

STATISTICAL ANALYSIS PLAN

Title: A Comparative Crossover Study on the Safety, Efficacy, and Patient Reported Satisfaction of the PureWick™ System with an Established Comparator Overnight in the Home Setting for Incontinence in Adult Males

Protocol No.: UCC-24HC013

NCT No.: NCT06850259

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Version & Date: Version 1.0 – July 1, 2025

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General Information	
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CIP/CPSP Version:	1.0

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1.0 INTRODUCTION

1.1 Background and Rationale

Nocturnal enuresis, or overnight urinary incontinence, is a significant concern among men, particularly as they age. Studies indicate that the prevalence of urinary incontinence in men ranges widely, with various factors contributing to its occurrence. Urinary incontinence affects a substantial portion of the male population, with future directions focusing on better management and treatment options. Furthermore, cognitive impairment or dementia significantly increases the risk of incontinence, emphasizing the need for targeted interventions in these groups. Urinary incontinence in home care settings not only affects the quality of life but also presents severe challenges in daily living. There is a profound impact of urinary incontinence on the lives of elderly men, as it can lead to social isolation and decreased quality of life. These findings collectively underscore the importance of addressing nocturnal enuresis through comprehensive and individualized care strategies.

Current management options for male incontinence at home include behavioral techniques, lifestyle modifications, and medical interventions. Absorbent products and traditional external catheters are practical solutions for managing incontinence in home care settings, although they may impact the quality of life. Traditional sheath style male external catheters may not be effective for all males. Medications such as anticholinergics and desmopressin are effective in reducing urinary frequency and urgency. However, these management options can have drawbacks, including serious side effects from medications, the inconvenience of using absorbent products, and the psychological impact of living with incontinence. These challenges underscore the need for individualized care strategies to effectively manage male incontinence at home.

Difficult-to-manage urinary incontinence in men in the home setting poses health risks and can lead to severe consequences. It has long been understood that urinary incontinence is associated with increased risks of hospitalization, nursing home admission, and mortality. This underscores the critical need for effective management strategies to prevent these adverse outcomes. Similarly, it has been reported that urinary incontinence is linked to a higher likelihood of death, nursing home admission, and functional decline. These findings highlight the importance of addressing urinary incontinence promptly and effectively to mitigate its impact on overall health and quality of life. Without proper management, individuals may experience complications such as skin injury, falls, and a decline in mental health due to the stress associated with incontinence for these patients and their caregivers.

The study will collect clinical and qualitative preference data from adult male patients requiring urine output management overnight in the home setting, the results of which will advise reimbursement in the United States (U.S.). This pilot will inform the sample size and the methodology for a future randomized control trial.

1.2 Objectives and Endpoints

Table 1. Objectives and Endpoints

Objective Type	Objective	Endpoint
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Primary	To compare efficacy and safety of PureWick™ Male System (PureWick™ Male External Catheter & PureWick™ Urine Collection System) and sheath-style male external catheters.	- Efficacy – Daily capture rate via bed pad weights and captured volume. - Safety – Number of device-related Adverse events requiring medical intervention in each treatment group.
Secondary	- To assess participant device satisfaction and preference between the PureWick™ Male System (PureWick™ Male External Catheter & PureWick™ Urine Collection System) and sheath-style male external catheters after treatment completion. - To measure study device adherence/dislodgement - Tolerability - To assess the tolerance of PureWick™ System and sheath-style male external catheters over the expected duration of use.	- End of study preference questionnaire administered at study completion. - Proportion of device wear nights that the device became dislodged. - Number of nights of actual use of each device.
Exploratory	To assess impact of PureWick™ Male System and sheath-style male external catheters on sleep quality related Quality of Life.	PROMIS Sleep Disturbance score collected at baseline and every 7 days during treatment.

1.3 Acceptance Criteria and/or Investigation Hypothesis

None. No formal hypothesis test is planned for this pilot study.

