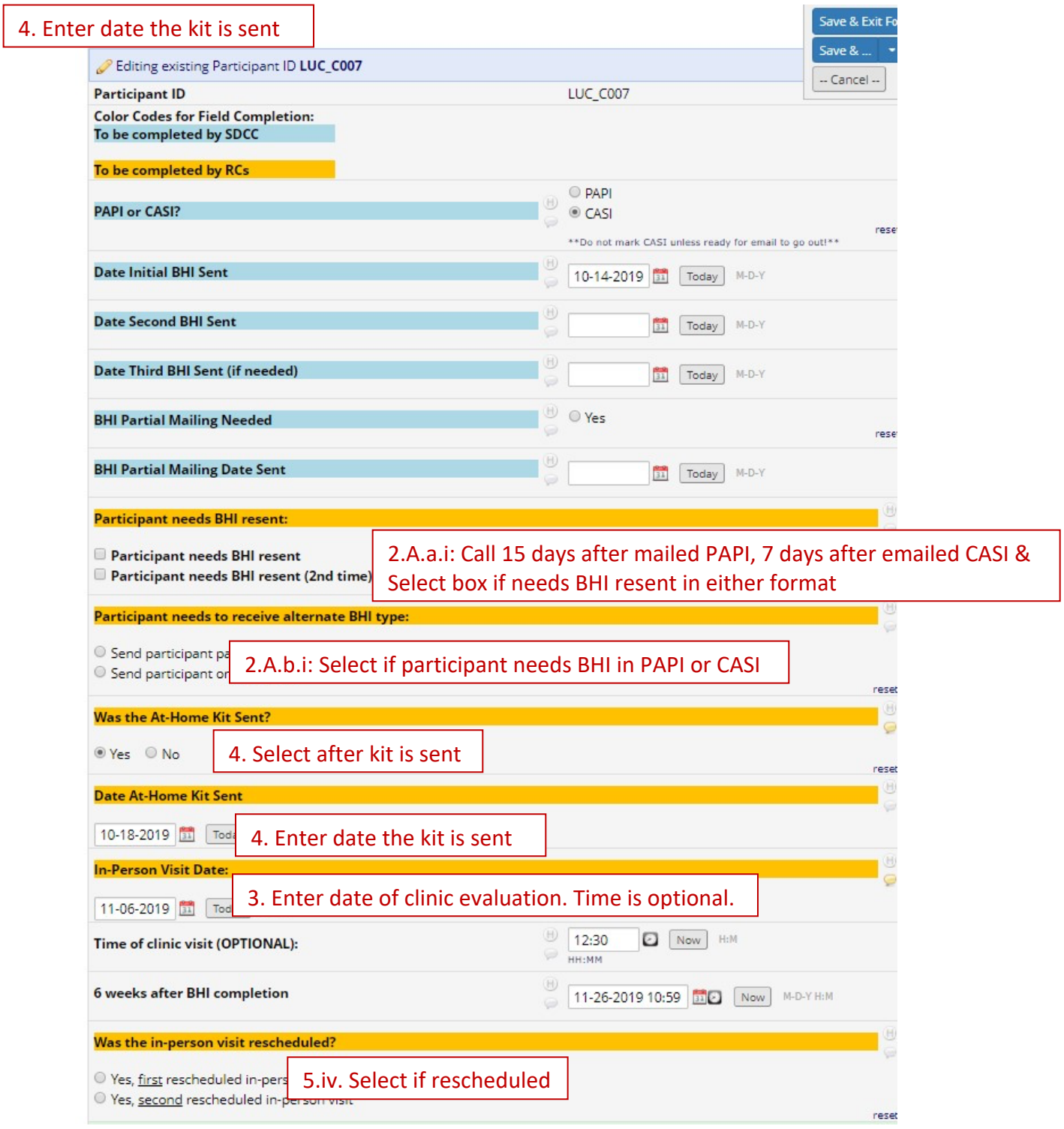
a. If a participant needs another survey sent to them:
    i. The RC will mark it in REDCap and SDCC will be notified to send another BHI

(see Data Entry Checklist, Form 11; screenshot is below, see 2.A.a.i)

b. If a participant needs to switch randomization groups (ex. a CASI participant would like a paper survey mailed to them), and you think the participant will drop out of the study if they don't receive the alternate BHI survey type:
   i. This can be marked in REDCap and SDCC will be notified (see Data Entry Checklist, Form 11 screenshot is below, see 2.A.b.i
)ii. This will also be collected on the reminder call checklist
c. If a participant would like to no longer be contacted about the study, complete a Participant Exit form to disenroll the participant from the study (see Data Entry Checklist, Form 11)
d. If a participant still does not complete the BHI within 30 calendar days of enrollment, the participant will be disenrolled
   - The RCs will be notified via email if a participant is disenrolled from the study

B. <u>If the BHI has been completed:</u> Once the BHI has been returned to SDCC, RCs will be notified via email to contact the participant to schedule the in-person evaluation. This in-person evaluation must be complete within within 6 weeks of BHI completion. This is the date that is listed in REDCap Form 11.

Form 11 Screenshot



3. Schedule In-Person Visit

After the RC is notified of BHI completion, the RC schedules the particpant's in-person visit ideally within 7-10 days of the scheduling call and no later than 5 weeks after notification of BHI completion. This will allow time for shipping and 3 days of diaries to be completed before the in person visit and within the 6 week post BHI completion window.

3.A. Menstruation. RCs should try to avoid scheduling the in-person visit for a day when the participant will be menstruating. If the participant is menstruating during the clinic visit, RCs will still complete all clinical tests and indicate testing that is done while on their period OR if not reliable (papertowel test and Urine Dip for heavy vaginal bleeding) and simply indicate on CRF in the notes section that participant was menstruating. For those women using a tampon, they should remove the tampon prior to the PTT and uroflow procedures and CRF should indicate that the participant was on menses and no tampon used.

3.B. Scheduling postpartum participants. For postpartum participants, the in-person evaluation must be scheduled to occur before the 12 week postpartum date. Any deviation beyond the 12 weeks postpartum or 6 weeks from BHI completion must be reviewed and approved by the VIEW Co-Leads (Constantine and/or Lukacz) team.

The date of the in-person visit will be entered into REDCap (see Data Entry Checklist, Form 11, see screenshot above, 3.B). The time may also be entered (optional).

3.C. Coordination. Scheduling of the in-person visit will include coordination of the participant, the judge, the evaluator and clinic room availability. Each site must determine the best way to handle this logistical challengage given local clinic procuedres and personnel scheduling considerations. It is preferred that all procedures and assessments be performed on the same day judge is asking the participant in the interview

4. Mail Kit At the time the RC schedules the in person evaluation, the RC will mail the at-home kit within the next business day via site preferred mail carrier. The kit will be packed in the approved purple shipping boxes. The contents of the kit will include:

1. Introduction/general instruction letter
2. $15 incentive for the completion of the BHI Part 1(for centers able to do so)
3. Pocket folder with 1-day and 2-day diaries plus instruction sheets, informed consent form, directions to clinic and any parking or transportation information deemed necessary by center RC
4. RC business card inserted in the folder
5. Voiding hat
6. PLUS shopping bag
7. Yellow tissue paper for packaging
8. Sticker (provided by SDCC) to close tissue wrapping

RC will enter the date the at-home kit was mailed into REDCap (see Data Entry Checklist, Form 11, screenshot above, see 4.)

