Clinical Investigational Plan

Pippa Fitness Pessary
Device Effectiveness and Safety Study

Unique Protocol Identification Number: LL101
National Clinical Trial (NCT) Identified Number: NCT05611970

Sponsor:
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STATEMENT OF COMPLIANCE

The trial will be carried out in accordance with International Council on Harmonisation Good Clinical Practice (ICH GCP) and United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (21 CFR Part 50, 21 CFR Part 54, 21 CFR Part 56, and 21 CFR Part 812).

National Institutes of Health (NIH)-funded investigators and clinical trial site staff who are responsible for the conduct, management, or oversight of NIH-funded clinical trials have completed Human Subjects Protection and ICH GCP Training.

The protocol, informed consent form, recruitment materials, and all participant materials will be submitted to the IRB for review and approval prior to use. Approval of both the protocol and the consent form must be obtained before any participant is consented. Any amendment to the protocol will be reviewed and approved by the IRB, if needed, before the changes are implemented to the study. All changes to the consent form(s) will be IRB approved; a determination will be made regarding whether a new consent needs to be obtained from participants who provided consent, using a previously approved consent form.

I agree to ensure that all staff members involved in the conduct of this study are informed about their obligations in meeting the above commitments.

Principal Investigator:

Name of Investigator (printed) _____

Signed _____

Date: _____

1 PROTOCOL SUMMARY

1.1 SYNOPSIS

Title: Pippa Fitness Pessary Device Effectiveness and Safety Study

Short Title: Pippa Pessary Study

Study Description: This is an open label, interventional, single arm, multi-clinic study where each adult female participant with stress urinary incontinence (SUI) serves as her own control (vaginal pessary use vs. no vaginal pessary). Approximately 90 adult women with stress urinary incontinence from 3 distinct clinics in ethnically and economically diverse settings will be recruited for the study. Participants will undergo clinical assessments, comparative pad weight testing (with and without intervention), and at-home device use (as compared to a control phase without device use). This study is deemed non-significant risk and this status has been confirmed with FDA.

Objectives: The overall objectives of this clinical study are to demonstrate the effectiveness and safety of the *Pippa Fitness Pessary* (device) when self-administered and used in a home environment. Specifically, this study will evaluate the effectiveness of the *Pippa Fitness Pessary* by assessing reduction in urine leakage in approximately 57 women with SUI. Up to ninety women will be recruited to ensure that leakage reduction can be assessed in approximately 57 women. Effectiveness will be assessed by percentage reduction in 1-hour pad weight gain, reduction of stress urinary incontinence episodes per day, and a quality-of-life questionnaire. The safety of the *Pippa Fitness Pessary* will be evaluated by assessing all adverse events, including the results of urinalysis and vaginal examination.

Primary Objectives:	The primary objectives are to demonstrate safety of the *Pippa Fitness Pessary* for over the counter (OTC) use and effectiveness of the *Pippa Fitness Pessary* in reducing urinary leakage and/or frequency of leakage episodes.
Secondary Objectives:	The secondary objective is to demonstrate improved quality of life.

Endpoints:

Primary Effectiveness Endpoint:	Composite endpoint consisting of >50% reduction in urine pad weight gain in 1-hour pad weight test and/or >50% reduction in mean daily episodes of leak episodes (pre/post pessary use).
Primary Safety Endpoint:	Collection and evaluation of all adverse events, analyzed by seriousness, severity and device-relatedness, including the results of urinalysis and vaginal examination.
Secondary Endpoints:	Change in Quality of Life as Measured by the IIQ-7 Questionnaire.

Study Population: Approximately 90 women will be recruited, ages 18 and up, who suffer from objectively-diagnosed Stress Urinary Incontinence (SUI); have a >3 month history of experiencing more than 3 episodes of SUI per week; and have not been diagnosed with any other form of urinary incontinence.

Phase: Pivotal trial (non-significant risk status)

Description of Sites/Facilities Enrolling Participants: The study will be conducted at 3-6 clinical centers within the United States, that specialize in treating SUI. Investigators will be selected based on training and experience in Female Pelvic Medicine and Reconstructive Surgery. The centers will be geographically distinct to allow access to a verity of ethnic and socio-economic populations.

Description of Study Intervention: A reusable vaginal pessary for stress urinary incontinence worn daily.

Endpoint Classification:	Effectiveness and Safety Study
Interventional Model:	Single Group, Open Study
Masking:	Open Label
Primary Purpose:	Effectiveness and Safety

Study Duration: 8 - 18 months

Participant Duration: < 4 weeks of activity

1.2 SCHEMA

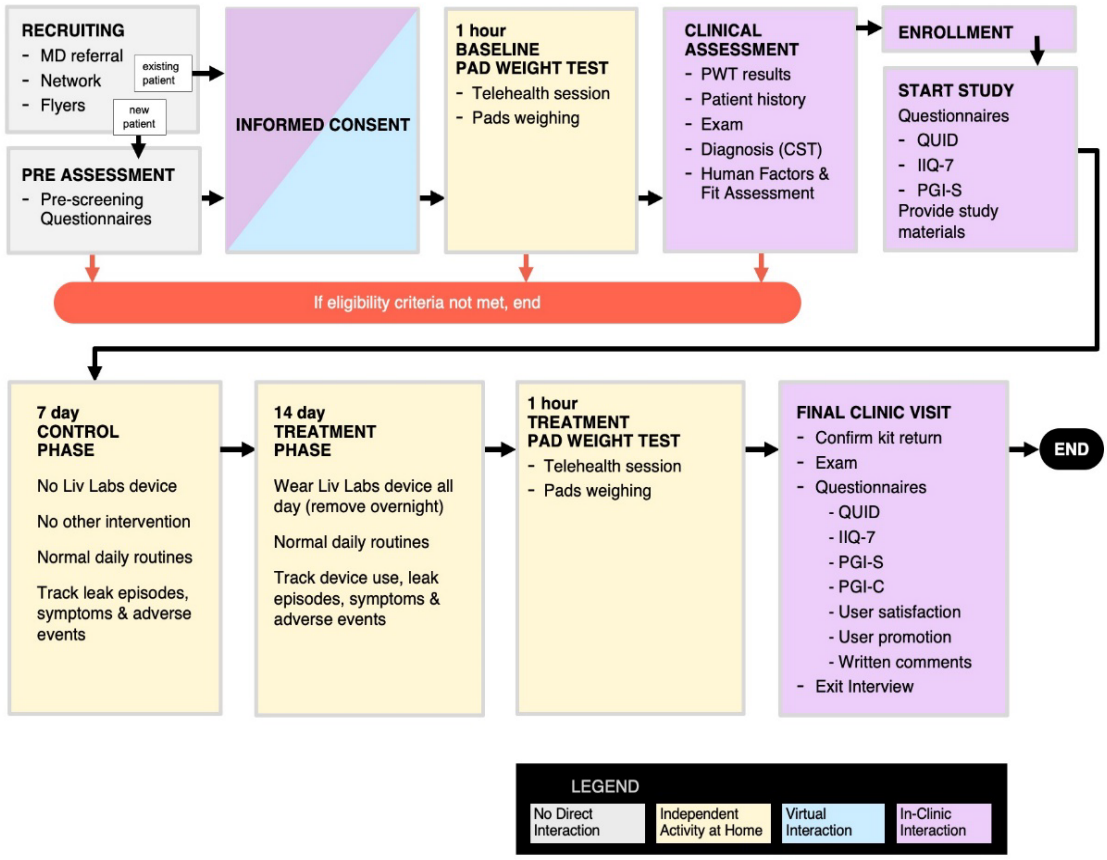

Figure 1.: Clinical Trial Schema

Recruiting

New patient study candidates will be recruited through physician referral, flyers, and web posting that may be shared across social networks. Existing patients will be contacted by the clinical team at the sites.

Pre-Assessment

New patient study candidates will be pre-screened via the web for self-reported frequency and likely stress urinary incontinence, based on the Three Incontinence Questions questionnaire (3IQ). If responses suggest SUI with leaking episodes at least three times weekly, or if the candidate is an existing patient whose symptoms are known, an appointment will be scheduled for informed consent.

Informed Consent

Potential Study candidates will be consented using the process described in Section 10.1.1. of this protocol. Potential study candidates may be consented electronically if site has current access to a 21 CFR part 11 compliant platform.

1-Hour Baseline Pad Weight Test (PWT[1,2])

Study candidates will execute a standardized 1-hour baseline PWT in a telehealth visit staffed by a licensed healthcare provider (such as a Doctor of Physical Therapy or a Registered Nurse) who has been trained on the study protocol and certified in Good Clinical Practice (GCP). Incontinence pads used in the test will either be provided at the consenting visit or express shipped to the study site for blinded weighing and collection of baseline pad weight data. If results indicate *at least* mild incontinence (pad weight gain of >1g[3]), the study candidate will be invited to the clinic for an in-person assessment.

Clinical Assessment

The in-person clinic visit will include 1) obtain and document medical history, 2) conduct a Cough Stress Test (CST) to confirm an SUI diagnosis, 3) perform a vaginal examination and symptom evaluation to ensure the participant has no active urinary or vaginal infection requiring treatment, 4) perform lab tests (urine culture, urinalysis and, for women of childbearing potential, a pregnancy test), 5) screen potential participants by remaining inclusion and exclusion criteria, and 6) perform human factors and fit assessments.

Enrollment

Results of the clinical assessment will determine who may be formally enrolled in the study. The SUI diagnosis assessment and fit assessment may deem the participant ineligible for enrollment due to a diagnosis of urgency urinary incontinence or mixed (stress and urgency) urinary incontinence or inadequate pessary fit. To simulate OTC use, study candidates will be asked to perform self-selection and assess device fit based on the product labeling (prior to confirmation by the PI).

Nota bene: Results of the laboratory tests from the screening visit (any pregnancy test, vaginal examination, urine culture and urinalysis) may deem a participant ineligible for enrollment due to positive pregnancy result, positive vaginal infection requiring treatment, or positive urinary infection requiring treatment, respectively. Thus, due to a laboratory test result, a provisionally enrolled study participant may need to be treated for infection and retested after a period of recovery, or she may need to be disenrolled from the study.

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[1] P. Abrams, J.G. Blaivas, S.L. Stanton, J.T. Anderson. The standardization of terminology of lower urinary tract function. *Scand J Urol Nephrol Suppl*, 1988, 114:5-19.

[2] A. Tubaro, W. Artibani, C. Bartram, et al., "Imaging and other investigations," in Incontinence: Basics and Evaluation, edited by P. Abrams, L. Cardozo, S. Khoury, and A. Wein A., vol. 1, Paris: Health Publication Ltd., 2005, pp. 775.

[3] Ibid, pp. 779.

Questionnaires

Consented study participants will complete several surveys including: a baseline Quality of Life Questionnaire (IIQ-7), Patient Global Impression of Severity (PGI-S), the Questionnaire for Urinary Incontinence Diagnosis (QUID), and the Pelvic Floor Disability Index (PFDI-20). After completing these surveys, study participants will be provided with materials for the in-home portion of the study.

Start Study

Enrolled study participants will receive for home use: a Study Participant Guide; a packaged *Pippa Fitness Pessary* kit (two differently sized pessaries, one applicator, and Instructions for Use); water-based lubricant; water-based cleanser; and a 1-Hour Treatment Pad Weight Test kit. They will be given an opportunity to ask questions and provided with a number to call as needed, throughout the study. For women of child-bearing potential, the study may be scheduled to not overlap with menstruation, according to the preference of the study participant.

7-Day Control Phase

Study participants will perform the control phase of the study at home. They will track leaking episodes for 7 consecutive days. During this time, they will go about their normal daily routines and will use no treatments or interventions (neither the investigational *Pippa Fitness Pessary* nor any other leak preventative). Study participants will receive daily text message reminders to track their leak episodes.

14-Day Treatment Phase

Study participants will begin using the investigational *Pippa Fitness Pessary* in the second week of the home use study. Participants will be instructed to wear the device during waking hours, but to remove and clean it before bedtime. Study participants will receive a daily text message reminder to wear their Pippa Fitness Pessary and track their leak episodes.