2.0 STUDY DESIGN

2.1 Study Design

In this prospective, open-label, crossover trial, approximately 15 men with Nocturnal Urinary Incontinence requiring the use of diapers or pads in bed will be 1:1 randomized to a treatment sequence using two devices (PureWick™ MEC and UltraFlex™ Self-Adhering Male External Catheter) and followed for approximately 16 days through 2 treatment phases. For purposes of this study, the PureWick™ Male System will be referenced to include the PureWick™ Male External Catheter used in conjunction with the PureWick™ Urine Collection System, including the tubing and the canister.

At the start of the study, participants will be consented and screened against inclusion/exclusion criteria. Participants that have met all eligibility criteria will be assigned a participant ID treatment order. Participants will complete an anatomical measuring procedure to determine sizing for the UltraFlex™ Self-Adhering Male External Catheter at the baseline visit. Participants will view the training video and/or review the IFU for the applicable product at the beginning of each treatment phase and have access to the Instructions for Use (IFU) to review. Participants will use the device assigned in treatment phase 1 overnight while sleeping for 1 week (7 days) before transitioning to the second assigned device in treatment phase 2. Prior to treatment phase 2, participants will have a washout period for a minimum of 2 days.

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The primary objectives are to evaluate safety (device related adverse events requiring medical intervention) and efficacy (daily capture rate). Safety will be evaluated using incidence rate of AEs requiring medical intervention and efficacy will be measured based on daily capture rate.

Nurses will visit patients' homes daily to assess primary endpoints and collect data. The nurses will also assess skin irritation daily using the Draize Scale.

The secondary objectives are to assess participants' satisfaction with and preference between the PureWick™ Male External Catheter and sheath-style male external catheters after treatment completion, device adherence/dislodgement, and device tolerance over the expected duration of use.

The exploratory objective will assess the impact of PureWick™ Male System and sheath-style male external catheters on sleep quality using self-reported PROMIS Sleep Disturbance assessments.

This study will assess the performance of, and participant reported satisfaction with the PureWick™ System in the home setting. The endpoints chosen for the study were selected based on peer-reviewed research and feedback from expert consultants, Centers for Medicare & Medicaid Services, applicable health authorities and urology key opinion leaders.

2.2 Study Population

Adult male participants requiring urine output management overnight in the home setting will be recruited for this study by the study site from their current patient list. Study sites may advertise and recruit new patients if eligible participants from the patient list have been exhausted.

To best mimic potential users of the PureWick™ System, participants ≥ 65 years of age will be enrolled.

2.2.1 Inclusion Criteria

In order to be eligible to participate in this study, an individual must meet all of the following criteria:

1. Adult male participants ≥ 65 years of age at the time of signing the informed consent
2. Male anatomy at the time of enrollment
3. Currently use diapers, pads, or equivalent at night for urine output management
4. Willing to comply with all study procedures in this protocol
5. Provision of signed and dated informed consent form

2.2.2 Exclusion Criteria

Subjects are excluded from the study if any of the following criteria apply:

1. Has frequent episodes of bowel incontinence; or
2. Has chronic urinogenital infections, active genital herpes; or
3. Has Urinary retention; or
4. Has experience using study devices in the home setting within the last year; or

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5. Is agitated, combative, and/or uncooperative and may remove the external catheter; or
6. Has any wound, open lesion or irritation on the genitalia, perineum, or sacrum; or
7. Any other condition that, in the opinion of the investigator, would preclude them from participating in the study; or
8. Is considered a vulnerable population.

2.3 Randomization and Blinding

Randomization will occur after informed consent is obtained and after study personnel ensures the participant meets all eligibility criteria. Subjects will be randomized 1:1 to the two sequences of treatment (using PureWick™ Male System as treatment 1 and UltraFlex™ Self-Adhering Male External Catheter as treatment 2, or the reversed order). This design allows the evaluation of elements such as the carryover effect, period effect, and sequence effect. Block randomization will be carried out using a fixed block size of 2.

This is an open-label study. Blinding is not applicable.

2.4 Sample Size

Approximately 15 participants will be enrolled. The sample size is planned based on operational and practical considerations and is adequate for the purpose of this pilot study.

2.5 Interim Analysis

Not applicable.

