General Information	
Report Date:	11-Sep-2024
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CIP Title:	A Comparative Crossover Study on the Safety, Efficacy, and Patient Quality of Life Comparing PureWick™ System with an Established Comparator in the Home Setting for Incontinence Overnight
CIP Number:	UCC-8007
CIP/CPSP Version:	5.0
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1.0 INTRODUCTION

1.1 Background and Rationale

The PureWick™® Female External Catheter (PureWick™ FEC) is an external drainage device to address the need for an effective, non-invasive method of managing urine output in adult incontinent women. The device utilizes suction to drain urine away from the patient through tubing that is connected to a collection canister. PureWick™ FEC can use either wall suction (acute care setting) or a free-standing PureWick™ Urine Collection System (home setting/skilled nursing facility). In the U.S., PureWick™ FEC is a Class I, 510(k) exempt device. In Europe, the PureWick™ FEC is a Class I, CE marked, non-sterile device.

The study will collect clinical and quality of life data from patients requiring urine output management overnight in the home setting, which will aid reimbursement in France and the United States (U.S.). This pilot will inform the sample size and the frequency of nursing visits for the future home-setting, randomized control trial.

1.2 Objectives and Endpoints

Table 1. Objectives and Endpoints

Objectives and Endpoints	Objective(s)	Endpoint(s)
	Primary To compare efficacy and safety of PureWick™ System and Hollister® Female Urinary Pouch External Collection Device	Primary • Efficacy – Daily capture rate via bed pad weights and captured volume. • Safety – Daily skin irritation score using the Draize Scale

	Secondary • To assess impact of PureWick™ System and Hollister® Female Urinary Pouch External Collection Device on Nocturnal Incontinence related Quality of Life and sleep disturbance. • Tolerability – To assess the tolerance of PureWick™ System and Hollister® Female Urinary Pouch External Collection Device over the expected duration of use • To assess participant comfort and ease of use of PureWick™ System and Hollister® Female Urinary Pouch External Collection Device • To assess participant final preference between the PureWick™ System and Hollister® Female Urinary Pouch External Collection Device after treatment completion	Secondary • Nocturia Quality of Life (N-QOL) score collected at baseline and every 2 weeks during treatment • PROMIS Sleep Disturbance questionnaire at baseline and every 7th days during treatment. • Tolerability – Number of days of actual use of both devices & Discontinuation rate attributed to the device's inconvenience or discomfort • Overall comfort and ease of use scores on a 5-point Likert scale (brief questionnaire) collected at the end of each treatment phase • Conduct end of study interview. Asking for details of participant's use preference of both devices during treatment phase.

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

This is a prospective, open-label, 2 by 2, crossover trial to evaluate the safety, efficacy, and patient quality of life of PureWick™ System in comparison with Hollister® Female Urinary Pouch. Participants are randomized 1:1 to use PureWick™ System in phase 1 and Hollister® Female External Pouch in phase 2, or to use Hollister® Female Urinary Pouch in phase 1 and PureWick™ System in phase 2. Each phase lasts 4 weeks, with a 2-4 week washout period between phase 1 and phase 2. Capture rates and Draize Scale are assessed daily during both phases. Nocturia-Quality of life is assessed at baseline and every 14 days during phases 1 and 2. PROMIS Sleep disturbance is assessed at baseline and every 7 days during phases 1 and 2. User preference questionnaires are completed at the completion of each treatment phase with final user preference between the PureWick™ System and Hollister® Female Urinary Pouch External Collection Device after completion of both treatments. The primary efficacy endpoint is the mean of daily capture rate. The primary safety endpoint is the mean of daily assessments of Draize Scale.

2.2 Study Population

Adult female 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 >18 years of age will be enrolled. It is desired that at approximately 90% of participants are >65 years of age. This study will enroll approximately 30 participants.