1-Hour Treatment Pad Weight Test

After using the *Pippa Fitness Pessary* for two weeks, study participants will complete the 1-Hour Treatment Pad Weight Test in a televisit staffed by a licensed healthcare provider who has been trained on the study protocol and certified in Good Clinical Practice (GCP). The test will be identical to the baseline test, except that the study participant will perform the test while wearing the investigational device.

Final Clinic Visit

The final clinic visit will take place after the in-home protocols have been completed. The device and associated materials will be collected from participants. The visit will include final safety evaluation via vaginal examination and urinalysis. Study participants will repeat the Pelvic Floor Disability Index (PFDI-20), Quality-of-Life Questionnaire (IIQ-7), Patient Global Impression of Severity (PGI-S), and the Questionnaire for Urinary Incontinence Diagnosis (QUID). Participants will also complete the Patient Global Impression of Change (PGI-C) and surveys measuring user satisfaction and likelihood to

recommend the device. Participants will undergo an exit interview and provide written comments.

1.3 Schedule of Activities (SoA)

Procedure	Screening (2 hrs)	Day 1 (1 hr)	Days 2-8 (1 wk)	Days 9-23 (2 wks)	Day 24 (1 hr)	Final Visit Day 25 (1 hr)
Recruitment	X					
Questionnaires/ Survey - 3IQ - Severity self pre-screening - Inclusion criteria self pre-screening	X					
Informed Consent	X					
1-Hour PWT	X				X	
Demographics	X					
Medical History	X					
Physical Exam	X					X
Urinalysis	X					X
Pregnancy Test (if needed)	X					
Cough Stress Test	X					
HF & Fit Assessments	X					
Concomitant Medications Case Report Form (ConMeds CRF)	X					X
Pre-Study Questionnaires - PGI-S - QUID - IIQ-7 - PFDI-20		X				X
Leak Tracking w/o Pessary			X			
Leak Tracking w/Pessary				X		
Post-Study Questionnaires - PGI-C - PGI-S - QUID - IIQ-7 - PFDI-20 - Likelihood to recommend - User satisfaction - User experience - Observational study interest						X
Exit Interview						X
Adverse Event Collection		X	X	X	X	X
Complete CRFs		X	X	X	X	X

1.4 Subject Follow-up and Allowed Windows

Study-related follow-up assessments occur between Study Days 2-8, Days 9-23, and at Study Exit (Day 25), with windows shown below. The study's schedule of assessments is shown above in section 1.3.

Follow-Up Contact	Allowed Window
Control Phase Follow-Up*	Day 2-8
Treatment Phase Follow-Up*	Day 9-23
Day 24 - Treatment PWT	Day 22-25
Final Clinic Visit	Day 25-30

*Phone follow-up.

** If day lands on a weekend or holiday, the subject may be scheduled on the next business day.

2 INTRODUCTION

2.1 STUDY RATIONALE

This study seeks to evaluate the effectiveness and safety of the *Pippa Fitness Pessary*, a pessary intended for temporary management of urine leakage caused by stress urinary incontinence (SUI) in women, 18 years and older. The study design has been guided by a review of the literature and co-authored by subject matter experts engaged in daily clinical care and numerous clinical research studies of the study population.

SUI can present as a daily concern or, for many women, only in the context of specific physical activities, be they chosen (as with jogging) or involuntary (as with a sneeze). The *Pippa Fitness Pessary* is designed to be self-managed and used on an as-needed basis, i.e.: for a trip to the gym, during a hike, or all-day. Thus, effectiveness must justify the per-use effort. Although dryness is the logically ideal outcome, some women may find leak reduction meaningful.

The selection of a within-subject pad weight study design aligns with the intended use of the device as a situational self-treatment option for women with varying degrees of symptom severity. The primary and secondary endpoints incorporate both objective measures of leak reduction and a validated quality-of-life assessment. The statistical analysis plan of safety and effectiveness draws upon available data from testing of a predicate pessary device (Revive, K183468).

The recruitment of adult women with suspected SUI will involve three distinct, geographically-dispersed clinics, enabling recruitment of a diverse study population. The sample size for the study (recruiting up to 90 participants to meet a goal of 57 completions) is based on power calculations with summary data from predicate studies.

Finally, the safety analysis for this study will include results of urinalysis, vaginal examination, and evaluation of adverse events, as is recommended in the FDA Guidance (*Guidance for Industry and Food and Drug Administration Staff -- Clinical Investigations of Devices Indicated for the Treatment of Urinary Incontinence* (Issued March 8, 2011).

The protocol utilizes daily digital reminders that should improve the accuracy of participants' self-report on leaking episodes, adherence to the study protocol, and the reporting of any adverse events.

2.2 BACKGROUND

Urinary incontinence is a common issue for women. It is estimated that one in three women leak urine involuntarily, and that approximately 25 percent of women will seek medical advice for the condition at some point, typically after suffering with it for several years. The most common form of incontinence is stress urinary incontinence (SUI). SUI is the involuntary leaking of urine that occurs during exercise, sneezing, coughing, and laughing. During these activities, the abdominal muscles apply pressure to the bladder and urethra, and a combination of weakened pelvic floor muscles and urethral hypermobility allows urine leakage to occur. Stress incontinence affects adult women, particularly after vaginal childbirth when the muscles of the pelvic floor are stretched and weakened. Other causes include aging into menopause, high-impact sports, chronic cough and obesity.

Market research suggests that most women manage their SUI day-to-day with a combination of activity avoidance and incontinence pads. Too often women who do seek medical treatment only consider surgery, discounting the restorative potential of physical therapy and shying away from vaginal pessaries. Physician-inserted, prescription-only fitted pessaries, while proven effective and safe, are inconvenient to maintain because they require both clinicians and patients to engage in an indefinite routine of follow-up visits. Many physicians are reluctant to recommend fitted pessaries for this reason.

Women suffering from SUI lack direct access to an Over-the-Counter (OTC) pessary that can be reused without replacing at least one component. Currently marketed OTC pessaries are either disposable after a single use or include disposable components that may only be used once. All such devices include a cotton string for device retrieval. The multi-use device requires that any old string be removed, and a new cotton string be threaded and attached by the user, for each instance of device re-use. A significant number of adverse events reported in the FDA's MAUDE database relate to breakage of the string and the subsequent need for professional medical attention to remove the pessary.

The *Pippa Fitness Pessary* was designed to address barriers to pessary trial, adoption, and use. It is intended to offer users device effectiveness and safety that is on par with currently marketed OTC disposables, in a handy, fully reusable, engineered form without the need to change a string, that both patients will find comfortable and that doctors will find credible.

2.3 RISK/BENEFIT ASSESSMENT

2.3.1 KNOWN POTENTIAL RISKS

Potential risks include the following short-term risks:

- Sensitivity to the materials used in the device; however, the probability is low due to the high purity, medical-grade silicone in use and testing demonstrating biocompatibility of the device
- Irritation to the vaginal area, cramping or other discomfort

- Vaginal bleeding/spotting or excess discharge
- Urinary Tract Infection (UTI)
- Vaginal infection
- Toxic Shock Syndrome (TSS)
- Urine retention
- Infection if the device is not used as indicated
- Breach of confidentiality

There are no known long-term risks associated with this study.

2.3.2 Known Potential Benefits

Patients undergoing successful intravaginal pessary treatment for SUI have been shown to have improvement in quality of life, so long as the device is being used. The quality of life improvement seen in patients undergoing successful SUI treatment include physical mitigation of symptoms which results in potential increase in social interaction, increased confidence, reduced anxiety, and increase in physical activity.

Non-surgical treatment options are important to the subject population. SUI device interventions that demonstrate effectiveness and safety could significantly improve the quality of life for a condition that most patients do not like to discuss, even with their physicians. Surgical options are typically used as a last resort. For this reason, the potential benefits associated with this study outweigh the risks involved.

The potential benefits to participants during this study include treatment of their SUI, increased quality of life, increased social activity (including exercise), psychological improvement, and increased confidence due to decreased urinary leakage.

2.3.3 Assessment of Potential Risks and Benefits

The risk profile of the *Pippa Fitness Pessary* (investigational device) is considered to be low. Risks to participants in this study are comparable to those routinely encountered with using commercially available vaginal pessaries.

The device is not intended as an implant or for use in supporting or sustaining human life and does not present serious risk to the health, safety, or welfare of a subject. Thus, this study is a non-significant risk study under the criteria in 21 CFR 812.3(m). In a meeting with FDA regarding the proposed study, FDA stated agreement that the study qualified as a non-significant risk device study.

The materials used in the manufacturing of this device are medical-grade. During the screening process, a vaginal examination and urinalysis will be performed to rule out vaginal infection or UTI, respectively. For pre-menopausal women of childbearing potential, a urine pregnancy test will be administered. The device will be tested at the screening visit to ensure fit. Each of the participants will receive an

identification number during enrollment. This number will be the only identifying information on the Case Report Form. The PI will maintain the participant information in a secure location. The Sponsor shall have access to the study data after it has been de-identified to analyze the data to determine the success of the study. Patient names will only be seen during monitoring by the study sponsor or inspections by regulatory authorities.

Each of the devices used in this study will be labeled “Caution: Investigational device. Limited by United States law to investigational use”. If manufacturing lots differ for the study devices, this will be recorded.

Patients undergoing successful intravaginal pessary treatment for SUI have been shown to have improvement in quality of life. The quality-of-life improvement in patients undergoing successful SUI treatment with an intravaginal pessary include mitigation of physical symptoms (leaking) which result in potential social and psychological benefit. Successful pessary treatment for SUI could also lead to greater ability to enjoy exercise and increased confidence due to decreased urinary leakage. The potential benefits to participants thus outweigh potential risks.

3 OBJECTIVES AND ENDPOINTS

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS
Primary		
Effectiveness of the device in reducing urinary leakage in adult women with SUI - percentage reduction in 1-hour pad weight gain - reduction of episodes of incontinence Safety for over the counter (OTC) use	A composite primary endpoint comprising of subjects achieving >50% reduction in pad weight gain and/or achieving 50% reduction in episodes of leaking - treatment vs. control Collection of all adverse events, analyzed by seriousness, severity and device-relatedness, including the results of urinalysis, and vaginal examination	Reviewed with FDA
Secondary		
Demonstrate improved quality of life	Reduction in scores on the IIQ-7 from control by > 3.7.	Use of IIQ-7 conforms to FDA guidance

4 STUDY DESIGN

4.1 OVERALL DESIGN

The purpose of the pivotal study is to gather clinical data to support applications for marketing authorization from the U.S. FDA and regulatory health agencies outside the U.S., with the objectives of evaluating the effectiveness and safety of the *Pippa Fitness Pessary* in a home environment, comparing standardized 1-hour baseline and treatment pad weight studies as well as reduction in leaking episodes during 7 days at home without use of the *Pippa Fitness Pessary* to 7 days at home with use of the *Pippa Fitness Pessary* (within the 14-day period of device use). This is an open label, interventional, single arm, multi-clinic study where each adult female participant with stress urinary incontinence (SUI) serves as her own control (vaginal pessary use vs. no vaginal pessary). Up to 90 adult women with stress urinary incontinence served by 3 distinct clinics in ethnically and economically diverse settings will be recruited for the study so that treatment may be evaluated in approximately 57 women.
The study will comprise three distinct elements:

1. Clinic Visits: to evaluate patient health, confirm SUI diagnosis, confirm eligibility via inclusion and exclusion criteria, assess human factors and device fit, collect baseline and treatment data on symptom severity, urinary symptom distress, daily life impact, and user experience; and

2. Comparative Pad Weight Testing (with and without intervention): to establish objective data on device effectiveness using a standardized method; and

3. At-Home Device Use (compared to a control phase): to establish objective data on device effectiveness under realistic conditions that will vary by study participant.

The study will follow a standardized process for each participant lasting 4-5 weeks from recruitment to participant completion, as follows:

Pre-Assessment Process
Recruiting materials will provide links to an online survey. Interested participants who are not existing patients will first be screened for likelihood of study eligibility. If a candidate's responses suggest eligibility, she will be provided with summary information about the study and scheduled for informed consent.