Kit Process/Checklist:

1. To have on hand before kit assembly:
    a. ICF (site-specific, approved)
    b. Cover letter (ready to modify)
    c. PID (stickers or just to reference)
    d. Participant contact information
    e. Participant appointment date and time

   f. RC business card
   g. Gift card (if applicable)
   h. Bladder diaries
   i. Tote
   j. Bladder hat
   k. Purple folder
   l. Yellow tissue paper
   m. Packaging tape
   n. Avery mailing labels
2. Print participant mailing label (if not batch printed in advance)
3. Modify cover letter with participant name, address, and appointment date
   a. Print
4. Assemble purple mailing box
5. Affix mailing label to box
6. Label each page of both bladder diaries with PID
7. Attach RC business card to the purple folder
8. Assemble the folder documents:
   a. ICF
   b. Bladder diaries labeled with PID
9. Line the mailing box with tissue paper
10. Fill the box:
   a. Tote
   b. Bladder hat
   c. Completed folder
   d. Cover letter
   e. Gift card
11. Close the box and secure with packaging tape
12. Drop off with postal service

5. Bladder Diary Completion Reminder

5. A 4 – Day Visit Call Reminder. RCs will be notified by email 4 business days before the participant's scheduled clinic visit
   1. The RC should call, email or text the participant to remind them of the upcoming visit and confirm bladder diaries are complete.
   2. Remind participant of visit time, location, parking, etc.
   3. Confirm that the participant is not pregnant. If pregnant, she will need to be excluded from the study
   4. RC should also use this call as an opportunity to provide the participant with more detailed information about the bladder assessments that will be performed at the visit, and tell them that they will be asked to undress from the waist down and given a gown or sheet
   5. If the participant has **not completed the diaries**:
      a. The RC should confirm if the bladder diaries can be completed by visit date. If they cannot complete the diaries prior to the visit, the RC should reschedule the in person visit. If the participant says they can complete the diaries before the in person visit, follow step b

b. The RC will need to recontact the participant 1-2 day before the visit date.
    i. If the participant has STILL **not completed the diaries**:
        1. The RC will reschedule the participant within the 6 week window of initial completion of BHI.
        2. For the postpartum population, because there is a very tight time window for participants to follow up before 12 weeks postpartum deadline, if a postpartum participant is unable to complete one or both diaries before the scheduled visit AND the visit cannot reasonably be rescheduled within the time window the participant should still be scheduled and come in for the in person evaluation.
            a. If it is possible for them to do one of the diaries, it is preferable that the 1-Day Frequency-Volume Bladder Diary be completed, but we will take whatever they are able to complete.
            b. If it is not possible for them to complete any of the diaries before the scheduled visit and the visit cannot be rescheduled inside the window, or in the opinion of the coordinator the likelihood of completion is low, the appointment should be kept and proceed without the diary information. Non-Diary completion should be noted on the Clinic Visit form and any reasons why should be entered in REDCap
    ii. Participants who do not complete the diaries will not receive stipend for diaries.
    iii. Participants may be rescheduled up to 2 times within 6 weeks of the bladder diary completion date. Further extensions beyond 2 reschedules will be left to the individual discretion of the RC, considering RC opinion of likelihood of participant completion. The RC may use their judgement to withdraw the participant from the study at any time if the participant is unlikely to be compliant with study procedures.
    iv. Every time the participant is rescheduled, update the in-person visit date in REDCap and mark that the person has been rescheduled (see Data Entry Checklist, Form 11, screenshot above, 5.iv)
6. Add pertinent notes to the In-Person Noted Field in REDCapForm 11.

5B. 2-Day Visit Reminder Call.

1. Call participant 2 days prior to visit to remind them of date & time
    a. REDCap will auto-matically notify RC by email of 2-Day Visit Remindre Call
2. If diaries were not complete at 4-day call but participant said they could complete them, check to see if they are complete
3. Add pertinent notes to the In-Person Noted Field in REDCapForm 11.

In-Person Day of Visit Process

The order of events for the in-person visit may differ depending on several factors (e.g. participant voicing an immediate need to void, availability of the Judge to perform the initial interview and availability of Clinical Evaluator or equipment to perform testing). Below are all of the items that need to occur at the in-person visit, preferably in this order. Exceptions to the order are indicated with an asterisk:

- Informed consent
- Verification of Bladder Diary legibility consistent with scanning requirements
- Judge interview

- Initial judge rating (see #10 below)
- Clinical Tests (clinical procedures)*
- Judge second rating (see #16 below)

* If possible, the clinical tests will be completed following the Judge interview and rating number 1. These tests should only be performed before a Judge interview if the participant arrives with an "uncomfortably" full bladder and voiding cannot be delayed until after the Judge interview or the judge is not available for the interview.

Note that the judge interview and clinical testing as well as initial judge rating should be performed on the same day. The judge second rating must be performed within 7 days of the first judge rating, and preferably on the same day as the visit.

1. Informed Consent

The RC will review the Consent Form with the participant, answer any questions, obtain the paricipant's signature, and sign and date the form themselvels. The RC will tell the participant who the judge is and briefly review the judge interview and study procedures. If required by research center, the RC will provide the participant with a signed copy of the consent. Nothing should be collected from the participant and the bladder diaries should not be reviewed until the consent form is signed.

Once the consent has been completed, the Confirmation of Consent form can be completed in REDCap. Included in the Confirmation of Consent form in REDCap is the field for adding participants to the NIH Repository if checked during signing of the consent form. Also in the Confirmationof Consent form is the field to document participant consent to be added to the PLUS Registry to be contacted for further research.

2. Review the Diaries

The in-person visit research coordinator (RC) will collect the bladder diaries and review for legibility. If numbers or entries are not legible, the RC may ask the participant to correct any illegible entries. The RC should NOT review or otherwise ask questions about the accuracy or completeness of the diary. If data points are missing, this will not be the responsibility of the RC to reconcile. If diaries are not available, despite the numerous attempts to ensure compliance, the participant will still undergo clinical testing and be evaluated by the Judge. In this scenario, the participant will not receive compensation for the diaries. If diaries were completed but left at home or forgotten, they can be mailed back in a prepaid stamped envelope to the research center and compensation provided after return of the completed diaries.

3. Pre-Clinical Testing Questions

Prior to starting the clinical testing, ask the participant the following question and proceed as noted based on the participant's response:

Do you feel like you could empty your bladder now?

a. No I just went → Have the participant drink fluids and complete the initial judge interview and any other items. Perform a bladder scan after 15-30 minutes until >150 mL of urine and she feels she can void before beginning paper towel test.

b. No I really don't, but didn't just empty my bladder → Complete initial judge interview and any other items. Confirm that she feels like she has enough to void and check volume. If participant doesn't feel like she could void but volume on scanner is >150 mL → give fluids to drink and wait 15 to 30 min until she feels she can void before beginning paper towel test.

c. Yes I could go now → Perform a bladder scan and proceed if > 150 mL. If there is not >150 mL of urine then have the participant drink fluids, complete initial judge interview and any other items. Perform bladder scan after 15-30 min until >150mL of urine and she feels she can void before beginning paper towel test.

d. Yes I can barely hold it → Perform bladder scan and if >150 mL of urine, it is okay to proceed with paper towel test and additional testing prior to judge interview. If <150 mL then proceed with testing and check box on CRF that she is unable to hold urine and follow with initial judge interview. Do NOT provide results of any clinical testing to judge prior to judge interview.