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 Female Participants >18 years of age at the time of signing the informed consent.
2. Currently use diapers or equivalent at night for urine capture (“Change complet” (FR))
3. Willing to comply with all study procedures in this protocol
4. Provision of signed and dated informed consent form

2.2.2 Exclusion Criteria

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

1. Has frequent episodes of bowel incontinence without a fecal management system in place; or
2. Has moderate to heavy menstruation and cannot use a tampon or menstrual cup; or
3. Has Urinary tract, vaginal or other chronic infections, active genital herpes; or
4. Has Urinary retention; or
5. Is agitated, combative, and/or uncooperative and may remove the external catheter or pouch; or
6. Has any wound, open lesion or irritation on the genitalia, perineum, or sacrum; or
7. Has any pre-existing neurological, psychiatric, or other condition that would

confound quality of life assessment or would make it difficult to self-report on quality-of-life questionnaires in the opinion of the investigator; or

8. Is known to be pregnant at time of enrollment (for women of childbearing age); or
9. Any other condition that, in the opinion of the investigator, would preclude them from participating in the study.

2.3 Randomization and Blinding

Subjects will be randomized 1:1 to the two sequences of treatment (using PureWick™ FECs in phase 1 and Hollister® Female External Pouch in phase 2, or the reversed order). This design allows the evaluation of elements such as the carryover effect, period effect, and sequence effect. To begin treatment phase in either the U.S. or France, using a prepared randomization schedule participants will be randomized 1:1 to use either PureWick™ FEC in phase 1 and Hollister® FUP in phase 2, or vice versa. Block randomization will be carried out using a fixed block size of 2 and stratified by investigational site and geography.

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

2.4 Sample Size

Approximately 30 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

Procedure	Screening / Enrollment	Daily Study Home Visits												
		Ph 1 Baseline Day 1	Ph1 Day 2-14	Ph1 Day 15	Ph1 Day 16-28	Ph1 Day 29	Ph1 Day 30	Wash out Day 29-42 (+14 days)	Ph2 Baseline Day 1	Ph2 Day 2-14	Ph2 Day 15	Ph2 Day 16-28	Ph2 Day 29	Ph2 Day 30
Informed consent	X													
Inclusion and exclusion criteria	X													
Demography	X													
Medical history	X													
Katz ADL Index	X													
Participant ID Assignment and Randomization	X													
Introduction to Home Nurses (On site or Virtual)	X													
Visual Skin Assessment & Draize Scoring (Both site and Nurses)		X	X	X	X	X	X		X	X	X	X	X	X
Nurses Confirm Study Supplies		X							X					

Procedure	Screening / Enrollment	Daily Study Home Visits												
		Ph 1 Baseline Day 1	Ph1 Day 2-14	Ph1 Day 15	Ph1 Day 16-28	Ph1 Day 29	Ph1 Day 30	Wash out Day 29-42 (+14 days)	Ph2 Baseline Day 1	Ph2 Day 2-14	Ph2 Day 15	Ph2 Day 16-28	Ph2 Day 29	Ph2 Day 30
Nurses Have Participant Complete N-QOL		X		X*		X*			X		X*		X*	
Nurses Have Participant Complete PROMIS Sleep Disturbance		X	X* Day 8	X* Day 15	X* Day 22	X* Day 29			X	X* Day 8	X* Day 15	X* Day 22	X* Day 29	
Nurses Conduct Device Training w/Participants		X							X					
Nurses Pre-weigh urine canister or graduated cylinder		X							X					
Nurses Pre-Weigh Overnight Pads and Mesh underwear (if applicable)		X	X	X	X				X	X	X	X		
Participants wear investigational device		X	X	X	X				X	X	X	X		

Procedure	Screening / Enrollment	Daily Study Home Visits												
		Ph 1 Baseline Day 1	Ph1 Day 2-14	Ph1 Day 15	Ph1 Day 16-28	Ph1 Day 29	Ph1 Day 30	Wash out Day 29-42 (+14 days)	Ph2 Baseline Day 1	Ph2 Day 2-14	Ph2 Day 15	Ph2 Day 16-28	Ph2 Day 29	Ph2 Day 30
Nurses Measure Urine Output			X	X	X	X				X	X	X	X	
Nurses Post-Weigh Overnight Pads and Mesh Underwear (if applicable)			X	X	X	X				X	X	X	X	
Participant Completes Preference and Ease of Use Survey*						X*							X*	
Participant Completes End of Study Preference Survey														X*
AE review (If applicable)														
SAE review (If applicable)														
Device Deficiencies (If applicable)														

GFM-10082C

*To be completed per treatment schedule or upon treatment discontinuation, whichever comes first.