Informed Consent Process
Voluntary informed consent will be given by every study candidate prior to the initiation of any study-related procedures. The Investigator/designee will explain the study to each study candidate and they must indicate voluntary consent by signing and dating the approved informed consent form. The Investigator must provide the study candidate with a copy of the consent form in a language the participant understands. The Investigator will maintain documentation that informed consent was obtained prior to the initiation of any study-specific procedures.

1-Hour Baseline Pad Weight Test

Consented study candidates will execute a 1-Hour Baseline Pad Weight Test at a telehealth visit with a healthcare provider based on guidelines developed by the International Continence Society (ICS)[4]. Study participants will follow a timed process that includes emptying their bladders, drinking 500 milliliters of water, resting, walking, climbing up and down a flight of stairs, and performing a set of physical activities as follows:

- Standing up from sitting (10 times)
- Jumping jacks (10 times)
- Picking up a small object from the floor (5 times)
- Running in place (1 minute)
- Low-hopping in place (20 seconds)
- Coughing vigorously while sitting (10 times)

Test facilitation will be standardized across study sites by means of tools, training, and practice. Study participants will wear activity trackers to enhance comparative data analysis.

Study participants will be provided an initial pad weight test kit. It will include:

- a reusable water bottle with a 500 mL marking;
- an activity tracking device with digital display;
- two (2) incontinence pads bagged in odor- and leak-proof, resealable 4 mil zipper bags that have been pre-labeled and pre-weighed for de-identified data collection; and
- a pre-addressed, postage-paid FedEx return mailer suitable for shipping exempt human specimens.

Healthcare providers conducting each session will use the following standardized tools:

- a facilitation guide for the complete session, and
- a data collection tool for recording test participant behavior.

Upon completing the PWT, study candidates will return-ship the used and re-bagged incontinence pad(s), and the activity tracking device in a provided FedEx mailer. Incontinence pads used in the test will then be weighed and baseline pad weight data recorded at the clinical sites. If a candidate meets the baseline inclusion criteria for SUI and severity, an appointment will be made for her to come to the clinic for the clinical stage of assessment. The appointment will be timed to avoid a menstruating study candidate's monthly cycle.

Clinical Assessment & Enrollment

Consented study candidates will be evaluated in clinic for the purposes of confirming a diagnosis of SUI and for ensuring proper fit of the *Pippa Fitness Pessary*. The procedure is outlined below in **Figure 2**.

[4]Krhut J, Zachoval R, Smith PP, Rosier PF, Valanský L, Martan A, Zvara P. *Pad weight testing in the evaluation of urinary incontinence.* Neurourol Urodyn. 2014 Jun;33(5):507-10. doi: 10.1002/nau.22436. Epub 2013 Jun 24. PMID: 23797972.

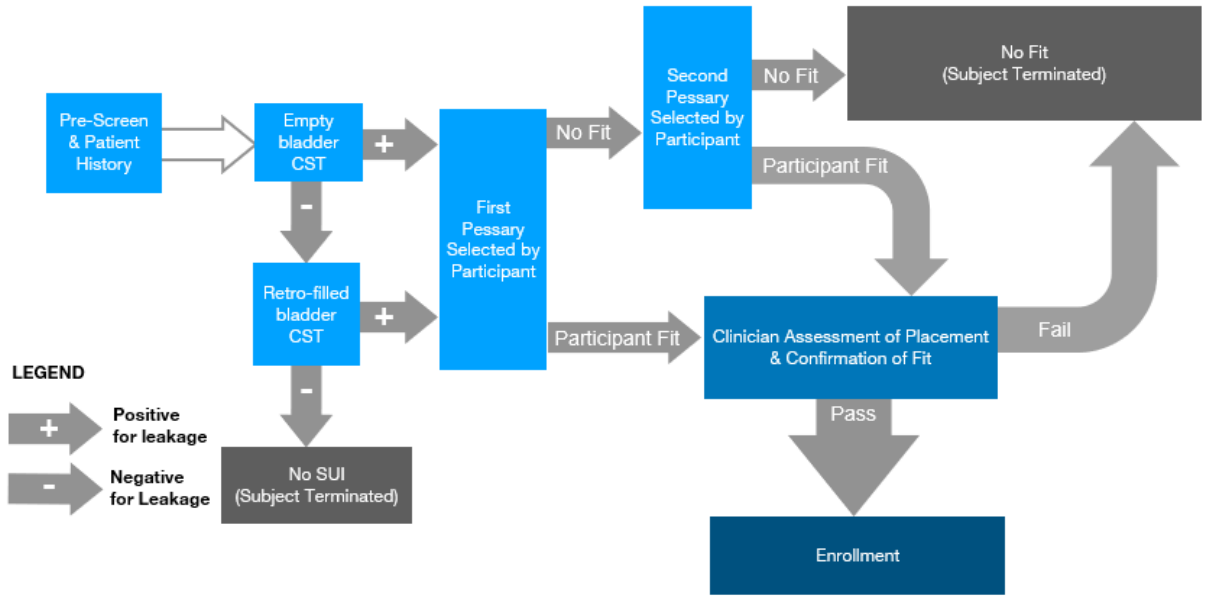

Figure 2. Protocol for the in-clinic SUI diagnosis, human factors, and device fit procedures.

Human Factors and Fit Assessments: As part of the screening process, and following a positive diagnosis of SUI using a CST,[5] a human factors assessment will be performed, followed by a fit assessment. The human factors portion will assess self-administration and device placement accuracy. Proper device fit will be evaluated first through study candidate perception and then through expert confirmation by a clinician.

Self-Administration Assessment: Each study candidate will be provided with a packaged *Pippa Fitness Pessary* kit and instructed to proceed as she would at home. She will be further instructed to inform the clinician when she believes she has finished the process. The study candidate will perform self-selection and device self-administration using only the labeling and without any training by study staff. She may or may not remove and reinsert the first selected *Pippa Fitness Pessary*. She may or may not swap out the first selected *Pippa Fitness Pessary* for the other one. The observing clinician will document any issues with device assembly, insertion, and removal. Once the study candidate announces she has finished the process, the clinician will elicit the candidate's feedback on perceived fit. The study candidate will then remove the device without clinician assistance. If the study candidate chooses on

[5]The cough stress test (CST) is recommended in the evaluation of female patients to identify the signs of SUI and is used as an outcome measure following SUI treatment. The patient coughs and is observed for urine loss synchronous with the cough. If the patient leaks with the onset of the cough and terminates with its cessation, the test is positive and confirms the presence of SUI. The International Continence Society (ICS) has provided guidance on the CST with the introduction of the ICS Uniform Cough Stress Test (ICS-UCST), and an ICS education module has been developed to standardize the performance and reporting of the CST used in the clinical and outcome assessment of women with urinary incontinence. When compared with multichannel urodynamic evaluations, the CST demonstrates good sensitivity and specificity for SUI. https://onlinelibrary.wiley.com/doi/epdf/10.1002/nau.23519#

her own to try the other *Pippa Fitness Pessary*, she will again be asked to provide feedback regarding her perception of fit.

Proper Fit Assessment: If the study candidate does not think either device fits, she will be excluded from the study. Otherwise, she will be instructed to reinsert the *Pippa Fitness Pessary* she prefers, again without assistance. The clinician will then verify proper device placement and confirm fit. In the absence of confirmed fit, the study candidate will be excluded from the study. If the study candidate has passed all other inclusion and exclusion screens, then proper fit of the *Pippa Fitness Pessary* will confirm the candidate's eligibility for the home-based study, and she will be enrolled.

Start Study
Enrolled study participants will complete three questionnaires to provide baseline symptom severity, urinary symptom distress, and daily life impact data. These questionnaires are the validated Questionnaire for Urinary Incontinence Diagnosis (QUID), the Incontinence Impact Questionnaire Short Form (IIQ-7), Patient Global Impression of Severity (PGI-S), and the Pelvic Floor Disability Index (PFDI-20). They will then be provided with all at-home study materials.

Home-Based Study Protocol
Enrolled study participants will be sent home from the clinic with a *Pippa Fitness Pessary Kit*, a PWT kit and a Study Participant Guide. In broad strokes, the home-based study will include one week of monitoring urine leakage episodes during normal routines (the 7-day control phase) and two weeks of monitoring urine leakage episodes during normal routines *and* while wearing the investigational device (the 14-day treatment phase). Reminders will be sent by text message every morning and evening.

Week 1 will constitute the control phase and will require participants to simply go about their ordinary lives. Twice-daily (morning and evening) text messages will be sent to each subject to remind her to track her leaks, which will be the only study task for this phase.

Weeks 2 and 3 together are the treatment phase and will require participants to wear the *Pippa Fitness Pessary* during waking hours, while going about their ordinary lives. Daily reminders by text message will continue throughout the 14-day period.

1-Hour Treatment Pad Weight Test
A telehealth visit will be scheduled with a healthcare provider after week 3 to repeat the original pad weight test, but with investigational device treatment. Each study participant's actual *baseline* test activity will have been documented and retained for reference. To ensure comparable within-subject baseline vs. treatment test conduct, any modification for participant ability will be replicated. (For example, if a participant ceases running in place at 45 seconds in the baseline test, she will only be asked to run in place for 45 seconds on the treatment test.) As before, this test requires the study participant to return-ship the pad weight test materials via FedEx for pad weight data collection and analysis by the centralized research team.

Final Clinic Visit
After completing the period of treatment, participants will return to the clinic with the *Pippa Fitness Pessary* (for subsequent reconciliation against Device Accountability Logs by the Site Monitor and disposed of per the site's biohazard protocol). Participants will be debriefed with the same four

validated questionnaires used in the pre-study period, namely: QUID, IIQ-7, PFDI-20 and PGI-S. Additionally, they will complete the Patient Global Impression of Change (PGI-C); a user experience satisfaction questionnaire; a *likelihood to recommend* question; an open-ended request for any additional comments; and a brief exit interview.

4.2 Scientific Rationale for Study Design

This study is an interventional, open label, single-arm, clinical study in which participants will serve as their own controls. This study will enroll participants deemed eligible per the Inclusion/Exclusion Criteria listed. These criteria were informed by relevant FDA guidance and predicate device studies.

This study will evaluate the effectiveness of the *Pippa Fitness Pessary* (device) by assessing percentage reduction in urine leakage and/or frequency in approximately 57 women with SUI (up to 90 will be recruited). Effectiveness will be assessed by percentage reduction in 1-hour pad weight gain, frequency of stress urinary incontinence episodes, and a quality-of-life questionnaire.

We used a precision approach to determine the appropriate sample size and power for the study. For our primary composite endpoint (>50% reduction in pad weight gain on the 1-hour pad weight test and/or on mean daily leak reports) we estimated a response rate of at least 70% based on our own earlier work and on the Poise Impressa study (Ziv et al.). With the desired precision of this estimated response rate set to 0.10 and a confidence level of 0.90, the estimated sample size would be 57.

For the primary composite endpoint, the null hypothesis is that the responder proportion (percentage of participants with >50% reduction in pad urine weight and/or >50% reduction in mean daily number of leakage events) is <=70%. The alternative is that it is >70%.

For the analysis of our primary composite outcome, the dichotomous subject success in pad leakage reduction of greater than 50% and/or a reduction in mean daily leakage episodes greater than 50%, a binomial proportion test will be used. In analyzing the individual components, a comparison of the mean percent reduction in leakage compared to zero will be performed using a 1-sample t test.

To also ensure that our 1-hr pad weight differences between baseline and pessary treatment would be statistically significant, we checked that a sample size of 57 with a type 1 error rate (alpha) of 0.05, one-sided, would provide sufficient power. We based our estimates of a standard deviation in pad weight change to be 18% (conservative estimate based on the Poise Impressa study, Ziv et al.) and found that we would only need 50 subjects to have at least 90% power to see at least a 50% reduction in pad urine weight as an exploratory single endpoint.

Thus, to be conservative, we will recruit up to 90 participants to ensure a sample size of completers of 57 participants.

This sample size should also be sufficient for the analysis of self-report measures of leak frequency, quality-of-life, and our other exploratory endpoints.