4. Judge interview and Initial Judge Rating (Unaided) - The RC will provide the Judge with the Judge Initial Rating Form (Form 5) before the Judge interviews the participant

a. The judge interview and the initial Judge rating and will be on the same day as the clinical tests but the second judge rating may be on a separate day but within 1 week of the in-person visit.
b. Judges should not rate their own patients.
c. As mentioned above, it is preferred that the judge interview the participant before the clinical tests. If necessary, however (e.g. participant can't hold it) the interview, may be done after the clinical tests.
d. If the clinical tests are done before the Judge interview, the Judge is **not** to see the results of the clinical tests before seeing the participant.
e. Each judge rating form requires the judget to make two ratings. The first rating of these rates will be an absolute rating of the ***overall/absolute*** health of the person's bladder. The judge will write down a rating on 0 (worst) to 10 (best) on Form 5 and provide up to three reasons for that rating.

The judge should also record the start time and end time of the participant interview (time the judge spent talking to the participant) in 24-hour/military time.g. The second judge rating occurs once the clinical prodcedures are completed and forms (or copies of forms) given to the judge. This process if outlined on page 31.

5. Clinical Testing

As part of the clinical testing, collect particiant height (feet & inches) and weight (lbs) and enter it on the Clinic Test Form (Form 4),

5a. Bladder Volume Assessment (e.g. BladderScan)

Background:

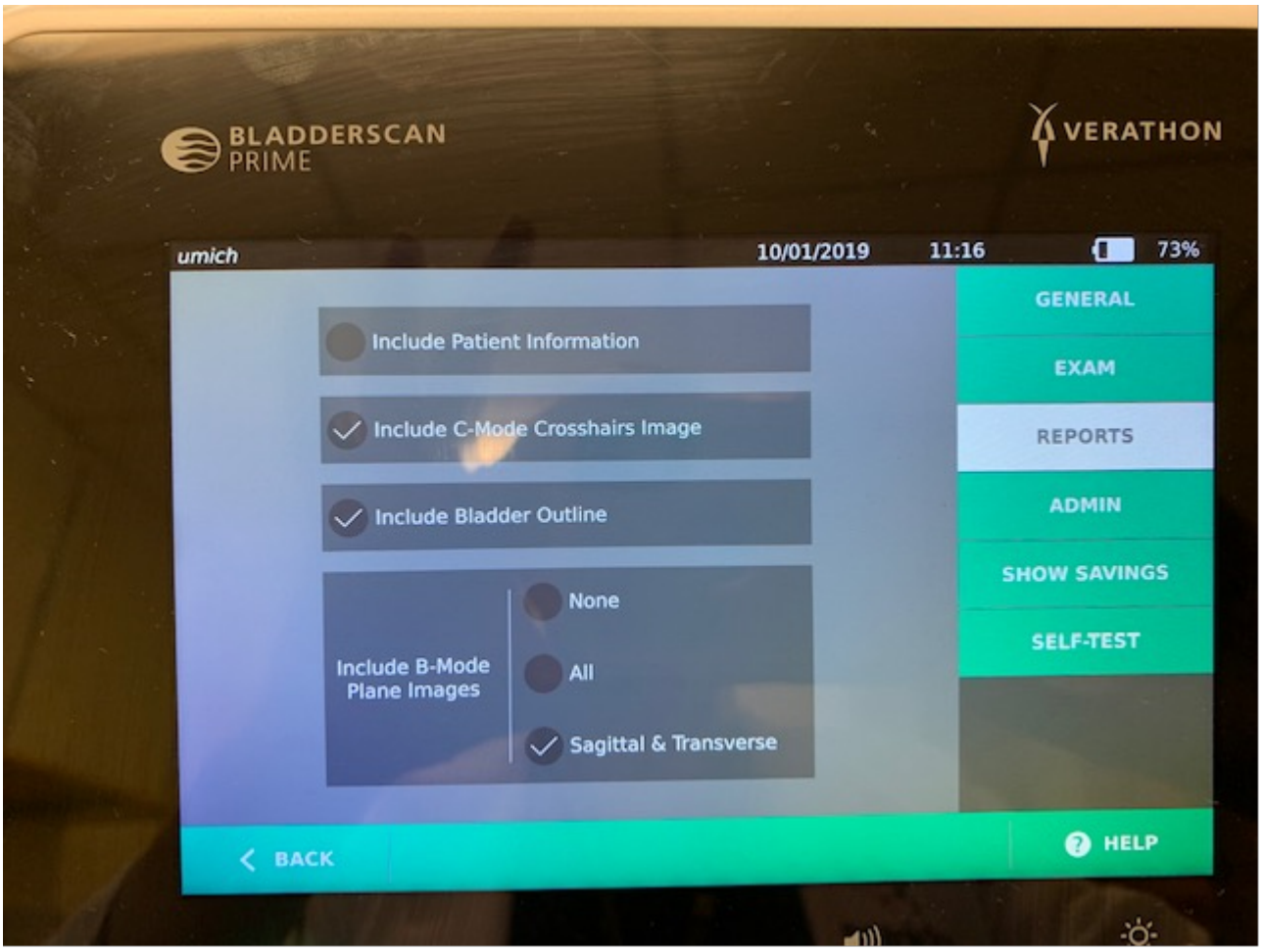
1. The bladderscan will be conducted as part of the clinical tests to assess for the adequate urine volume (≥150 mL) to perform the Paper Towel Test (PTT) and to determine post-void residual (PVR) following a uroflow test.
2. BladderScan Prime Plus, a 3-D ultrasound system, will be used to measure the amount of urine in the bladder. The core components of the system are a console with a touch-screen display, a scanning probe containing the ultrasound transducer, a printer and a battery charger with rechargeable lithium ion batteries. Note that new paper for the scanner can only be ordered through Verathon.
3. Before the visit begins, turn on Scanner and check battery life. Go to settings and note accurate date, select B mode and ensure that print settings are set to B mode. Check printing paper for adequate amount to complete scheduled visits for day.

4. The participant will self-report bladder fullness or urge sensation (inferred by participant's level of need to void). In order to complete the Paper Towel Test, there should be ≥150 milliliters (mL) of urine in the bladder. If there is < 150 mL in the bladder, then the participant is instructed to drink at least 8 ounces of fluids (e.g. water, juice, etc.). The bladder assessment is repeated after allowing for time for filling of the participant's bladder. Generally, the bladder fills at 30 to 100 mL per hour. Depending on how low the volume is before starting the scanning, the participant may need to wait an hour or more for a full enough bladder. The bladder scan may be repeated approximately every 15 to 30 minutes until there is ≥ 150 mL of urine. The participant can continue to drink fluids until there is ≥ 150 mL of urine.
5. The bladder scan battery charger should be kept plugged in with replacement battery inserted for easy access to evaluator in clinical setting.

Procedure

- The participant is instructed to disrobe from the waist down and a sheet provided to cover below the pubic bone. The participant may keep on socks during the procedure if desired.
- Wash/sanitize hands and put on gloves.
- Turn on the scanner and select from which side of the participant you are scanning**.** Ensure the diagram on the hand held device is oriented in the same direction as the participant.
- With the participant lying in the supine position (head elevated no more than > 30 degrees), with abdominal muscles relaxed, the participant's pubic bone is palpated.
- An ample quantity of ultrasonic gel should be placed with as few air bubbles as possible midline on the participant's abdomen approximately 3 cm (one inch) above the pubic bone. Gel can alternately be placed on the probe itself (or both abdomen and probe).
    - Be sure there are no areas of gaps between the probe and the participant's skin, and that enough pressure is applied to maintain adequate skin contact until the scan is completed. If necessary, more gel should be added to insure proper contact.
- The probe is held by grasping with the cable running up the wrist and forearm.
- The probe is gently pressed to the lower abdomen through the gel just above the pubic bone aiming away from the participants head and more toward the feet and the diagram on the top of the scanning probe should be oriented in the same direction as the participant. The probe cable should be oriented at 90 degrees to the digital plane of the participant
    - If an obese (large girth) participant is being scanned, lift as much abdominal adipose tissue out of the way of the scanning probe as possible. More pressure should be applied to the probe in order to reduce the amount of adipose tissue through which the ultrasound probe is passed.
- The green button on side of probe is then pressed or press the "Scan" icon on the console screen. The real B-mode ultrasound image appears on the console screen. Target the bladder by doing the following:
    - Angle the probe slightly from the participant's left to right until the dark bladder area is centered in the vertical green line on the aiming screen. Once the bladder is centered, angle the probe slightly up or down the participant's midline to obtain the largest possible dark area.