2.6 Study Procedure

Table 2. Schedule of Activities

Assessment	On-Site Visit	Treatment 1 (In-Home Assessments)		Washout Period (2 Days ¹)	Treatment 2 (In-Home Assessments)		
	Screening/ Enrollment	Baseline	Night 1-7 (Device Use)		Baseline (Crossover)	Nights 1-7 (Device Use)	End of Treatment
Device Demonstration ²	X						
Informed Consent	X						
Inclusion & Exclusion Criteria	X						
Demography	X						
Medical History	X						
Participant ID Assignment and Treatment Order Randomization	X						
Introduction of Home Nurse (On-Site)	X						
Participant Self-Reported Skin Assessment	X						
Participant to Complete Anatomical Measurement	X						

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	On-Site Visit	Treatment 1 (In-Home Assessments)			Treatment 2 (In-Home Assessments)		
Assessment	Screening/ Enrollment	Baseline	Night 1-7 (Device Use)	Washout Period (2 Days ¹)	Baseline (Crossover)	Nights 1-7 (Device Use)	End of Treatment
Nocturnal Enuresis (NE) attribute survey	X						
Nurse Visual Skin Assessment & Draize Scoring		X	X		X	X	
Nurse Confirm Study Supplies		X			X		
Participant to View Device Training Video and/or Instruction for Use (IFU)		X			X		
Nurses takes Pre-weight		X	X		X	X	
Participant wears device overnight			X			X	
Nurse takes post-weight			X			X	
Nurse documents Device Dislodgement			X			X	
Nurse administers PROMIS Sleep Disturbance Questionnaire		X		X ³			X ³
End of Study Preference Questionnaire ⁴							X
Nurse completes End of Study Disposition							X
AE/SAE Review ⁵							
Device Deficiencies ⁵							

1 -- Minimum of 2 days for the washout period. If the participant has a skin issue, the washout period can be extended up to 7 days. The nurse should call the participant to confirm if the skin issue was resolved prior to scheduling the Treatment 2 Baseline visit

2 --To occur prior to consenting the participant

3 -- PROMIS Sleep Disturbance questionnaire to be completed after device use night 7 in each treatment phase

4 -- To be completed at completion or discontinuation of treatment phase 2. Questionnaire should only be completed if each device was used for at least one night

5 - Collect if applicable

3.0 INTENDED STATISTICAL SOFTWARE AND DATA INFORMATION

3.1 Intended Statistical Software

SAS Version 9.4 (SAS Institute, Cary, NC) or above will be used to perform analyses and generate outputs.

3.2 Data Information

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Analysis datasets and a document outlining the specification of analysis datasets will be stored in a version-controlled environment.

4.0 ANALYSIS POPULATION SET(S)

4.1 Populations Definitions

The following populations are defined:

Population	Description
Enrolled	Subjects who sign ICF.
Intent-to-Treat (ITT)	Subjects who sign ICF and are randomized to a treatment sequence.
Per-Protocol (PP)	ITT subjects without major protocol deviation.

ITT population will be used for the analyses of endpoints. Sensitivity analyses may be conducted using PP population.

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5.0 STATISTICAL ANALYSIS / CALCULATIONS

5.1 *Derived Variables*

Daily capture rate (%) is defined as: captured urine weight / (captured urine weight + leaked urine weight) *100, where

- Captured urine weight is defined as:
 - PureWick: Canister with lid (without tubing attached) post-use weight (g) - Canister with lid (without tubing attached) pre-use weight (g), and
 - UltraFlex: (Graduated cylinder post-use weight (g) - Graduated cylinder pre-use weight (g))+(Used urine collection bag with tubing attached in canister (no lid) post-use weight (g) - Unused urine collection bag with tubing attached in empty canister (no lid) pre-use weight (g))
- Leaked urine weight is defined as:
 - bed pad 1 post-use weight (g) – bed pad 1 pre-use weight (g) when the answer for “Was 2nd bed pad used?” is equal to “No” on Case Report Form (CRF) page PureWick(TM) Male External Catheter Placement or UltraFlex(TM) Self-Adhering Male External Catheter Placement and
OR
 - (pad 1 post-use weight (g) – bed pad 1 pre-use weight (g)) +(pad 2 post-use weight (g) – bed pad 2 pre-use weight (g)) when the answer for “Was 2nd bed pad used?” is equal to “Yes” on Case Report Form (CRF) page Male External Catheter Placement or UltraFlex(TM) Self-Adhering Male External Catheter Placement

A void of which (captured urine weight + leaked urine weight) < 10 g is considered not evaluable for the purpose of analyzing capture rate.