The primary safety endpoint was adopted from the FDA's guidance for urinary incontinence studies. Safety analysis will include results of urinalysis, vaginal examination, and evaluation of adverse events. The study site will contact each subject at least twice during the study to check compliance with the study protocol and record any adverse events the subject may have experienced. At the final study visit, the investigator will inquire about the occurrence of AE/SAEs since the initial visit. All adverse events will be characterized according to their relatedness to the device and their seriousness and severity. The safety analysis will include a descriptive assessment of the types and frequency of adverse events observed, with comparison to those observed during the control phase.

4.3 End of Study Definition

A participant is considered to have completed the study if she has completed all phases of the study including the last visit shown in the Schedule of Activities (SoA), Section 1.3.

The end of the study is defined as completion of the last visit by the last participant.

5 Study Population

5.1 Inclusion Criteria

Inclusion Criteria: To be eligible to participate in this study, an individual must meet all of the following criteria:

1. Female, ≥18 years of age
2. Diagnosed with SUI by a physician using a cough stress test (positive test)
3. Confirmed *Pippa Fitness Pessary* fit in clinic by a physician or qualified clinician (e.g., Nurse Practitioner, Registered Nurse)
4. Have a >3 month history of experiencing more than 3 episodes of SUI per week
5. English literacy sufficient to understand the nature of the study and sufficient to read and understand the informed consent form
6. Provision of a signed and dated informed consent form
7. Willingness to use the Pippa Fitness Pessary during the study and comply with study procedures
8. Willingness to forego use of any vaginal insert (e.g.: vaginal pessaries, bladder supports, estrogen rings, tampons, and menstrual cups) while the Pippa Fitness Pessary is in place
9. Willingness to cease use of any other form of urinary incontinence treatment for the duration of the study
10. Willingness and ability to interact with study staff by email, phone, text message and video conferencing software throughout study

5.2 Exclusion Criteria

Exclusion Criteria: An individual who meets any of the following criteria will be excluded from participation in this study:

1. Known urethral stricture, bladder neck contracture, spastic bladder, vesicoureteral reflux, bladder stones, and/or bladder tumors
2. Concurrent bladder specific medications (including beta agonists or anticholinergics) that affect urination and the use of any other prescription medication and/or over-the-counter medication and/or dietary supplements (including herbal supplements and those taken as teas) that affect urination, except in those instances where they are medically necessary and can be actively supported at a stable dosage throughout the active study period
3. Known prolapse beyond hymen or any POP-Q point > 0
4. Known hypersensitivity to silicone rubber

5. Pelvic floor surgery including anterior bladder repair and urethral slings
6. Vaginal, perineal, or uterine surgery, or abortion (spontaneous or induced) within the past 3 months
7. Any injectable treatments, or prior surgeries for incontinence
8. Class III Obesity (BMI > 40.0 kg/m^2)
9. Currently suffering from urinary tract or vaginal infection
10. Pregnant or planning to become pregnant within 3 months, or within 3 months postpartum
11. History of Toxic Shock Syndrome or consistent symptoms
12. Previously diagnosed with urge-predominant or mixed predominant urinary incontinence, functional incontinence, incontinence due to a central or spinal cord neurological condition (such as multiple sclerosis, neurogenic bladder, Parkinson's, spina bifida), insensate incontinence, or overflow incontinence
13. Screening laboratory values outside the reference range considered significant by the investigator which might impact the safety of the participant or outcome of the study
14. Unsuccessful fit assessment during screening
15. Any other reason the investigator decides the potential participant should not participate in the study
16. Self-reported difficulty emptying bladder
17. Difficulty inserting or wearing an intra-vaginal device

5.4 Screen Failures

Participants will be pre-screened prior to calendaring an appointment. If they fail the pre-assessment, they will be thanked for their interest but told that they are not eligible for the study. If they fail the 1-hr PWT, they will not be scheduled for an in-clinic screening visit, but will be provided with the stipend, as outlined in the Informed Consent Form (ICF). If participants fail the screening procedure during the clinic visit, they will be thanked for their participation and be provided with the stipend, as outlined in the ICF

5.5 Strategies for Recruitment and Retention

The study staff will recruit women with stress urinary incontinence from 3-6 distinct clinics in ethnically and economically diverse settings.
An ethnically and racially diverse mix of participants will be recruited.

A mix of methods will be used to facilitate recruiting, ranging from flyers in clinics and nearby facilities to physician referrals and emails and Web news to patient networks. This information will be replicated in substantially similar Web and email forms. Existing clinic patients with a diagnosis of SUI will not

undergo pre-assessment. Instead they will be instructed to call directly for an informed consent call and will be shipped the first pad weight test kit, or they will be scheduled for an office visit for informed consent review and signature. Up to 90 participants will be recruited to ensure that approximately 57 are able to complete the study.

- Participants will receive reminders by mobile text messages each morning and evening of the leak-tracking study phase.
- Subjects will be contacted via phone call at least once during each phase of the study, to ensure that the subject is compliant and does not have any concerns. During these calls, the site staff will remind the subject to complete her leak diary each day.

6 STUDY INTERVENTION

6.1 STUDY INTERVENTION(S) ADMINISTRATION

6.1.1 STUDY INTERVENTION DESCRIPTION

A pessary is an intravaginal prosthetic that, in the case of stress urinary incontinence (SUI), seeks to affect mechanical changes to restore proper urethral function.

The subject device, the *Pippa Fitness Pessary,* is a system of reusable device components comprising a stress urinary incontinence pessary and vaginal applicator (**Figure 3**). The device is single patient, multi-use, and self-administered without training. The device is intended for both over-the-counter (OTC) and prescription use.

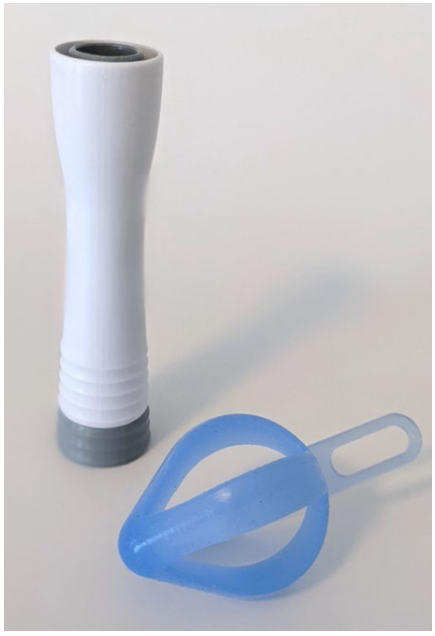

Figure 3:
Pippa Fitness Pessary System

The *Pippa Fitness Pessary* is made of flexible medical-grade silicone with no attachments to irritate vaginal tissue and no sharp edges to cause injury or discomfort. It is engineered to compress and expand intravaginally. The device package includes two diameters: 42mm and 50mm, to serve most women in need. It will require no precise sizing, fitting, patient training or clinic visits. Both sizes should be effective and safe for most women, but one size may be more comfortable or easy to position for a given user. It will be recommended that users try both sizes (starting with the 42 mm size) and select the one they prefer for regular use. When placed intravaginally, the device presses longitudinally along the urethra to reduce or prevent involuntary urine loss while also preventing involuntary expulsion. Placed correctly, it will not impede intentional urination. The hollow form allows vaginal excretions to pass through and prevents the vaginal sealing found with some SUI pessaries. **Figure 4**, below, shows an anatomical cross section both with and without the Pippa Fitness Pessary.

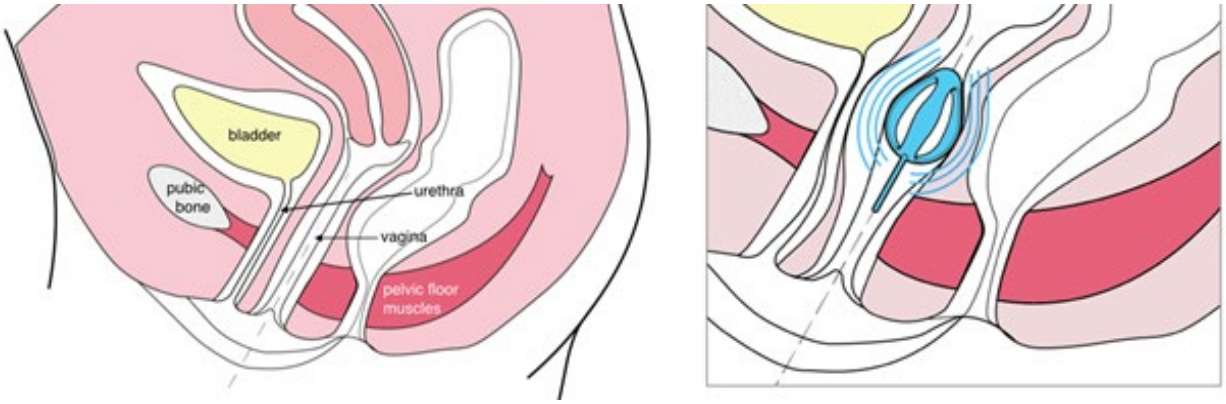

Figure 4: Anatomical cross section without (L) and with (R) *Pippa Fitness Pessary*

The reusable *Pippa Fitness Pessary* is shaped as a hollow silicone ovoid, comprising a tapered leading end from which extend radially four elongate surface elements that reconnect at a base, from which further extends a loop, by which the device may be pulled (out of one's body) or hung (as if to dry on a wall hook). The *Pippa Fitness Pessary* was carefully designed for comfort and ease of use. A reusable vaginal applicator is required to assist with correct self-administration of the device. The applicator comprises injection-molded plastic cylinders, assembled for use. **Figure 5** below shows the Pippa Fitness Pessary in its expanded form and **Figure 6** below shows it in its compressed form.

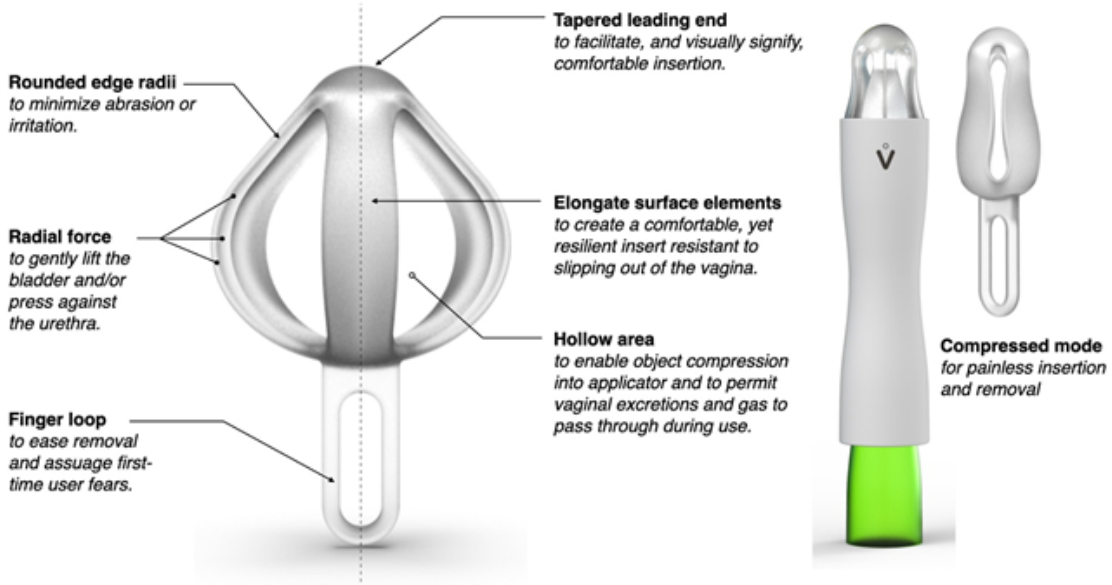

Figure 5: Design Features (expanded) **Figure 6: Design Features (compressed)**

The user-contacting materials used in the *Pippa Fitness Pessary* are listed in **Table A** below.

Table A - *Pippa Fitness Pessary* Materials

Component	Material	Tissue Contact	Duration
Pessary	medical-grade silicone	mucosal membrane	Less than 24 hours at a time.
Applicator (two pieces)	polypropylene	mucosal membrane	Less than 24 hours. The applicator should be in contact with the vagina for only a few seconds during placement.