- A green outline (*BladderTraq*) will appear around the detected edges of the bladder.
- When the largest possible dark area is obtained, the green probe button should be pressed or tap icon “Scan” on the screen to allow the scanning process to begin.
- The probe should be held securely while the scan is in process.
- The end scan tone sounds when the scan is completed.
- Press the icon “Done” on the console screen.

- Aiming guiding is successful if bladder is centered in the field of view and all bladder edges are visible. There should be no grey areas. Bladder scanning is then successful and the results optimized for accuracy. If the bladder volume is outside the edges and is >150 mL there is no need to repeat the scan. If the bladder volume is <150 mL and is not centered in the field, the scan should be repeated to obtain an accurate measurement.
- Press the icon “Print” on the console. The printer should be set up to print both the b and c mode.
- 

- Take the report from the printer. If extra copies of the results are desired, press the Print icon a second time.
- Tape the report on the Bladder Scan Printout Form (Form 4A). You will also be putting the PVR bladder scan report on this form, so be sure you tape the report on one side of the form. After the in-person Visit, scan this form and put it in Box (Bladder Scan Printouts Folder)

- Be sure to name the file something like BladderScan_SITE_ID (ex. BladderScan_UMICH_C002)

- Note the following parameters on the Clinical Test Form under **#1 Bladder Scan volume prior to Paper Towel Test:**
  - Check Box for: Printout ☐ Yes ☐ No
  - Volume: _____mL
  - Check Box if ☐ scanned volume is < 150 mL and the participant was unable to "hold or wait for scan prior to voiding"
  - If the BladderScan is not completed, check ☐ Not done and write an explanation in the space provided

  Participants should be reminded when scheduling appointments to come in with a full bladder. If participant empties her bladder prior to the procedures, then they should be asked to drink 8 to 16 oz of fluids and rescanned when they feel full or after 15 to 60 minutes until ≥150 mL of urine.

Checking for accuracy: If inaccurate, need to repeat procedures until no error messages. For the pre Paper Towel Test, if scanned volume is >150 mL, rescanning is not necessary, but if scanning is inaccurate for the post void residual test, the test should be repeated until accurate.

- Yellow "greater than" (>) symbol appears: The actual bladder volume may exceed the displays result. The participant should be re-aimed and re-scanned if this happens.
- Bladder not centered in the field of view (within green tracker): Angle the probe in the direction of the bladder on the display in order to optimize results.
- Edge scan: if one side of the bladder is not within a field of view, then a portion of the bladder was not included in the scan. The system displays a "greater than" symbol (>) before the measured result, indicating that the actual bladder volume may exceed the displayed result. The probe should be moved or angled in the direction of the bladder on the display in order to optimize results.
- Pubic bone interference: if a grey area appears, this indicates that the pubic bone is inside the field of view. Although the bladder may be centered and measurement may be complete, there is the possibility that the pubic bone is obscuring part of the bladder. The system displays a "greater than" sign (>) before the measured result, indicating the actual bladder volume may exceed the displayed result. The probe may be moved or angled in order to optimize results.

CLEANING AND DISINFECTING

- Wipe the excess gel off the participant's abdomen with a washcloth or tissues.
- Clean the probe after each scanning
- Wipe any ultrasound gel completely off the probe using a wet cloth or towelette indicated for cleaning medical devices. To disinfect the probe, use a germicidal towelette with an active ingredient class. The following is a list of low-level disinfectant classes that have demonstrated efficacy with the system:
  - Alcohol or alcohol compounds
  - Chlorine and chlorine compounds

- Plutonium ammonium and hydrogen peroxide

- Do not allow gel or other contaminants to dry on the system or probe. This makes removal more difficult. Always wipe in the direction from the clean surface to a dirty surface to minimize overlap of the wiping pattern.
- Do not immerse the console or probe in cleaning or disinfecting solution or other liquids. Do not subject the instrument to steam or any other products.

5b. Standing Stress Paper Towel Test (PTT)

Background

1. The PTT will be conducted as part of the clinical tests to assess for stress incontinence
2. Quantifies amount of leakage as a continuous level variable. By using an ordinary standardized trifolded brown paper towel, even a small volume of urine loss down to a fraction of a drop spreads into a readily observable and measurable wetted area. All PTT will be conducted with a consistent brand of paper towels provided for this study.

Procedure:

- The clinical evaluator will need to be present to ensure proper completion of the PTT and to collect and measure the area on the towel within 10 seconds of completing the test.
- The test will be performed with a comfortably full bladder confirmed by the participant's sensation of fullness and by a bladder volume of $\geq$150 mls indicated on the BladderScan ultrasound
- Wash/sanitize hands and put on gloves.
- Place a blue pad (chux) on the floor for participant to stand on.
- Ask the participant to stand on the blue pad, with feet shoulder width apart.
- With the folded paper towel flat in your palm, ask the participant to place the paper towel lightly against the perineum (advise that the test is being done to demonstrate leakage and hence don't press on the perineum to hold back leakage).
- Be sure the participant keeps the trifold paper towel flat in their palm, and does not fold it over onto itself to create a thicker towel.
- Instruct the participant to do 3 single hard coughs.
    - These should be very hard coughs so as not to produce a "false negative" on the PPT.
    - These should be coughs that the woman does ***without*** an intentionally/consciously contracting of her pelvic floor muscles. The instruction "do not hold back" or "do not intentionally contract your pelvic muscles" standardizes the test procedure.
    - It is helpful to add instructions such as: "Cough as though you have very bad bronchitis." If the coughs are "too light" and the towel remains dry, she can try again to produce 3 hard coughs.
    - If she saturates the paper towel at the first cough or second cough, (such that urine is not

contained on it and runs down legs or pools onto the blue pad) there is no need for her to cough again. She has already demonstrated that her leakage maxes out the absorptive capacity of the paper towel.

- With gloved hands, take the paper towel from the participant and lay it on the counter for measurement within 10 seconds of the test.
- Observe and mark the paper towel with a determination of results as follows:
  - Observe the towel carefully! Sometimes vaginal secretions are transferred to the paper towel. These are noticeable as a shiny substance sitting on the surface of the towel and poorly absorbed into the towel. It is readily distinct from the dark wetted area of urine. These towels should be marked with a large **X** on the towel for no urine leakage.
  - If the towel is unmarred with vaginal secretions or with wetted area from urine, these towels should be marked with a large **X** on the towel for no urine leakage.
  - If the towel is wet from urine loss, at 10 SECONDS outline the wetted area using a ball-point pen to trace around it. If there is more than one wetted area (sometimes over the 3 coughs leakage hits a different spot on the towel), outline each of the wetted areas. Ignore that the wetted area will continue to spread beyond the marked area after 10 seconds in cases of higher volume leakage. By protocol, wetted area is determined at 10 seconds or less.
  - Using a clear plastic ruler, measure the longest and widest diameter of the circled wetted area, in millimeters (mms). If there are additional circled wetted areas, only measure and record the circled area longest and widest diameter

    i. Do not attempt to calculate wetted area by hand. Rather, record separately the length of the wetted area and the width of the wetted area on a data collection form.

    ii. Note the measurements on the Clinical Test Form under **#2 Paper Towel Test:**

      - Mark ☐ Overflow if there is any circled wetted area that ran off the edge of the paper towel
      - Length in mm: _____
      - Width in mm:_____
      - If the Paper Towel Test is not completed, check ☐ Not done and write an explanation in the space provided

2. After the PTT is completed, the participant should be offered towels for cleaning and/or patting dry, as needed, and a chance to wash her hands.