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

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 signed ICF.
Intent-to-Treat (ITT)	Subjects who signed ICF and randomized to a treatment sequence.
As-Treated (AT)	ITT subjects, grouped by actual treatment sequence, if different from planned 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 carried out using AT or PP population.

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(TM): Canister final weight (g) - Canister starting weight (g), and
  - Hollister(R): Graduated cylinder final weight (g) - Graduated cylinder baseline 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) Participant Placement or Hollister(R) Female External Collection Pouch Participant 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 PureWick(TM) Participant Placement or Hollister(R) Female External Collection Pouch Participant Placement
    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)) +(Mesh underwear post-use weight (g) – Mesh underwear pre-use weight (g) when theDaily answer for “Was 2nd bed pad used? ” is equal to “Yes” and when the answer for “Did participant use the mesh underwear provided while using the study device?” is equal to “Yes”(This scenario only applies to PureWick™ group.).
  - OR
  - (pad 1 post-use weight (g) – bed pad 1 pre-use weight (g)) +(Mesh underwear post-use weight (g) – Mesh underwear pre-use weight (g) when the answer for “Was 2nd bed pad used? ” is equal to “No” and when the answer for “Did participant use the mesh underwear provided while using the study device?” is equal to “Yes” (This scenario only applies to PureWick™ group.).

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. For the primary efficacy endpoint, if capture rate assessments are missing for part of a treatment phase, derivation of the primary efficacy endpoint will be based on available data. For the primary safety endpoint, the main analysis will be based on available data. Sensitivity analyses may be performed for the primary safety endpoint where missing data is imputed using methods including linear interpolation or last-observation-carry-forward.

5.2.1.2 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.

5.2.1.3 Multiplicity Control

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 rates is evaluated daily during participant phase 1 and phase 2. Daily capture rate (%) is defined as:

captured urine weight / (captured urine weight + leaked urine weight) *100

The primary efficacy endpoint is derived by computing the mean of daily capture rate during each phase. Descriptive statistics of the primary efficacy endpoint, including mean, standard deviation, median, and range will be provided by treatment and phase. A scatter plot for Capture Rate (y axis) vs. Day # (x axis), with different colors representing PureWick and Hollister and different panels representing study subject will also be provided. The summary statistics (mean, 95% CI for mean, median) for paired difference in mean daily capture rate between the two treatment arms and p-value from Wilcoxon signed rank test or Paired t-test will be provided. Normality test will be performed before the test, if the data is normally distributed then Paired t-test will be used, otherwise Wilcoxon signed rank test will be used. Sensitivity analyses using linear mixed model (with treatment, phase, and study day 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 computing the mean of Draize Scale assessed daily during each phase. The daily mean of erythema (redness) score, edema (swelling) score, bleeding score, and total score will be calculated. Total score is the sum of erythema score, edema score, and bleeding score. Descriptive statistics of the primary safety endpoint, including mean, standard deviation, median, and range will be provided by treatment, and phase. Paired difference in mean daily Draize Scale between treatment will be provided. A scatter plot for Draize Scale (y axis) vs. Day # (x axis), with different colors representing PureWick and Hollister and different panels representing study subject will also be provided.

5.2.3 Secondary Endpoint

5.2.3.1 Questionnaire Nocturia Quality of Life (N-QoL)

The questionnaire consists of 13 items. However, the global QoL item (question 13) should be removed from the N-QoL and scored separately from the core 12 items. Question responses are scored from 0 to 4 (0 = lowest QoL, 4 = highest QoL). There are two sub-domains: sleep/energy (questions 1-5 and 7) and bother/concern (questions 6 and 8-12). Each sub-domain is made up of 6 items. The score for each sub-domain will be analyzable only if all six questions have responses. The total score is independent of the sub-domain scores, therefore patients will be allowed to miss up to one question and still have an analyzable total score.
The raw total score will be transformed onto a standardized scale of 0-100 using the following formula:

$$Transformed\ Total\ Score = \frac{The\ sum\ of\ the\ component\ items\ score}{Possible\ raw\ score\ range} * 100$$

Domain scores are transformed using the same formula. Thus 0 is the worst QoL and 100 is the best QoL.
The questionnaire will be completed on Day 1, Day 15 and Day 29 of both study phases. We will categorize the questionnaire timepoint as baseline, week 1-2 (day 2-17) and week 3-4 (> day 17), respectively. If day 15 is missing, the latest record between day 2 and 17 will be used for week 1-2; if day 29 is missing, the latest record after day 17 will be used for week 3-4. Descriptive statistics will be provided by each questionnaire timepoint, treatment, and phase. A scatter plot for N-QoL (y axis) vs. Day # (x axis), with different colors representing PureWick and Hollister and different panels representing study subject will also be provided. Linear mixed model may be used, with treatment, phase, and day number as the fixed effect, and participant as the random effect.