6.2 Preparation/Handling/Storage/Accountability

6.2.1 Acquisition and accountability

All participant study materials will be provided by Liv Labs. Materials will include printed participant study guides; packaged *Pippa Fitness Pessary* kits (two differently sized pessaries, one applicator, and Instructions for Use); water-based lubricant; water-based cleanser; pad weight test kits (instructions, activity monitor (pedometer), pre-weighed incontinence pads, FedEx mailers); a commercial-grade electronic balance; and a proper balance calibration mass. These study materials will be stored securely at each of the clinics at which study candidates and participants will be seen. All pads will be mailed back by participants to a central location. Pads will be weighed upon return and then disposed of.

6.2.2 Formulation, Appearance, Packaging, and Labeling

The *Pippa Fitness Pessary* is a system of reusable device components comprising a stress urinary incontinence pessary and vaginal applicator. The *Pippa Fitness Pessary* is constructed of medical-grade silicone and the applicator is constructed of polypropylene. The device is single patient, multi-use, and self-administered without training. The device is intended for over-the-counter (OTC) and prescription use. It will be provided to participants in a box that contains 2 pessaries (42mm and 50 mm), an applicator, a plunger, and instructions for use. Participants will also be provided with water-based cleanser and lubricant to be used as needed. The instructions for use (IFU) are provided in Appendix A.

6.2.3 Product Storage and Stability

The IFU in Appendix A instructs the participant to wash the device with a water-based cleanser and to store the Pippa Fitness Pessary in a cool dry place.

6.2.4 Preparation

The materials for the treatment period of the study will be provided to each participant during the initial clinic visit. The investigational device and applicator are described in the IFU (Appendix A). Participants will be provided with a tailored Study Participant Guide that describes what to do on each day of the at-home study phase. Participants will also be provided with a pad weight testing kit that includes instructions, an activity monitor (pedometer), pre-weighed incontinence pads, and a pre-addressed FedEx mailer. Participants will receive daily text reminders. Advice about pessary use will not be provided.

6.3 Measures to Minimize Bias: Randomization and Blinding

Although the participants will know when they are in the treatment period (using the *Pippa Fitness Pessary*), the study personnel weighing the pads after use will be blinded with regard to participant name or what phase of the trial they are in. The pads will be labeled with coding that de-identifies each study participant. Therefore, research analysts will not associate participant scores between all the tests, reducing expectations about results based on prior assessments. Analysts may only associate results for individual participants after completion of all statistical analyses.

6.4 Study Intervention Compliance

Participant compliance will be monitored throughout the study by follow-up telephone calls made by the site during the at-home phase of the study.

6.5 Concomitant Medication

Prescription medications taken during study participation will be recorded on the case report forms (CRFs). For this protocol, a prescription medication is defined as a medication that can be prescribed only by a properly authorized/licensed clinician. Only prescription medications are to be reported in the ConMeds CRF. Over-the-counter medications will be documented if they are taken for the purpose of resolving an Adverse Event that occurs during the study. This information shall also be collected during the medical history evaluation. There are no known concomitant medications for the treatment of SUI.

7 Study Intervention Discontinuation and Participant Discontinuation/Withdrawal

7.1 Discontinuation of Study Intervention

Adverse event monitoring will begin upon study enrollment (not during screening phase). Potential adverse events will be monitored during the follow-up telephone calls made by the site during the at-home phase of the study. All adverse events will be reported to the Sponsor within 48 hours. The study will be suspended or discontinued if required by an evaluation of the severity and possible causality of the adverse events. This study may be temporarily suspended or prematurely terminated if there is

sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to the investigator, funding agency, the sponsor and regulatory authorities. If the study is prematurely terminated or suspended, the PI will promptly inform the IRB and will provide the reason(s) for the termination or suspension and the study sponsor will inform the FDA if the study was terminated due to an unanticipated adverse device effect that presents an unreasonable risk to subjects.

Circumstances that may warrant termination or suspension include, but are not limited to:

• Determination of unexpected, significant, or unacceptable risk to participants

• Insufficient compliance to protocol requirements

Study may resume once concerns about safety, protocol compliance, and data quality are addressed and satisfy the Sponsor, IRB and FDA.

7.2 Participant Discontinuation/Withdrawal from the Study

Participants will be clearly informed that they are free to withdraw from the study at any time. Study personnel will work with each participant having problems to determine if they should continue the study. If any participant discontinues the study, the reasons for termination will be recorded. Every attempt will be made to complete the study exit visit and collect all study-related products.

7.3 Lost to Follow-Up

If for some reason a participant cannot be reached after three (3) attempts (using a combination of phone calls, emails, and/or MyChart) and pad shipments or device return requests go unanswered, then she will be considered lost to follow-up. Attempts to contact such a participant by mail, to determine a reason for this, and any reasons reported, will be recorded for later analysis.

8 Study Assessments and Procedures

8.1 Effectiveness Assessments

The primary effectiveness endpoint is a composite endpoint used to describe responders to the use of the Pippa Fitness Pessary to reduce urinary leakage. The two component endpoints defining a responder are:

1. >50% reduction in pad weight gain for the 1-hour pad weight test with vs without the pessary. This component outcome is defined as:

$$\frac{\text{(1-hr PWT urine weight without pessary) – (1-hr PWT urine weight with pessary)}}{\text{(1-hr PWT urine weight without pessary)}} > .50$$

and/or

2. >50% reduction in the average daily reports of number of urine leaks per day during periods with and without the pessary. This component outcome is defined as:

$$\frac{\text{(Mean \# of leaks/day without pessary) - (Mean \# of leaks/day with pessary)}}{\text{(Mean \# of leaks/day without pessary)}} > .50$$

Our secondary endpoint will be Change in Quality of Life as measured by the Incontinence Impact Questionnaire Short Form (IIQ-7) measured at baseline and at the end of the treatment phase.

Other effectiveness data to be analyzed include:

(1) Net Promoter Score (likelihood that participant would recommend the device)

(2) Patient Global Impression of Severity (PGI-S)

(3) Patient Global Impression of Change (PGI-C)

(4) Pelvic Floor Disability Index (PFDI-20)

8.2 Safety and Other Assessments

The clinician's initial physical exam and screening procedure will ensure that all participants are appropriate for the study.

Daily reminders will be sent to participants via text message. These text messages will include a routine reminder for the participant to contact the site in the case of questions or concerns. Such questions or concerns may range from confusion on logistical procedures associated with the study, to mild

discomfort or vaginal discharge, or to a possible serious adverse event. Study participants will be encouraged to call the study coordinator immediately if she has a serious concern. The study guide will also indicate that the participant should call 911 in the event of a medical emergency.

Serious adverse events will be communicated to the Data Safety Monitor for the study within a 48-hour period, with the exception of deaths and immediately life-threatening events. Deaths and immediately life-threatening events, whether related or unrelated to the study device, shall be recorded on the SAE form and submitted to the Data Safety Monitor, IRB and the Sponsor, Liv Labs, Inc., within 24 hours of site awareness. The study sponsor will report the UADE to FDA.

Unanticipated adverse device events (UADEs) will be reported to the Sponsor and Data Safety Monitor within 24 hours of site awareness.

Safety analysis will also include results of urinalysis and vaginal examination taken at the end of the study.

8.3 Adverse Events and Serious Adverse Events

8.3.1 Definition of Adverse Events (AE)

An adverse event is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device and whether anticipated or unanticipated. (ISO 14155:2020(E))

8.3.2 Definition of Serious Adverse Events (SAE) & Unanticipated Adverse Device Effect

A Serious Adverse Event (SAE) is defined as an AE or suspected adverse reaction that, in the view of either the Investigator or Sponsor, results in any of the following outcomes (ISO 14155:2020(E)):

(1) death;
(2) serious deterioration in the health of the subject, users, or other persons as defined by one or more of the following: (a) a life-threatening illness or injury, (b) a permanent impairment of a body structure or a body function including chronic diseases, (c) in-patient or prolonged hospitalization, or medical or surgical intervention to prevent life-threatening illness or injury, or permanent impairment to a body structure or a body function;
(3) fetal distress, fetal death, a congenital abnormality, or birth defect including physical or mental impairment.

An Unanticipated Adverse Device Effect (UADE) is defined as any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects (21 CFR 812.3(d)).

8.3.3 Classification of an Adverse Event

All AEs will be assessed by the PI using a protocol-defined grading system. The following guidelines will be used to describe severity:

• Mild – Events require minimal or no treatment and do not interfere with the participant's daily activities.

• Moderate – Events result in a low level of inconvenience or concern with the therapeutic measures. Moderate events may cause some interference with functioning.

• Severe – Events interrupt a participant's usual daily activity and may require systemic drug therapy or other treatment. Severe events are usually potentially life-threatening or incapacitating.

8.3.3.1 Severity of Event

The PI will record all reportable events with start dates occurring any time after enrollment occurs through the last day of study participation. At the end-of-study clinic visit, the investigator will inquire about the occurrence of AE/SAEs throughout the home study. Events will be followed for outcome information until resolution or stabilization.

8.3.3.2 Relationship to Study Intervention

The PI's assessment of an AE's relationship to the study device is part of the documentation process, but it is not a factor in determining what is or is not reported in the study. All AEs must have their relationship to the study device assessed. To help assess, the following guidelines are used:

• Related – The AE is known to occur with the study device type, there is a reasonable possibility that the study device caused the AE, or there is a temporal relationship between the study device and the event. Reasonable possibility means that there is evidence to suggest a causal relationship between the study device and the AE.

• Not Related – There is not a reasonable possibility that the administration of the study device caused the event, there is no temporal relationship between the study device and event onset, or an alternate etiology has been established.

8.3.3.3 Expectedness

The PI will be responsible for determining whether an AE is expected or unexpected. An AE will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information previously described for the study device. Potential risks are noted in Section 2.3.1.

8.3.4 Time Period and Frequency for Event Assessment and Follow-Up

Adverse event assessments will be noted by the study clinician for the initial clinic visit and for the end-of-study final clinic visit. . If any of the adverse events are serious, these will be noted, followed up with phone contact with the participant, and arrangements made for care.

All AEs including local and systemic events will be captured on the appropriate CRF. Information to be collected includes event description, time of onset, clinician's assessment of seriousness and severity, relationship to study product (assessed only by those with the training and authority to make a diagnosis), and time of resolution/stabilization of the event. All AEs occurring while on study must be documented appropriately regardless of relationship to the study device. All AEs will be followed to adequate resolution or stabilization. Any medical condition that is present at the time that the participant is screened will be considered as baseline and not reported as an AE. However, if the study participant's condition deteriorates at any time during the study, it will be recorded as an AE.

8.3.5 Adverse Event Reporting

AEs will be documented using the Case Report Form. This will include assessments from the two (2) clinic visits as well as the two follow-up telephone calls..

The PI will record all reportable events with start dates occurring any time after enrollment occurs through the last day of study participation. At the final study visit, the investigator will inquire about the occurrence of AE/SAEs since the last visit. Events will be followed for outcome information until resolution or stabilization.

8.3.6 Serious Adverse Event Reporting

The study clinician will complete a SAE Form within the following timelines:

- All deaths and immediately life-threatening events, whether related or unrelated, will be recorded on the SAE Form and submitted to the Data Safety Monitor, IRB and the Sponsor, Liv Labs, Inc. within 24 hours of site awareness. See Section 10.1.5, Key Roles for contact information.

- Other SAEs, regardless of relationship, will be submitted to the Sponsor and Data Safety Monitor within 48 hours of site awareness.

- All UADEs will be reported to the Sponsor and the Data Safety Monitor within 24 hours of site awareness.

- The Sponsor will notify the IRB of any device-related SAE and the IRB and FDA of any UADE as soon as possible, but in no case later than 10 working days after the Sponsor first receives notice of the UADE.
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- UADEs will be reported to study participants as soon as possible, but in no case later than 10 working days after the Sponsor first receives notice of the UADE. Participants will also be informed of their right to discontinue the study at any time.