5c. Uroflowmetry (Flowstar)

Background:

1. The Uroflow test will be conducted as part of the clinical tests to measure the volume of urine voided, the speed with which it is voided, and how long the voiding takes.
2. The Flowstar is a stand-alone uroflow system that consists of the following equipment: 1) flow sensor, 2) flow stand, 3) funnel and urine container, 4) commode, and 5) AC adapter –power supply. Flowstar

has a built-in printer connected to the Flowmeter. The sensor measures flow and volume. Replacement paper can be ordered through Office Depot.

3. The test begins automatically when a urine flow (participant starts to pee) is detected. Flow and urine volume are recorded in real-time, so the results are immediately available.
4. Checklist prior to test:
    - Check for proper placement of the: flow scale, volume scale and urine collection container on the flow sensor prior to turning machine on.
    - A clean, disposable urine collection container should be used for each participant.
    - Operation mode must be set to Automatic so flow test will start when voiding occurs.
    - Switch on the Flowstar - "Waiting for flow" mode is selected and the Waiting LED flashes.
    - Have toilet paper readily available and a receptacle for discarding, as paper should not be discarded in the uroflow.

Procedure:

- After the PTT is completed, the participant will be asked to urinate on the uroflow commode. The recommended voiding position is sitting.
- Immediately before the test is conducted, the participant should be asked to wipe off any vaginal secretions with a dampened towelette used for collecting clean catch urine specimens.
- Provide the following instructions before leaving the room for the participant to void in private:
    - Wipe urethra and vaginal area clean as if they were collecting a urine specimen at the doctor's office
    - Sit on the commode
    - Void completely like you normally would
    - Discard tissues where appropriate for the setting
    - Come back to exam room (if uroflow in separate room)
    - Please do not touch any of the uroflow equipment
- Take the report from the printer. If extra copies of the results and curves are desired, press the Print button. On the printout, the flow curve and voided volume curve are printed in real-time. Siroky plots do not need to be printed. The voided volume is the total volume voided.
- Note the following parameters on the Clinical Test Form under **#3 Uroflow**:
    - Check Box for: Printout ☐ Yes ☐ No
    - Voiding Time: _____ sec
    - Flow Time:_____sec
    - Time to Peak Flow :_____sec
    - Peak Flow: _____mL/sec
    - Average Flow: _____mL/sec

- Voided Volume:_____mL
- If the Uroflow is not completed, check ☐ Not done and write an explanation in the space provided

- Save at least 30 mL of urine from the container to test for Urine dipstick (see procedure).
- Tape the report on the Uroflow Printout Form (Form 4B). After the In-person Visit, scan this form and put it in Box (Uroflow Printouts Folder)
  - Be sure to name the file something like Uroflow_SITE_ID (ex. Uroflow_UMICH_C002)
-

Care of the Flowstar:

- The system should be cleaned after each test.
- With gloved hands, wipe down the commode seat with approved detergent..
- Clean funnel with water and/or spray detergent between each participant and wipe dry.
- Clean the Flow sensor, remove any moisture from sensor and the flow stand with a soft dry cloth.
- Discard the container and place a new urine collection container after each uroflow test.
- The urine collection container and funnel can be cleaned in a medical dishwasher or instrument washer according to the local practice and regulations.

5d. Post-Void Residual (PVR) Assessment

Background:

1. A post void residual is performed by bladder scanner after completion of the PTT and uroflowmetry test with the volume measured and recorded. This is done to assess the completeness of emptying.

Procedure: See **Bladder Volume Assessment (e.g. Bladder Scan)**

- Note the following parameters on the Clinical Test Form under **#4 Post void residual (PVR) with scan**:
  - Check Box for Printout: ☐ Yes ☐ No
  - Volume _____mL
  - If the PVR is not completed, check ☐ Not done and write an explanation in the space provided
- Tape the report on the Bladder Scan Printout Form (Form 4A). After the in-person Visit, scan this form and put it in Box (Bladder Scan Printouts Folder)
  - Be sure to name the file something like BladderScan_SITE_ID (ex. BladderScan_UMICH_C002)

5e. Dipstick Urinalysis

Background:

1. The Dipstick Urinalysis will be conducted as part of the Clinical tests to assess for the presence of leukocytes, nitrites, and/or blood.
2. All centers will use Siemins 10 G dipstick test strips
3. Test the urine within two hours after voiding.
4. Check the expiration date on the reagent strip bottle before use to be sure it has not expired.
5. Dipsticks are sensitive to air; containers should never be left open to air.

Procedure:

- Wash/sanitize hands and put on gloves.
- Pour urine from the uroflow urine collection container into a sterile specimen container
- The container should allow for the entire reagent strip to be submerged in the urine.
- Remove strip from the bottle, replace cap.
- Do not touch the test pads on the strip.
- Dip all the test pads on the strip into the urine and immediately remove the strip. If reading the strip visually, begin timing.
- Drag the edge of the strip against the container rim to remove excess urine.
- Blot the edge on a paper towel or tissue, reading visually.
- Compare each test pad to the corresponding row of color blocks on the bottle label (or laminated card).
- Read each pad at the time shown on the label, beginning with the shortest time.
- Hold the strip close to the color blocks and match carefully. Read the pads in good lighting.
- Discoloration or darkening of the test pads may indicate deterioration.
- The following are considered positive findings. See section 17 – Distress Protocol for instructions for positive findings.
    - Leukocytes (LEU) $\geq$ +1 (small) plus Nitrites positive
    - Nitrites (NIT) positive (alone- w/o Leukocytes)
    - Leukocytes + 2 (whether or not Nitrites positive)
    - Blood (BLO) $\geq$ +2 (moderate) will be considered a positive response.
- The clinical evaluator should provide the results to the RC along with the other bladder test results. These results will be provided to the judge and any abnormalities will be addressed after the judge performs the initial evaluation.
- Note the following parameters on the Clinical Test Form under **#5 Dipstick**:
    - LEU: ☐ (negative) ☐ Trace ☐ 1+ (small) ☐ 2+ (moderate) ☐ 3+ (large)
    - NIT: ☐ Negative ☐ Positive

- PRO: ☐ Negative ☐ Trace ☐ 1+ (30) ☐ 2+ (100) ☐ 3+ (300) ☐ 4+ (2000 or more)
- BLO: ☐ Negative ☐ Non-Hemolyzed (trace or moderate)
  ☐ Hemolyzed (trace) ☐ +1 (small) ☐ 2+ (moderate) ☐ 3+ (large)
- SG: _____
- GLU: ☐ Negative ☐ 100 ☐ 250 ☐ 500 ☐ 1000 ☐ 2000
- If the Dipstick is not completed, check ☐ Not done and write an explanation in the space provided

5f. Distress Protocol

If any of the following occur during the clinic testing, RCs need to notify local clinical PDWG member/VIEW representative or clinical investigator or judge (after initial interview) for referral to PCP, urology or other clinical provider per local site clinical practice.