5.2 *Analysis Methods*

5.2.1 General Considerations

5.2.1.1 Handling of Missing Data

Endpoint data may be missing due to reasons including lost to follow-up or withdrawal of consent. Reason for missing endpoints will be reported. For the primary efficacy endpoint, if capture rate assessments are missing for part of the study period, derivation of the primary efficacy endpoint will be based on available data.

5.2.1.2 Comparability of Groups

Baseline characteristics and potential confounders will be compared between treatment sequence groups. Subgroup analysis or regression may be used if potential confounding effect is suspected.

5.2.1.3 Poolability of Data

The effect of investigational site will be evaluated using regression models, with primary endpoint as the dependent variable, and treatment, investigational site, and the interaction term between treatment and investigational site as fixed effects.

5.2.1.4 Multiplicity Control

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No formal hypothesis test is planned for this pilot study. P values and confidence intervals may be provided for exploratory purposes and are unadjusted for multiplicity.

5.2.2 Primary Endpoint

5.2.2.1 Primary Efficacy Endpoint

Capture rate is evaluated daily during participant treatment 1 and treatment 2. Nightly capture rate (%) is defined as:

$$\text{captured urine weight} / (\text{captured urine weight} + \text{leaked urine weight}) * 100$$

The primary efficacy endpoint is derived by computing the mean of nightly capture rate during each treatment. Descriptive statistics of the primary efficacy endpoint, including mean, standard deviation, median, and range will be provided by treatment. A scatter plot for Capture Rate (y axis) vs. Device Use Night # (x axis), with different colors representing PureWick and UltraFlex and different panels representing study subject will also be provided. The summary statistics (mean, 95% CI for mean, median) for paired difference in mean nightly capture rate between the two treatment arms will be provided. Sensitivity analyses using linear mixed model (with device, treatment phase, device use night, volume, and sleep duration as the fixed effect, and participant as the random effect), beta regression (with treatment, phase, and study day as the fixed effect, and participant as the random effect) will also be performed.

5.2.2.2 Primary Safety Endpoint

The primary safety endpoint is derived by counting the number of device-related adverse events requiring medical intervention for each treatment. Descriptive statistics of the primary safety endpoint, including mean, standard deviation, median, and range will be provided by treatment. Paired difference in the number of device-related adverse events between treatments will be provided.

5.2.3 Secondary Endpoint

5.2.3.1 End of Study preference questionnaire

Items in the questionnaire will be summarized as categorical variables (using frequency count and percentage).

5.2.3.2 Proportion of device wear nights that the device became dislodged

The proportion of device wear nights that the device became dislodged will be summarized using descriptive statistics by treatment. Paired difference between treatment will be provided.

5.2.3.3 Tolerability - Number of nights of actual use of each device

The calculation for the number of days of actual use will involve counting the non-missing records for each device, determined by the number of non-missing Device Use Night # entries. Subsequently, the number of nights of actual use will be summarized using descriptive statistics by treatment. Paired differences between treatments will also be provided.

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5.2.4 Exploratory Analysis

5.2.4.1 Questionnaire PROMIS Sleep Disturbance

The questionnaire consists of 4 items with a total raw score ranging from 4 to 20 (sum of the 4 questions). The total raw score will be translated into a T-score for each participant using the score conversion table from the PROMIS sleep scoring manual (Table 3). All questions must be answered in order to produce a valid score using the scoring tables. The T-score rescales the raw score into a standardized score with a mean of 50 and a standard deviation (SD) of 10. If a participant has skipped a question, the HealthMeasures Scoring Service (https://www.assessmentcenter.net/ac_scoringervice) will be used to generate a final score. Items in the questionnaire will be summarized both as categorical variable (using frequency count and percentage) and as continuous variables (using mean, standard deviation, median, and range) by treatment.