All SAEs and UADEs will be followed until satisfactory resolution or stabilization. Other supporting documentation of the event may be requested by the Sponsor and should be provided as soon as possible. The Sponsor will be responsible for notifying the FDA of any UADE as soon as possible but in no case later than 10 working days after the Sponsor's initial receipt of the information.

8.3.7 Reporting Events to Participants

If any serious adverse events are associated with the study logistics or treatment phase of the study, study personnel will pause the trial and notify all participants within 72 hours of the Sponsor or PI determining that a serious adverse event is likely associated with the study logistics or treatment.

8.3.8 REPORTING OF PREGNANCY

If any study candidate tests positive for pregnancy at the clinic visit, she will be informed of the test result as the basis for her exclusion from the study.

9 Statistical Considerations

9.1 Statistical Hypotheses

- **Primary Effectiveness Endpoints:**

The primary effectiveness endpoint is a composite endpoint used to describe responders to the use of the *Pippa Fitness Pessary* to reduce urinary leakage. The two component endpoints defining a responder are:

1. >50% reduction in pad weight gain for the 1-hour pad weight test with vs without the pessary. This component outcome is defined as:

$$\frac{\text{(1-hr PWT urine weight without pessary) - (1-hr PWT urine weight with pessary)}}{\text{(1-hr PWT urine weight without pessary)}} > .50$$

and/or

2. >50% reduction in the average daily reports of number of urine leaks per day during periods with and without the pessary. This component outcome is defined as:

$$\frac{\text{(Mean \# of leaks/day without pessary) - (Mean \# of leaks/day with pessary)}}{\text{(Mean \# of leaks/day without pessary)}} > .50$$

We plan to ensure that our study is powered to be able to show a significant difference between baseline and treatment measures for each component outcome, but primarily we will ensure that our

study is powered to show a responder rate of success of at least 70%. A responder in this case would be a participant who showed a greater than 50% reduction in 1-hour pad weight gain between baseline and pessary use and/or a greater than 50% reduction in mean daily reported leakage episodes between baseline and pessary use.

For the primary composite endpoint, the null hypothesis is that the responder proportion (percentage of participants with >50% reduction in pad urine weight gain and/or >50% reduction in mean daily number of leakage episodes) is <=70%. The alternative is that it is >70%.

To investigate the component endpoints of our composite endpoint:

1. The null hypothesis for the 1-hour pad weight test is that the reduction in urine weight gain due to use of the Pippa Fitness Pessary is <=50%, and the alternative hypothesis is that it is >50%.
2. For the daily reports of leakage episodes, the null hypothesis is that the reduction in leakage episodes due to use of the Pippa Fitness Pessary is <=50%, and the alternative hypothesis is that it is >50%.

Our additional primary endpoint relates to safety. Safety reporting using urinalysis, vaginal examination, and evaluation will be descriptive and narrative in nature. Additionally, the participants' self report of AEs will be descriptive and later classified into relative groupings and quantitatively summarized.

Secondary Endpoint:
Our secondary endpoint will be change in quality of life (QoL) as measured by the IIQ-7 Quality of Life Questionnaire at baseline and post-treatment. Although we also will measure changes in the Patient Global Impression of Severity (PGI-S), the Pelvic Floor Disability Index (PFDI-20) and the Questionnaire for Urinary Incontinence Diagnosis (QUID) as exploratory measures, the secondary endpoint analysis will be based on changes in the IIQ-7 scores.
The IIQ-7 Questionnaire is to be completed at baseline and after the treatment period. The questionnaire contains 7 questions regarding areas which may have been influenced or changed by accidental urine loss. These questions are assigned a value of 0 = Not at All; 1 = Slightly; 2 = Moderately; and 3 = Greatly. The Questionnaire is scored by taking the average score of items and then multiplying that value by 33 1/3 to put scores on a scale from 0 to 100. A lower score is considered less impact to quality of life and a higher score reflects more impact to quality of life. In the same manner, a reduction in scores from control reflects improved quality of life. A reduction in score of > 3.7 is considered the Minimum Clinically Important Difference (MCID). The IIQ-7 score reduction of > 3.7 will be our secondary outcome.

9.2 Sample Size Determination

We used a precision approach to determine the appropriate sample size and power for the study. For our primary composite endpoint (>50% reduction in pad weight gain on the 1-hour pad weight test and/or on mean daily leak reports) we estimated a response rate of at least 70% based on our own

earlier work and on the Poise Impressa study (Ziv et al.). With the desired precision of this estimated response rate set to 0.10 and a confidence level of 0.90, the estimated sample size would be 57.

Estimated Proportion	0.70
Desired precision of estimate	0.10
Confidence level	0.90
Population size	Large
Sample Size	57

To also ensure that our 1 hour pad weight differences between baseline and treatment would be statistically significant, we checked that a sample size of 57 with a type 1 error rate (alpha) of 0.05, one-sided, would provide sufficient power. We based our estimates of a standard deviation in pad weight change to be 18% (conservative estimate based on the Poise Impressa study, Ziv et al.) and found that we would only need 50 subjects to have at least 90% power to see at least a 50% reduction in pad urine weight for an exploratory analysis of just pad weight differences.

Thus, to be conservative, we will recruit up to 90 participants to ensure a sample size of completers of 57 participants.

This sample size should also be sufficient for the analysis of self-report measures of leak frequency, quality of life, and our other exploratory endpoints.

9.3 Populations for Analyses

The effectiveness and safety analyses will be based on the Intent to Treat (ITT) population. We will also do comparative analyses for the Modified Intent to Treat and Per Protocol populations.

Intent to Treat Population (ITT): Any subject enrolled who receives a pre-weighed pad for the control phase. Enrollment is expected to be 70 subjects. Enrolled study participants are those who meet all inclusion and exclusion criteria and who are issued pads and a device. An ITT approach is possible if at least partial primary endpoint outcome data are available (in this case, either a 1-Hour Treatment Pad Weight Test or at least one treatment leak report). We will handle missing data due to dropouts by using the last observation carried forward (LOCF) method, whereby the last available measurement for each individual at the time point prior to withdrawal from the study is retained in the analysis (in our case, all data up to the time of withdrawal).[6] The ITT population will be used for the primary effectiveness analysis.

Modified Intent to Treat Population (mITT): Any subject enrolled who remains in the study through the control phase, has started the treatment phase, has taken the 1-Hour Treatment Pad Weight Test and has at least 1 leak report data point. We will analyze the mITT data as an exploratory analysis.

[6] Gupta SK. Intention-to-treat concept: A review. Perspect Clin Res. 2011;2(3):109-112. doi:10.4103/2229-3485.83221.

Per Protocol Population (PP): Any subject getting through the entire treatment period and having complete data (baseline and treatment 1-hour pad weight data as well as complete leak report data). We will also analyze the PP data as an exploratory analysis.

Safety Population (SP): Same as ITT.

9.4 Statistical Analyses

9.4.1 General Approach

De-identified data will be combined into analysis data sets using an electronic database that is validated, secure, password-protected and has an audit trail of all changes made to the data after initial entry.

9.4.2 Analysis of the Primary Effectiveness Endpoint(s)

For the analysis of our primary composite outcome, the dichotomous subject success in pad leakage reduction of greater than 50% and/or a reduction in mean daily leakage episodes greater than 50%, a binomial proportion test will be used. In analyzing the individual components, a comparison of the mean percent reduction in leakage compared to zero will be performed using a 1-sample t test. The ITT population will be used for the primary effectiveness analysis. We will handle missing data due to dropouts by using data up to the last observation carried forward (LOCF) method, whereby the last available measurement for each individual at the time point prior to withdrawal from the study is retained in the analysis (in our case, all data up to the time of withdrawal).[6] For the composite primary endpoint, this means that the 1-hour Treatment Pad Weight Test will be required. For the daily reported leak episodes, we will consider data up until the time of withdrawal during the treatment period. We will also conduct sensitivity analyses for missing data, using various methods, to evaluate the whole spectrum of the treatment effect.

9.4.3 Analysis of the Secondary Endpoint(s)

Similarly, a 1-sample t test will be used to investigate change in the quality-of-life measure (IIQ-7) with versus without use of the *Pippa Fitness Pessary*.

9.4.4 Safety Analyses

No formal testing of adverse events or their characteristics will be performed. Reporting is described above. Analyses will include a summary table and tables for relationship to the study treatment and seriousness and severity.

9.4.5 Baseline Descriptive Statistics

Demographic variables, questionnaire data and physical exam / medical history findings taken at baseline will be summarized with descriptive statistics.

End-of-study data on safety outcomes, overall satisfaction with the *Pippa Fitness Pessary*, Net Promoter Score (indication of how likely one is to recommend the device to others), PGI-C, QUID, PFDI-20 and PGI-S will also be summarized with descriptive statistics.

9.4.6 Planned Interim Analyses

None planned.

9.4.7 Sub-Group Analyses

None planned.

9.4.8 Tabulation of Individual Participant Data

A spreadsheet will be used to consolidate and store the study data.

9.4.9 Exploratory Analyses

None planned.

10 Supporting Documentation and Operational Considerations

10.1 Regulatory, Ethical, and Study Oversight Considerations

10.1.1 Informed Consent Process

Consent forms describing in detail the study device, study procedures, and risks will be given to the participant, and documentation of informed consent is required prior to starting intervention/administering the study device. The following consent materials are submitted with this protocol: Pippa Fitness Pessary Device Effectiveness and Safety Study Informed Consent.

Informed consent is a process that is initiated prior to the individual's agreeing to participate in the study and continues throughout the individual's study participation. Extensive discussion of risks and possible benefits of participation will be provided to the participants and their families. Consent forms will be IRB-approved, embody the elements of informed consent required by 21 CFR 50.25, and the participant will be asked to read and review the document. A research team member will explain the research study to the participant and answer any questions that may arise. All participants will receive a verbal explanation in terms suited to their comprehension of the purposes, procedures, and potential risks of the study and of their rights as research participants. Participants will have the opportunity to carefully review the consent form and ask questions prior to signing.

The participants will have the opportunity to discuss the study with their surrogates or think about it prior to agreeing to participate. The participant will sign and date the informed consent document prior to any procedures being done specifically for the study. The participants may withdraw consent at any

time throughout the course of the trial. A copy of the signed informed consent document will be given to the participants for their records. The rights and welfare of the participants will be protected by emphasizing to them that the quality of their medical care will not be adversely affected if they decline to participate in this study.

Original informed consent forms will be maintained in the study participant's case history. In addition, the study participant's case history will document that the participant provided consent prior to participation in the research.

10.1.1.1 Consent/assent and Other Informational Documents Provided to participants

Candidates for the study will be provided with the Pippa Fitness Pessary Device Effectiveness and Safety Study Informed Consent; the IFU for the device; and the Study Participant Guide.

10.1.2 Study Discontinuation and Closure

The study will be discontinued after at least 57 participants have completed all phases of the trial and we have analyzed the resulting data.

The study will be suspended or discontinued if required by an evaluation of the severity and possible causality of adverse events. This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to the investigator, funding agency, the sponsor and regulatory authorities. If the study is prematurely terminated or suspended, the PI will promptly inform the IRB and will provide the reason(s) for the termination or suspension and the study sponsor will inform the FDA if the study was terminated due to an unanticipated adverse device effect that presents an unreasonable risk to subjects.
Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to participants
- Insufficient compliance to protocol requirements

The study may resume once concerns about safety, protocol compliance, and data quality are addressed and satisfy the Sponsor, IRB and FDA.

10.1.3 Confidentiality and Privacy

Participant confidentiality is strictly held in trust by the participating investigators, their staff, and the sponsor(s) and their agents. This confidentiality is extended to cover testing of biological samples in addition to the clinical information relating to participants. Therefore, the study protocol, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study or the data will be released to any unauthorized third party without prior written approval of the Sponsor.

The study monitor, other authorized representatives of the Sponsor, representatives of the IRB or company supplying study materials or regulatory health authorities may inspect all documents and records required to be maintained by the investigator, including but not limited to, medical records (office, clinic, or hospital) and pharmacy records for the participants in this study. The clinical study site will permit access to such records.

The study participant's contact information will be securely stored at each clinical site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as dictated by local IRB and Institutional regulations, but at least for a period of 2 years after the latter of the following two dates: The date on which the investigation is terminated or completed, or the date that the records are no longer required for purposes of supporting a marketing application.