1) If the participant can't urinate at all (on uroflow or in private bathroom) and there is > 500 mL on bladder scan
2) Post void residual (>150) – have them void again in bathroom and recheck. If still > 150mL then referral. The RC should enter the initial PVR results on the Clinical Tests (Form 4)

(3) If the following values are present on the dipstick:

- Leukocytes (LEU) $\geq$ +1 (small) plus Nitrites positive
- Nitrites (NIT) positive (alone- w/o Leukocytes)
- Leukocytes + 2 (whether or not Nitrites positive)
- Blood (BLO) $\geq$ +2 (moderate) will be considered a positive response.

Participants will be notified by the judge and/or PLUS center clinical person if any further referral or evaluation by PCP is recommended. Information can be provided to the participant using the Distress Protocol Form (Form 12).

6. After Clinical Testing

13a. Provide judge test results and 1-day diary for Second Judge Rating

Make a copy of the Clinic Test Form (Form 4), Bladder Scan Printout Form (Form 4A), Uroflow Printout Form (Form 4B), and 1-Day diary to provide to the Judge. If your site cannot copy the 1-Day bladder diary on 11x17 size paper, the diary may be copied page-by-page on 8 ½ x 11 size paper.

The evaluator is NOT to discuss anything that occurred during the clinic visit with the judge, including any unique circumstances. The evaluator may record such circumstances on page 2 of the clinic visit form (Form 4)

but only gives the judge page 1. If anything is noticed accidentially by a judge, the evaluator should note on page 2 of clinic form.

6b. Second Judge Rating

After reviewing the test results from the Clinic Visit forms and the information on the 1-Day diary, the Judge will complete a second rating of the participant using the Judge Second Rating form (Form 6).

1. The second rating will be based on the judge's assessment of the woman's bladder health to similarly situated women (i.e. age, history, general health status, etc).
2. In addition, the judge may access health information available to them (e.g. looking in the participant's electronic medical record if available).
3. If the judge feels that additional clinical testing is required to make the second rating, this will be indicated on Form 6. If the results from the testing will be available within a month of the initial rating, the form may be completed after that information is avaibale. If the test results will not be reasonably available in that time frame, this should be indicated on the form as a reason for not being able to provide the second rating.
4. Please provide this second rating as soon as possible after the first rating (ideally within 7 days, unless waiting on testing)

6c. Stipend distribution

We anticipate some participants may not complete every study measure or visit. Thus, compensation will be prorated. Participants will receive $35 for completion of the bladder diaries and $50 for completion of the in-clinic evaluation. The type of reimbursement will be managed by each research center and may include gift cards or checks depending on local standards.

6d. Enter In-Person Visit Forms into REDCap

The Clinic Test Form (Form 4), Judge Initial Rating Form (Form 5), and Judge Second Rating Form (Form 6) should be entered into REDCap within 14 days after the In-Person Visit.

Data Entry & Forms

Clinical Population Case Report Forms (CRFs)

1. Screening Forms – Available in Box, Printed by RCs
    a. VIEW Screening Form (Form 1)
    b. Contact Information Form (Form 2)
    c. Tracking/Enrollment Form (Form 3)
2. BHI Packet – Sent directly to participants by SDCC
3. Diaries – Sent to centers by SDCC, mailed to participant by RCs
    a. 1-Day Diary
    b. 2-Day Diary
4. Clinic Tests Form (Form 4) – Available in Box, Printed by RCs
    a. Bladder Scan Printout Form (Form 4A) - Available in Box, Printed by RCs
    b. Uroflow Printout Form (Form 4B) - Available in Box, Printed by RCs
5. Judge Initial Rating Form (Form 5) – Available in Box, Printed by RCs

6. Judge Second Rating Form (Form 6) – Available in Box, Printed by RCs
7. Judge Demographics Form (Form 7) – Available in Box, printed by RCs
8. Participant Exit Form (Form 8) – Available in Box, Printed by RCs
9. Adverse Event Form (Form 9) – Available in Box, Printed by RCs
10. Protocol Deviation Form (Form 10) – Available in Box, Printed by RCs
11. REDCap Data Entry Checklist (Form 11) – Available in Box, Printed by RCs
12. Distress Protocol Form (Form 12) – Available in Box, Printed by RCs

Participant Screening Form (Form 1)

- The screening form completed and entered into REDCap for all participants, even those that do not qualify
- The data for this form is entered before a participant can be randomized and enrolled in the study

Contact Information Form (Form 2)

- The contact information for all participants that qualify for the study
- The data for this form is entered by RCs before a participant can be randomized and enrolled in the study

Participant Exit Form (Form 8)

Participant exit forms are completed in the following circumstances:

Participant is lost to follow-up
Participant no longer wants to participate
Declined completing consent
No-show to in-person visit and RC does not want to continue participant participation
Declined to participate at in-person visit
Participant death
Bad Address
- This box should be checked if a mailing bounces back due to a bad address

Do not contact
- This box should be checked if a participant should no longer be contacted for a variety of reason

Clinical Tests Form (Form 4)

- Form to capture data from the clinical tests during the in-person visit
- This form is completed by the RCs and entered into REDCap by the RCs

Judge Initial Rating Form (Form 5)

- First rating form for judge during in-person visit
- This form is completed by the judge and entered into REDCap by the RCs

Judge Second Rating (Form 6)

- Second rating form for judge during in-person visit
- This form is completed by the judge and entered into REDCap by the RCs

Judge Demographics Form (Form 7)

- A short form completed by each Judge at the research centers
- This form is completed by the judge and entered into REDCap by the RCs at any point before the Judge begins seeing participants

REDCap Data Entry Checklist (Form 11)

- Tracking fields for Clinical Population participants
- These fields are completed by the RCs as needed throughout the course of the study
- The fields completed by the RCs include the following:
  - Participant needs BHI resent
    - Mark here if a participant needs the BHI resent. SDCC will be notified and the BHI will be resent to the participant.
  - Participant needs to receive alternate BHI type
    - Mark here if a participant is randomized to PAPI but would like to do the BHI electronically
      - SDCC will be notified and the participant will be sent a link to complete the BHI
    - Also mark here if a participant is randomized to CASI but would like to do the BHI on paper
      - SDCC will be notified and the participant will be sent a paper BHI
  - At-Home Kit sent & Date At-Home Kit sent
    - Once the participant is ready for their at-home kit, mark "yes" and enter the date the At-Home kit was sent.
  - In-Person Visit Date (date_mdy)
    - The Clinic Visit Date captures the date of the in-person clinic visit
    - If the in-person visit is rescheduled, this date needs to be updated.
  - Was the in-person visit rescheduled?
    - If the in-person visit had to be rescheduled, mark whether it was the first time or the second time the participant was rescheduled.

Participant PID Labels - Avery 5167

PID labels will be available in Box (VIEW Study/PID Labels) for research centers to use on study forms.

There will be 12 labels per participant:

Form	# of PID Labels
1-Day Bladder Diary	3
2-Day Bladder Diary	6
Clinic Visit Form	1
Judge Initial Rating Form	1
Judge Second Rating Form	1

Clinical Scanning Procedures

Scanned Documents

1. 1-Day Bladder Diary
2. 2-Day Bladder Diary
3. BladderScan and Uroflow printouts

Within one week the RC will scan the Bladder Diaries into Box for SDCC or batch for bulk shipment to SDCC on a monthly basis

Scanning the Diaries

Both diaries are printed on 11 x 17 (tabloid) pages. They are double-sided and do not need to be cut or altered in any way before scanning , except that the pages of the 2-day diary need to be separated (staple removed) before being scanned.