5.2.3.2 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.
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	
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

5.2.3.3 Tolerability - Number of days of actual use

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 Day # entries. Subsequently, the number of days of actual use will be summarized using descriptive statistics by treatment. Paired differences between treatments will also be provided.

5.2.3.4 Tolerability - Discontinuation rate due to device discomfort or inconvenience

Rate of not completing a treatment phase due to device discomfort or inconvenience will be summarized using descriptive statistics.

5.2.3.5 Comfort, Ease of Use and Confidence

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.

5.2.4 Exploratory Analysis

5.2.4.1 Correlation between capture rate and N-QoL

- Scatter plot:
  - N-QoL (y axis) vs. Capture rate (x axis) for week 1-2, with different colors representing PureWick and Hollister
    - The average nightly capture rate for each subject will be computed and used as x axis
  - N-QoL (y axis) vs. Capture rate (x axis) for week 3-4, with different colors representing PureWick and Hollister
    - The average nightly capture rate for each subject will be computed and used as x axis
- Table: Summary statistics (n, mean, SD, median, min, max) for N-QoL (week 1-2 and week 3-4) by two capture rate groups (<= median vs. > median), the data will be presented separately for PureWick and for Hollister. The calculation for the median capture rate will be as follows: compute the average of nightly capture rate for each subject , then determine the median for week 1-2 (day 1-14) or week 3-4 (day 15-28) for each device.

5.2.4.2 Correlation between Draize scale and N-QoL

- Boxplot
    - N-QoL week 1-2 (y axis) vs. Draize scale maximum per subject per device (x axis), with different colors representing PureWick and Hollister
    - N-QoL week 3-4 (y axis) vs. Draize scale maximum per subject per device (x axis), with different colors representing PureWick and Hollister
- Scatter plot
    - N-QoL week 1-2 vs. Draize scale average per subject per device (x axis), with different colors representing PureWick and Hollister
    - N-QoL week 3-4 vs. Draize scale average per subject per device (x axis), with different colors representing PureWick and Hollister

5.2.4.3 Correlation between Draize scale and capture rate

- Scatter plot: Capture rate (y axis) vs. Draize scale average per subject per device (x axis), with different colors representing PureWick and Hollister
- Scatter plot: Capture rate (y axis) vs. Draize scale (x axis), with different colors representing PureWick and Hollister and different panels representing study day
- Scatter plot: Capture rate/ Draize scale (y axis) vs. study day (x axis)

6.0 SUMMARY OF GENERAL STUDY DATA

6.1 Subject Disposition

Subject disposition data is collected on the 'Disposition - Phase 1 Completion Status', 'Disposition - Phase 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.

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 variables include:

- Age at time of Informed Consent (years)
- Sex (Female)
- Ethnicity (Hispanic or Latino, Not Hispanic or Latino, Not Reported, and Unknown)
- Race (American Indian or Alaskan Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, White, Not Reported, and Unknown)
- Medical history

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

Adverse Events (AEs) and Serious Adverse Events (SAEs) data will be presented based on treatment phases: the PureWick Phase includes all AEs/SAEs that occurred during the PureWick treatment phase, and the Hollister Phase includes all AEs/SAEs that occurred during the Hollister treatment phase. AEs/SAEs that occurred during the washout period will

be included in the analysis for the device used in Phase 1 treatment if treatment was performed for phase 1. If treatment was not performed in one of the phases, the AEs will be included in the other phase where treatment was performed for the subject.

8.0 INTERIM ANALYSIS PLAN

Not applicable.

9.0 REFERENCES

None.

10.0 APPENDIX

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

11.0 VERSION HISTORY

Vers #	Date (DD-MMM-YYYY)	Change Owner	Description of Change(s)
1.0	11-Sep-2024	Shuangshuang Fu	Original