Study participant research data, which is for purposes of statistical analysis and scientific reporting, will be transmitted to and stored in a secure server in the investigator's clinic. This will not include the participant's contact or identifying information. Rather, individual participants and their research data will be identified by a unique subject identification number. Any electronic study data entry and study management systems used by clinical sites will be secured and password protected. At the end of the study, all study databases will be de-identified and archived at the clinic and at the Sponsor organization.

10.1.4 Future Use of Stored Data

Data collected for this study will be stored at the clinical site and Sponsor facilities. After the study is completed, the de-identified, archived data that is stored at the Sponsor's facility under the supervision of the CEO may be used by other researchers, including those outside of the study. Permission to transmit data to the Sponsor will be included in the informed consent.

10.1.5 Key Roles and Study Governance

Sponsor	Liv Labs, Inc. 332 S Michigan Ave Suite 121 #5595 Chicago, IL 60604 Melody Roberts, CEO melody@liv-labs.com
Medical Monitor	SEE STUDY CONTACT LIST
Data Safety Monitor	SEE STUDY CONTACT LIST

10.1.6 Safety Oversight

The sponsor will contact the independent medical reviewer, to assist in assessing any safety concerns, if needed. The Investigator should be able and willing to provide further information on the specific event when requested by the study Sponsor. Details on the roles and responsibility of the medical monitor can be found in the Medical Monitoring Plan. 10.1.7 Clinical Monitoring

Clinical site monitoring shall be conducted to ensure that the rights, safety and welfare of human participants are protected, that the reported trial data are accurate, complete, and verifiable, and that the conduct of the trial is in compliance with the currently approved protocol/amendment(s), with GCP, and with applicable regulatory requirement(s). Any required onsite monitoring for this study will be performed by a qualified Sponsor representative. Details of clinical site monitoring are documented in a Clinical Monitoring Plan (CMP). The CMP will describe in detail who will conduct the monitoring, at what frequency monitoring will be done, at what level of detail monitoring will be performed, and the distribution of monitoring.

10.1.8 Quality Assurance and Quality Control

Following written SOPs, the monitors will verify that the clinical trial is conducted and data are generated, documented (recorded), and reported in compliance with the protocol, GCP, and the applicable regulatory requirements. The investigational site will provide direct access to all trial-related sites, source data/documents, and reports for the purpose of monitoring and auditing by the Sponsor, and inspection by local and regulatory authorities.

10.1.9 Data Handling and Record Keeping

10.1.9.1 Data Collection and Management Responsibilities

Data collection is the responsibility of the clinical trial staff at the site under the supervision of the site PI. The investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported.

Consenting records may be captured in electronic forms via REDCap (or similar software), which is a secure web application for managing online databases. Any software used for consenting will be compliant with 21 CFR Part 11, FISMA, HIPAA and GDPR.

Study data will be collected using standardized paper Case Report Forms. CRFs will be printed on 2-part NCR paper (or equivalent) so that both the site and Sponsor will have copies of the CRFs. Each CRF will be designed to accommodate the specific features of the trial design. Modification of a CRF will only be made if deemed necessary by the study sponsor. A CRF is required and should be completed for each included subject. The Investigator has ultimate responsibility for the collection and reporting of all data entered on the CRFs and any other data collection forms (source documents) and ensuring that they are accurate, authentic/original, attributable, complete, consistent, legible, timely (contemporaneous), enduring and available when required. The CRFs must be signed by the investigator to attest that the data contained therein are true. The site will be provided with general CRF Completion Guidelines that can be located in the Study Operations Manual, which will assist in data entry and data issues/questions. All persons allowed to enter or change CRF data must appear on the Delegation of Responsibilities Log.

During the at-home phase of the study, a digital messaging service (such as Twilio or Slick Text) will be used to automatically send daily reminders

A representative of the Sponsor will monitor CRFs to identify possible data errors. Data queries that arise on CRFs that have been retrieved from the site, will be resolved using a Data Clarification Form (DCF). All data discrepancies will be resolved prior to database lock.

10.1.9.2 Study Records Retention

Study documents (including device disposition, informed consents, source documents, correspondence, regulatory documents, contracts etc.) should be retained for a minimum of 3 years after the investigation is completed or terminated or the records are no longer required to support a marketing application (whichever date is later). No records will be destroyed without the written consent of the Sponsor, Liv Labs. It is the responsibility of the Sponsor to inform the investigator when these documents no longer need to be retained.

10.1.10 Protocol Deviations

A protocol deviation is any noncompliance with the clinical trial protocol or GCP requirements. The noncompliance may be either on the part of the participant, the investigator, or the study site staff. As a result of deviations, corrective actions are to be developed by the site and implemented promptly.

It is the responsibility of the site to use continuous vigilance to identify and report deviations within 3 working days of the scheduled protocol-required activity. All deviations must be addressed in study source documents and reported to the Sponsor. Protocol deviations must be sent to the IRB per their guidelines. The site PI/study staff is responsible for knowing and adhering to IRB requirements.

10.1.11 Publication and Data Sharing Policy

The study will be registered on ClincialTrials.gov before the first participant is enrolled.

10.1.12 Conflict of Interest Policy

The independence of this study from any actual or perceived influence, such as by the medical device industry, is critical. Therefore, any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication, or any aspect of this trial will be disclosed and managed. Furthermore, persons who have a perceived conflict of interest will be required to have such conflicts managed in a way that is appropriate to their participation in the trial.

10.3 Abbreviations

AE	Adverse Event	
CFR	Code of Federal Regulations	
CMP	Clinical Monitoring Plan	
CRF	Case Report Form	
CST	Cough Stress Test	
DCF	Data Clarification Form	
FDA	Food and Drug Administration	
GCP	Good Clinical Practice	
ICH	International Conference on Harmonisation	
ICS	International Continence Society	
IFU	Instructions for Use	
IRB	Institutional Review Board	
ITT	Intention-To-Treat	
NIH	National Institutes of Health	
PI	Principal Investigator	
PWT	Pad Weight Test	
SAE	Serious Adverse Event	
SOA	Schedule of Activities	
SUI	Stress Urinary Incontinence	
US	United States	

10.4 Protocol Amendment History

Version	**Date**	**Description of Change**	**Brief Rationale**
1.0	December 21, 2021	Original submission	
1.1	April 20, 2022	Change to data management	Ease of study execution
2.0	July 14, 2022	Update for independent IRB	Northwestern ceding to Advarra
3.0	May 16, 2023	Removing Northwestern Lab, eICF and subject payment details. Adding numbers to Eligibility Criteria and Visit Windows. Increasing the maximum number of sites to 6. Changing investigational device disposal policy.	Adapting protocol for Site Variation and Flexibility. Adding clarity to eligibility criteria and assessment time points. To have the ability to replace one site that was initiated but never enrolled.
4.0	July 11, 2023	Remove automated daily surveys during the at-home phase; including Appendix H – Daily Assessments. Better define exclusion criteria 5 and 7.	Over-complicated and unnecessary. Add clarity to the current exclusion criteria.

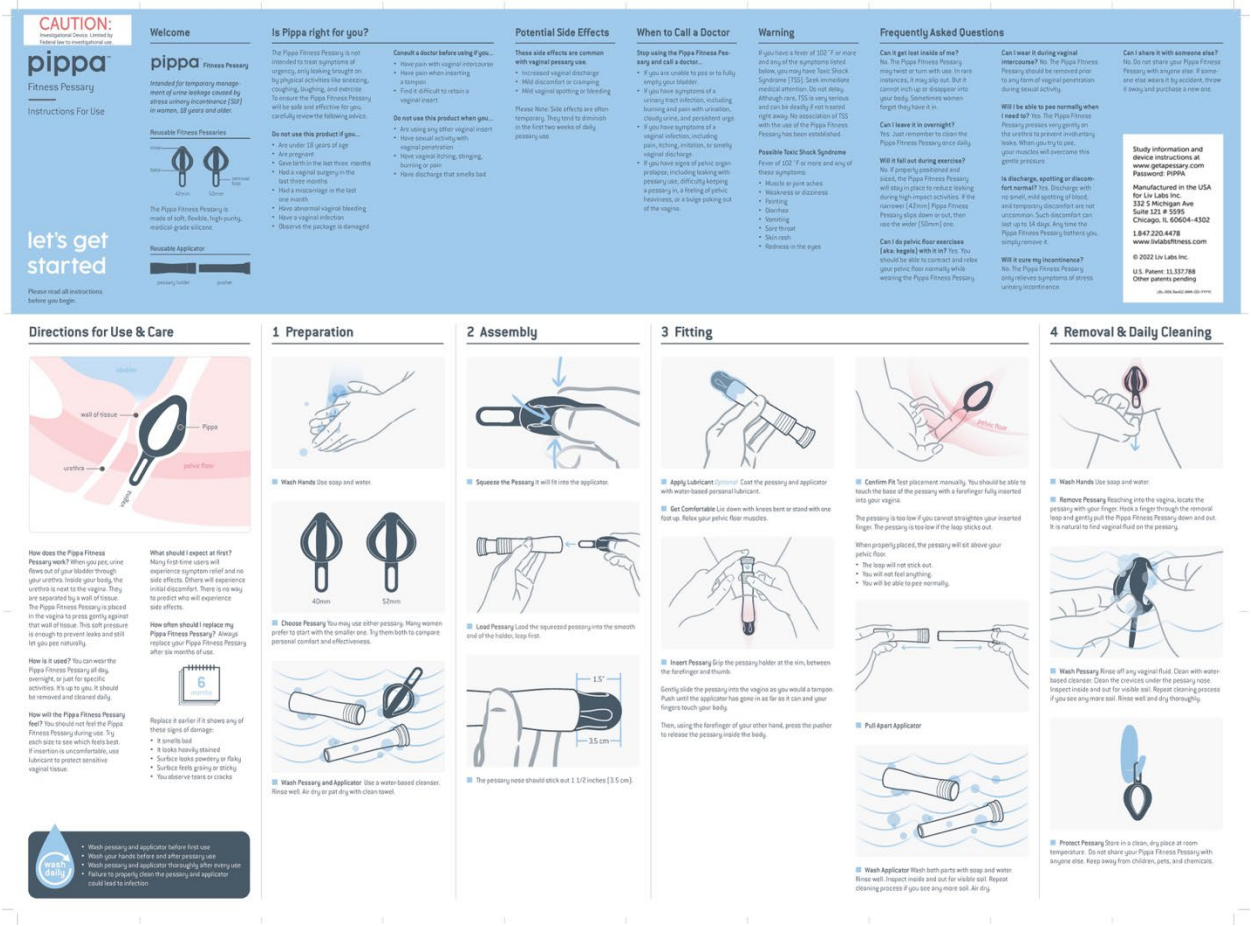
5.0	October 2, 2023	Add PFDI-20 questionnaire to baseline and final clinic visits. Remove contact information for Medical and Data Safety Monitors.	Collect additional information on secondary symptoms. Allow for contact information to be maintained outside of the protocol for ease of updating as needed.

11 APPENDICES

- Appendix A – Instructions for Use
- Appendix B – Screeners and Questionnaires
- Appendix C – Pad Weight Test Preparations Worksheet
- Appendix D – Pre-Enrollment Clinic Visit Invitation
- Appendix E – Study Participant Guide
- Appendix F – 12-Day Leakage Episodes Record
- Appendix G – Daily Communications

APPENDIX A – INSTRUCTIONS FOR USE

Instructions are provided in the device package. This large-format document folds out to display two sections: a written section detailing device benefits and risks and an illustrated section providing instructions for use. This document is the result of formal human factors testing. Full-scale version uploaded under Device Description Document.