Diaries should be scanned using the top feeder of your scanner. Some scanning procedures will be site dependent, based on scanner functionality.

Scanning settings: Be sure to scan 100% of the page, no special margin settings, do NOT delete blank pages, and scan front and back. Simply unfold the pages and lay them in the feeder tray with the cover page pointing up. There is no need to reorder or flip any pages.

Diaries will be scanned directly to a Box folder where SDCC will access the documents. The email address for scanning will be plus-viewscans@umn.edu.

If bladder diaries cannot be scanned, they may be batch mailed to the PLUS Operations mailbox once a month.

Scanning the Uroflow and Bladder Scan Printouts

The Uroflow and Bladder Scan Printouts need to be scanned and added to the VIEW Study/Uroflow and Bladder Scan Printouts folder.

The printouts cannot be scanned directly to plus-viewscans@umn.edu. They will need to be scanned to your computer and uploaded to the appropriate folder in Box. If RCs would like to scan these printouts directly to the Uroflow and Bladder Scan Printouts folder, they should contact Sara Putnam at SDCC (putnams@umn.edu) for the appropriate Box folder email address.

Data Management

Policy Provisions: Data is managed by SDCC. via REDCap and SNAP survey software. Access to the study's data in REDCap and SNAP will be restricted to the members of the study team by username and password.

Each participant will be assigned a unique study identification number by the corresponding research center where the participant is recruited, which will be used for all data contained in the database.

Study forms will be entered into REDCap at redcap.ahc.umn.edu

Data requests should be directed to Kyle Rudser (rudser@umn.edu) and Charles Cain (cainx191@umn.edu) at the SDCC. SDCC will provide de-identified data based on requests from VIEW study investigators. The format of the data will be agreed upon by both parties.

Box VIEW Study Folder Organization

1. Administrative Forms
    a. Staff Training Log
    b. Judge Demographics Form
    c. Participant Exit Form
    d. Adverse Event Form
    e. Protocol Deviation Form
    f. Distress Protocol Form
    g. Tracking/Enrollment Form
    h. REDCap Data Entry Checklist
2. Clinical Visit
    a. Clinical Test Form
    b. Bladder Scan Printout Form
    c. Uroflow Printout Form
    d. Judge Initial Rating Form
    e. Judge Second Rating Form
3. Decision Log
4. ICF
    a. Advarra Consent Documents
    b. Individual Site Consent Documents
5. Kit
    a. Kit cover letter
    b. 1-Day Bladder Diary Instructions
    c. 2-Day Bladder Diary Instructions
6. Measurement Tools and Articles
7. MOP
8. Participant Screening
    a. Participant Screening Form
    b. Participant Contact Information Form
9. PID Labels
    a. Individual Site PID labels
10. Protocol
11. Recruitment Materials
12. Research Center Budget
13. Supporting Documents & FAQs
    a. Bladder Diary FAQs
    b. Clinic Visit FAQs
    c. BHI FAQs
    d. Judge Instructions
14. Uroflow and BladderScan Printouts
    a. Uroflow Printouts
    b. BladderScan Printouts

Implementation Team Structure and Communication

Policy Provisions:

1) The VIEW clinical RCs will hold regularly scheduled calls on which study progress will be discussed. The SDCC liaison and the VIEW protocol implementation team liaison will be available to troubleshoot and relay any protocol or study procedure concerns, questions, or clarifications back to the VIEW implementation team.
2) The VIEW protocol implementation team will hold weekly calls on which study progress, outcomes, and any protocol adjustments will be discussed. The RC liaison to VIEW on that call and the SDCC liaison are responsible for relaying any protocol or study procedure concerns, questions, or clarifications back to the VIEW implementation team.
3) The SDCC will make a folder in Box with Decision Log which can be used by the Research Coordinators to track study implementation issues and their resolutions.

Regulatory Requirements

Central and Center-Specific IRB Submission Procedures

Procedure:

1) The SDCC has contracted with Advarra, an external IRB which governs the regulatory requirements of the study.
2) When protocol is approved, Advarra will provide approved protocol, stamped informed consent form and signed documentation of Reliance Agreements for IRB submissions at each research center.
3) RCs will submit approved protocol with Reliance Agreements at local IRB for approval or acknowledgment and upload this letter to Advarra website and submit to SDCC.
4) The RC at each participating research center will follow their local IRB guidelines for including study documents, recruitment materials, investigator CVs, or any other items required to complete local IRB review.
5) The VIEW study documents included in the central IRB submission by the SDCC are:
   - Protocol
   - Informed Consent form/s (written, verbal script)
   - Participant Screening form
   - Participant Contact information form
   - Medical History form
   - Socio-demographic form
   - Bladder Health items
   - External criteria measures included in questionnaire
   - Recruitment materials
   - Waiver of Partial consent (per each site's requirements)
   - Clinical
     - PAPI Cover letter
     - PAPI follow-up cover letter
     - CASI cover email
     - CASI follow up cover email
     - Kit cover letter
     - 2 Day Bladder health symptom diary and instructions sheet
     - 1 Day bladder health frequency volume diary and instructions sheet
     - Clinical Test Form
     - Judge Initial Rating Form
     - Judge Second Rating form
     - Judge Demographics form
6) The VIEW study documents can be accessed on the PLUS Box in the appropriate VIEW study folder in Box.
7) The RC at each research center is responsible for notifying the SDCC of local IRB decisions via email or weekly conference call.
8) The research activities at each center may begin once both central and local IRB approvals are received.

IRB Amendment Procedures

Procedure:

1) The VIEW Investigator team and/or SDCC will notify the RCs of any changes to the protocol, informed consent or pertinent study document via email and weekly conference call.
2) The SDCC is responsible for submitting the required protocol amendment to Advarra IRB.
3) The SDCC will upload amendment approvals into the appropriate VIEW study folder in Box and notify the research centers

IRB Continuing Review/ Investigator Progress Report

1) **SDCC will respond to requirements by the central IRB at Advarra, such as preparing and submitting continuing reviews. Approvals are sent to centers for uploading to IRB.**
2) **The SDCC will upload the IRB approval letter from Advarra into the appropriate VIEW study folder in Box within 7 days after receiving them.**
3) The RC at each research center is responsible for submitting any center specific continuing review documents to their local IRB.
4) The RC at each research center is responsible for notifying the SDCC of local continuing review approval via email or weekly conference call.
5) The RC is responsible for uploading any local approval letters to the VIEW study folders in the appropriate VIEW study Box within 7 days after receiving them.

Protocol deviations:

Data entered into redcap
Annual summary
AE/SAE form

Regulatory Binder/File Per Center Policy

This section outlines the documents required to maintain the Regulatory Binder/File. Original documents listed below should be maintained in a center-specific format as well as other appropriate documents for the conduct of this study.