Table 3. PROMIS Sleep Disturbance 4a - Short Form Conversion Table

Raw Score	T-score
4	32.0
5	37.5
6	41.1
7	43.8
8	46.2
9	48.4
10	50.5
11	52.4
12	54.3
13	56.1
14	57.9
15	59.8
16	61.7
17	63.8
18	66.0
19	68.8
20	73.3

6.0 SUMMARY OF GENERAL STUDY DATA

6.1 Subject Disposition

Subject disposition data is collected on the 'Disposition - Treatment 1 Completion Status', 'Disposition - Treatment 2 Completion Status', and 'Disposition – End of Study' CRF pages. The summary of the number of subjects enrolled, screen failure, randomized and not treated, randomized and treated, ITT subjects, completed the study, and discontinued from the study by reason of discontinuation will be provided. Screen failures will be summarized for each inclusion/exclusion criteria that were not met.

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6.2 Protocol Deviations

The number of subjects with protocol deviations for the ITT subjects will be summarized with descriptive statistics by the nature of the deviation. The major or minor deviations will be identified and classified as in Appendix 3 prior to data analyses of major reporting.

6.3 Demographics and Baseline Variables

Demographics and baseline characteristics will be summarized with descriptive statistics for the ITT population. Summary statistics for categorical variables will include frequency counts and percentages and for continuous variables will include mean, standard deviation, minimum, median, and maximum.

Demographics and baseline characteristics include:

- Age at time of Informed Consent (years)
- Sex
- Ethnicity (Hispanic or Latino, Not Hispanic or Latino, Not Reported, and Unknown)
- Race (American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, White, Not Reported, and Unknown)
- Primary diagnosis
- Medical history
- Vital Signs
- Participant Self-Reported Skin Assessment
- Nocturnal Enuresis (NE) Attribute Survey

6.4 Device Failure, Malfunctions and Defects

All device deficiencies will be summarized by the failure code for the ITT population.

7.0 SAFETY ANALYSIS

An overall summary including the number and percentage of subjects with at least one AE, total number of AEs, SAEs, UADEs, serious health threat, AEs by relationship to the Device/Procedure, and AEs by severity of the event will be summarized for the ITT subjects. In addition, the following summary tables will be provided:

- Number of AEs by System Organ Class (SOC) and Preferred Terms (PT)
- Number of SAEs by System Organ Class (SOC) and Preferred Terms (PT)
- Number of AEs by relationship to Study Device by System Organ Class (SOC) and Preferred Terms (PT)
- Number of AEs by relationship to Procedure by System Organ Class (SOC) and Preferred Terms (PT)

Listing of all AEs, SAEs, UADEs, and serious health threat will be provided.

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8.0 INTERIM ANALYSIS PLAN

Not applicable.

9.0 STATISTICAL OUTPUT VALIDATION PLAN

Primary endpoints will be double programmed. Other endpoints may be double programmed, peer reviewed or self-validated, depending on complexity and type of endpoint. The validation approach will be documented in the study-specific Programming Code Tracking Sheet and/or directly in the code used for validation.

10.0 REFERENCES

None.

11.0 APPENDIX

Appendix 1	Tables, Figures and Listing Shells
Appendix 2	Derived Data Specification
Appendix 3	Protocol Deviations: Major/Minor Classification

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1.0	01-Jul-2025	Shuangshuang Fu	Original

Signature Page for VV-TMF-356928 v1.0

Reason for signing: Finalize	Name: Shuangshuang Fu Role: Clinical Statistician Date of signature: 01-Jul-2025 20:20:31 GMT+0000
Reason for signing: Finalize	Name: Danielle Redmond Role: Medical Affairs Core Team Member Date of signature: 01-Jul-2025 21:20:54 GMT+0000
Reason for signing: Finalize	Name: Swathi Vasireddi Role: Clinical Statistical Programmer Date of signature: 02-Jul-2025 12:56:30 GMT+0000
Reason for signing: Finalize	Name: Kirsten Hammitt Role: Clinical Project Management, Site Management and Monitoring, and Clinical Safety Management Date of signature: 03-Jul-2025 15:53:10 GMT+0000
Reason for signing: Finalize	Name: Yanchang Zhang Role: Clinical Statistician Date of signature: 03-Jul-2025 16:19:49 GMT+0000

Signature Page for VV-TMF-356928 v1.0