1. Protocol
    a. Protocol versions used for the study and updates
    b. Sample Case Report Form (CRF)
2. Manual of Procedures, all versions and all updates
3. Participant enrollment logs
4. Technical and Administrative Memos
5. Participant Specific Material
    a. Current IRB approved version of Informed Consent Form (ICF)
    b. Other written material provided to study participants
        i. Diaries, questionnaires, instructions, etc.
        ii. All material must have IRB approval
6. Advertisements
    a. If used for participant recruitment
        i. Written (i.e. poster, flyer, newspaper, etc.)
        ii. Audio (i.e. radio, television, etc.)

   b. language and photographs used in advertisements must be IRB approved
7. IRB Approval
   a. IRB approval notification (annual renewals, modifications and amendments)
8. Curriculum Vitae (CV) and medical licenses
   a. Signed and dated by PI and Sub-Is
   b. Revised, updated, and signed every two-years
9. Delegation of Authority Log (DOA)
10. Staff Training Logs & certifications
   a. Human Subject Protection training certificates for all personnel involved in protocol implementation, data collection or data entry
11. Relevant Study Related Communications
12. SAE Reports

Safety

Participant Safety and Adverse Events (Form 9)

1) Unanticipated events not related to the VIEW study do not require IRB notification. Unanticipated or unexpected events can be noted in the VIEW participant's file. The research center PI will make the determination as to the nature of relatedness.
2) Unanticipated or Unexpected events are assessed according to the following criteria:
   • in terms of nature, severity, or frequency given the research procedures that are described in the protocol-related documents
   • or reasonably certain related to participation in the research
   • suggests that the research places subjects or others at a greater risk of harm (i.e., physical, psychological, economic, or social harm) than was previously known or recognized
   • in loss of privacy or confidentiality to the research participant
3) Adverse Events (AE) are assessed according to the following criteria:
   • the event has not been described in the VIEW protocol and/or Informed Consent in terms of nature, severity or frequency.
   • the event either caused harm or placed the participant at greater risk of harm (physical, psychological, economic, or social) than was previously known or recognized.
   • the event was related, or possibly related to participation in the VIEW study.
4) Additional requirements:
   • Each research center should follow its Institutional Review Board requirements in reporting unanticipated problems or adverse events.
   • Each research center RC is responsible for notifying the SDCC via REDCap and having site PI sign off on adverse event forms. Only the center where the event occurred is required to submit to their local IRB.
   • Each research center RC is responsible for filing submitted forms, IRB responses and other essential documentation in the VIEW regulatory binder and uploading to the PLUS Box folder.
   • Each research center where events were submitted will be required to submit a problem summary report at the time of continuing review. If needed, the problem summary report is generated by SDCC and sent to each center. Each research center should follow its Institutional Review Board's requirements for essential documents at time of continuing review.
   • All documents should be filed in the VIEW regulatory binder and uploaded to the PLUS Box folder.
   5) Serious Adverse Events (SAE) Investigators are required to submit any serious adverse events involving subjects enrolled at the site(s) that are determined to be **unexpected** and probably, possibly, or

definitely **related** to the test article or research procedures. SAEs are assessed according to the following criteria, and are defined to include any adverse experience resulting in the following:

- Persistent or significant disability or incapacity
- Hospitalization
- Life threatening
- Death

Procedure for Reporting Participant Safety and Adverse Events

1) The RC at each research center should follow its Institutional Review Board requirements at their center for reporting serious adverse events in a timely manner.
2) The RC at each research center is responsible for notifying the SDCC of adverse events via REDCap and the local PI via sign off on the AE form. Only the center where the event occurred is required to submit to the IRB.
3) The RC at each research center is responsible for filing submitted forms, IRB responses and other essential documentation to the VIEW regulatory binder and uploading to the PLUS Box folder.
4) The RC at each research center where events occurred will be required to submit a problem summary report at the time of continuing review.
5) Each research center should follow its Institutional Review Board's requirements for essential documents at time of continuing review.
6) All documents should be kept on file at the research center and approval letters uploaded to the PLUS Box folder.

Implementation Team Contact List

The VIEW implementation team is made up of at least one clinician member from each of the clinical centers and several members from the SDCC as outlined below:
Loyola (PIs Brubaker & Mueller) - Elizabeth Mueller
University of Alabama at Birmingham(PI Burgio) -Alayne Markland
University of California San Diego (PI Lukacz)-Emily Lukacz*
University of Michigan (PI Miller)- Lisa Kane-Low
University of Pennsylvania (PI Newman) - Diane Newman
Washington University (PI Sutcliffe)- Jerry Lowder
Yale (PI Rickey) - Leslie Rickey
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Advarra contact information
To contact Advarra, log into CIRBI and click on the "Contact IRB" button.

Study Checklist

VIEW Pre-Enrollment Process		
STEP	**DETAILS**	**COMPLETED**
1. Recruitment	Materials in Box (VIEW Study/Recruitment Materials folder)	
2. Screening and Enrollment	Materials in Box (see specific folders below)	
a. Complete Participant Screening Form & Contact Information Forms	Forms 1 &2: VIEW Study/Participant Screening Folder	
b. Fill out Enrollment/Tracking Form	Form 3: VIEW Study/Administrative Forms	
c. Enter Participant Screening & Contact Information Forms in REDCap	REDCap forms: Form 1:Participant Screening Form 2:Contact Info	
VIEW Post-Enrollment Process		
3. Randomization	Data entry in REDCap triggers SDCC notification for randomization and mailing/email of BHI	
4. BHI Completion	SDCC notifies RC if not complete. RC calls and follows up as needed	
a. If participant needs BHI resent, mark this in REDCap	Form 11:REDCap Data Entry Checklist (VIEW Study/Administrative Forms)	
b. If participant needs alternate BHI type (ex. paper), mark this in REDCap	Form 11:REDCap Data Entry Checklist (VIEW Study/Administrative Forms)	
c. If participant does not complete BHI, RC will be notified	The participant will be disenrolled and the RC will need to replace the participant on the tracking/enrollment form	
5. Schedule In-Person	Coordinate Judge, evaluator and clinical visit timing	
a. Try to avoid scheduling when participant may be menstruating		
b. Mark the date of the in-person visit in REDCap	Form 11:REDCap Data Entry Checklist (VIEW Study/Administrative Forms)	
6. Mail Kit	Mail kit within the next business day of scheduling in-person visit	
a. Mark that the kit was sent and the date in REDCap	Form 11:REDCap Data Entry Checklist (VIEW Study/Administrative Forms)	
7. Bladder Diary Completion Reminder	4-7 days prior to in-person visit. Repeat 1-2 days prior to in-person visit as needed. Reschedule as needed	
a. If the participant needs to be rescheduled, change the in-person visit date and mark in REDCap	Form 11:REDCap Data Entry Checklist (VIEW Study/Administrative Forms)	

In-Person Day of Visit Process and Checklist		
8. Informed consent	Sign and retain hard copy for files	
9. Review the diaries	1-day and 2-day, for legibility	
10. Pre-Clinical Testing Questions	Ask to participant before beginning the clinical tests or initial judge interview/rating	
11. Initial Judge Assesment and Rating	Provide the judge with Form 5: Judge Initial Rating Form (VIEW Study/Clinical Visit)	
12a. Bladder scan	Confirm greater than 150 ml	
12b. Paper towel test		
12c. Uroflowmetry		
12d. Post-void residual bladder scan		
12e. Urine dipstick		
12f. Distress Protocol	If at any time there is indication for referral, can be provided to participant during visit or any time after visit. Complete Distress Protocol form (Form 12) to provide to participant.	
13a. Provide judge test results and 1-day diary for Second Judge Rating	Clinic Test Form (Form 4), Bladder Scan Printout Form (Form 4A), Uroflow Printout Form (Form 4B), and 1-Day diary	
13b. Second Judge Rating	Within 7 days Judge fills out form and returns to RC	
13c. Stipend distribution	Provide participant with prorated reimbursement	
13d. Enter In-Person Visit forms in REDCap	Can be provided to participant during visit or any time after visit	