CAUTION:
Investigational Device. Limited by Federal law to investigational use.
pippa
Fitness Pessary
Instructions For Use
let's get started
Please read all instructions before you begin.
Welcome
pippa Fitness Pessary
Intended for temporary management of urine leakage caused by stress urinary incontinence (SUI) in women, 18 years and older.
Reusable Fitness Pessaries
40mm
50mm
The Pippa Fitness Pessary is made of soft, flexible, high-purity, medical-grade silicone.
Reusable Applicator
pessary holder
pusher
Is Pippa right for you?
The Pippa Fitness Pessary is not intended to treat symptoms of urgency, only leaking brought on by physical activities like sneezing, coughing, laughing, and exercise. To ensure the Pippa Fitness Pessary will be safe and effective for you, carefully review the following advice.
Do not use this product if you...
Are under 18 years of age
Are pregnant
Gave birth in the last three months
Had a vaginal surgery in the last three months
Had a miscarriage in the last one month
Have abnormal vaginal bleeding
Have a vaginal infection
Observe the package is damaged
Consult a doctor before using if you...
Have pain with vaginal intercourse
Have pain when inserting a tampon
Find it difficult to retain a vaginal insert
Do not use this product when you...
Are using any other vaginal insert
Have sexual activity with vaginal penetration
Have vaginal itching, stinging, burning or pain
Have discharge that smells bad
Potential Side Effects
These side effects are common with vaginal pessary use.
Increased vaginal discharge
Mild discomfort or cramping
Mild vaginal spotting or bleeding
Please Note: Side effects are often temporary. They tend to diminish in the first two weeks of daily pessary use.
When to Call a Doctor
Stop using the Pippa Fitness Pessary and call a doctor...
If you are unable to pee or to fully empty your bladder.
If you have symptoms of a urinary tract infection, including burning and pain with urination, cloudy urine, and persistent urge.
If you have symptoms of a vaginal infection, including pain, itching, irritation, or smelly vaginal discharge.
If you have signs of pelvic organ prolapse, including leaking with pessary use, difficulty keeping a pessary in, a feeling of pelvic heaviness, or a bulge poking out of the vagina.
Warning
If you have a fever of 102 °F or more and any of the symptoms listed below, you may have Toxic Shock Syndrome (TSS). Seek immediate medical attention. Do not delay. Although rare, TSS is very serious and can be deadly if not treated right away. No association of TSS with the use of the Pippa Fitness Pessary has been established.
Possible Toxic Shock Syndrome
Fever of 102 °F or more and any of these symptoms:
Muscle or joint aches
Weakness or dizziness
Fainting
Diarrhea
Vomiting
Sore throat
Skin rash
Redness in the eyes
Frequently Asked Questions
Can it get lost inside of me? No. The Pippa Fitness Pessary may twist or turn with use. In rare instances, it may slip out. But it cannot inch up or disappear into your body. Sometimes women forget they have it in.
Can I leave it in overnight? Yes. Just remember to clean the Pippa Fitness Pessary once daily.
Will it fall out during exercise? No. If properly positioned and sized, the Pippa Fitness Pessary will stay in place to reduce leaking during high-impact activities. If the narrower (40mm) Pippa Fitness Pessary slips down or out, then use the wider (50mm) one.
Can I do pelvic floor exercises (aka kegels) with it in? Yes. You should be able to contract and relax your pelvic floor normally while wearing the Pippa Fitness Pessary.
Can I wear it during vaginal intercourse? No. The Pippa Fitness Pessary should be removed prior to any form of vaginal penetration during sexual activity.
Will I be able to pee normally when I need to? Yes. The Pippa Fitness Pessary presses very gently on the urethra to prevent involuntary leaks. When you try to pee, your muscles will overcome this gentle pressure.
Is discharge, spotting or discomfort normal? Yes. Discharge with no smell, mild spotting of blood, and temporary discomfort are not uncommon. Such discomfort can last up to 14 days. Any time the Pippa Fitness Pessary bothers you, simply remove it.
Will it cure my incontinence? No. The Pippa Fitness Pessary only relieves symptoms of stress urinary incontinence.
Can I share it with someone else? No. Do not share your Pippa Fitness Pessary with anyone else. If someone else wears it by accident, throw it away and purchase a new one.
Study information and device instructions at www.getapessary.com
Password: PIPPA
Manufactured in the USA for Liv Labs Inc.
332 S Michigan Ave
Suite 121 # 5595
Chicago, IL 60604-4302
1.847.220.4478
www.livlabsfitness.com
© 2022 Liv Labs Inc.
U.S. Patent: 11,337,788
Other patents pending
Directions for Use & Care
bladder
wall of tissue
Pippa
urethra
pelvic floor
vagina
How does the Pippa Fitness Pessary work? When you pee, urine flows out of your bladder through your urethra. Inside your body, the urethra is next to the vagina. They are separated by a wall of tissue. The Pippa Fitness Pessary is placed in the vagina to press gently against that wall of tissue. This soft pressure is enough to prevent leaks and still let you pee naturally.
How is it used? You can wear the Pippa Fitness Pessary all day, overnight, or just for specific activities. It's up to you. It should be removed and cleaned daily.
How will the Pippa Fitness Pessary feel? You should not feel the Pippa Fitness Pessary during use. Try each size to see which feels best. If insertion is uncomfortable, use lubricant to protect sensitive vaginal tissue.
What should I expect at first? Many first-time users will experience symptom relief and no side effects. Others will experience initial discomfort. There is no way to predict who will experience side effects.
How often should I replace my Pippa Fitness Pessary? Always replace your Pippa Fitness Pessary after six months of use.
6 months
Replace it earlier if it shows any of these signs of damage:
It smells bad
It looks heavily stained
Surface looks powdery or flaky
Surface feels gritty or sticky
You observe tears or cracks
wash daily
Wash pessary and applicator before first use
Wash your hands before and after pessary use
Wash pessary and applicator thoroughly after every use
Failure to properly clean the pessary and applicator could lead to infection
1 Preparation
Wash Hands Use soap and water.
40mm
50mm
Choose Pessary You may use either pessary. Many women prefer to start with the smaller one. Try them both to compare personal comfort and effectiveness.
Wash Pessary and Applicator Use a water-based cleanser. Rinse well. Air dry or pat dry with clean towel.
2 Assembly
Squeeze the Pessary It will fit into the applicator.
Load Pessary Load the squeezed pessary into the smooth end of the holder, loop first.
1.5"
3.5 cm
The pessary nose should stick out 1 1/2 inches (3.5 cm).
3 Fitting
Apply Lubricant Optional Coat the pessary and applicator with water-based personal lubricant.
Get Comfortable Lie down with knees bent or stand with one foot up. Relax your pelvic floor muscles.
Insert Pessary Grip the pessary holder at the rim, between the forefinger and thumb.
Gently slide the pessary into the vagina as you would a tampon. Push until the applicator has gone in as far as it can and your fingers touch your body.
Then, using the forefinger of your other hand, press the pusher to release the pessary inside the body.
pelvic floor
Confirm Fit Test placement manually. You should be able to touch the base of the pessary with a forefinger fully inserted into your vagina.
The pessary is too low if you cannot straighten your inserted finger. The pessary is too low if the loop sticks out.
When properly placed, the pessary will sit above your pelvic floor.
The loop will not stick out.
You will not feel anything.
You will be able to pee normally.
Pull Apart Applicator
Wash Applicator Wash both parts with soap and water. Rinse well. Inspect inside and out for visible soil. Repeat cleaning process if you see any more soil. Air dry.
4 Removal & Daily Cleaning
Wash Hands Use soap and water.
Remove Pessary Reaching into the vagina, locate the pessary with your finger. Hook a finger through the removal loop and gently pull the Pippa Fitness Pessary down and out. It is natural to find vaginal fluid on the pessary.
Wash Pessary Rinse off any vaginal fluid. Clean with water-based cleanser. Clean the crevices under the pessary nose. Inspect inside and out for visible soil. Repeat cleaning process if you see any more soil. Rinse well and dry thoroughly.
Protect Pessary Store in a clean, dry place at room temperature. Do not share your Pippa Fitness Pessary with anyone else. Keep away from children, pets, and chemicals.

APPENDIX B – SCREENERS AND QUESTIONNAIRES

A. PRE-ASSESSMENT SCREENER

Hello!

Thank you for your interest in our study. Please answer the following questions honestly and to your very best knowledge, so that we can learn if you may qualify for further screening.

Thank you!

3IQ Screening Questionnaire

Q1: During the last three months, have you leaked urine (even a small amount)?
A1: Yes No
If no, end survey.

Q2: During the last three months, did you leak urine…
A2: (check *all that apply*):
- □ a. When you were performing some physical activity, such as coughing, sneezing, lifting, or exercise?
- □ b. When you had the urge or feeling that you needed to empty your bladder, but you could not get to the toilet fast enough?
- □ c. Without physical activity and without a sense of urgency?

Q3: During the last three months, did you leak urine *most often*
A3: (check *only one*):
- □ a. When you are performing some physical activities, such as coughing, sneezing, lifting, or exercise?
- □ b. When you had the urge or feeling that you needed to empty your bladder, but you could not get to the toilet fast enough?
- □ c. Without physical activity or a sense of urgency?
- □ d. About equally as often with physical activities as with a sense of urgency?

If the answer to question 3 is "a," then continue. If not, disqualify candidate.
End Message: Thank you for answering the questionnaire. You do not currently qualify for our study.

Frequency Confirmation

Q1: How many times in a week do you leak urine?
A1: 0, 1-2, 3 or more
If not "3 or more," end survey and disqualify candidate.

Q2: For how long have you leaked at least 3 times a week?
A2: less than 3 months, more than 3 months
If less than 3 months, disqualify candidate. Otherwise, move forward to inclusion and exclusion pre-screening questionnaires.

End Message: Thank you for answering the questionnaire. You do not currently qualify for our study.

Additional Criteria Self-Certification.

Q1: Are **ALL** of the following statements true for you?

- I am at least 18 years old.
- I am anatomically female. (I have a vagina.)
- I am willing and able to interact with study staff by email, phone, text message and video conferencing software.
- I have reliable home internet connectivity.
- I am willing and able to wear a vaginal insert that is similar in size to a tampon.
- I am willing to halt the use of other vaginal inserts (such as vaginal pessaries, bladder supports, estrogen rings, tampons, and menstrual cups) while the study device is in place.
- I am willing to stop the use of any other form of urinary incontinence treatment for the duration of the study.
- My BMI is less than <40.0 (If you do not know your BMI you may calculate it here: https://www.nhlbi.nih.gov/health/educational/lose_wt/BMI/bmicalc.htm)

A1a: If every statement above is true for you, click here: "All are true" (Continue to Exclusion Criteria Questions)

A1b: If one or more of the statements above are not true for you, click here: "Some are not true" (End screening Questionnaire and disqualify candidate)

End Message: Thank you for answering the questionnaire. Unfortunately, you do not currently qualify for our study.

Q2: Are **ANY** of the following statements true for you?

- I have been diagnosed with pelvic organ prolapse beyond the hymen
- I have hypersensitivity to silicone rubber
- I have recently been diagnosed with bladder stones and/or bladder tumors
- I have had pelvic floor surgery (Cesarean section is OK)
- I have had an abortion within the past three months
- I have had vaginal, perineal, or uterine surgery within the past 3 months
- I have had surgery for incontinence
- I have symptoms of a potential urinary tract or vaginal infection
- I am pregnant
- I am planning to become pregnant within the next 3 months
- I do have a history of Toxic Shock Syndrome
- I have been diagnosed with urgency urinary incontinence
- I have been diagnosed with mixed incontinence (both urgency and stress types)
- I have been diagnosed with overflow incontinence
- I have been diagnosed with functional incontinence
- My incontinence is related to a central or spinal cord neurological condition such as multiple sclerosis, neurogenic bladder, Parkinson's, or spina bifida
- I have difficulty emptying my bladder on a regular basis
- I have difficulty inserting or wearing an intra-vaginal device

A2a: If none of the above statements are true for you, click here: "None of these statements are true for me." (Continue: Move forward to Informed Consent process.)
A2b: If any of the above statements are true for you, click here: "At least one statement is true for me." (End screening Questionnaire and disqualify candidate)

> End Message: Thank you for answering the questionnaire. Unfortunately, you do not currently qualify for our study.

Q3: Check this box if you are currently within 3 months post-partum.

All inclusion and exclusion criteria will be evaluated and confirmed at the clinical visit.

B. PRE-STUDY QUESTIONNAIRES

Hello!

Thank you for enrolling in our study. Please answer the following questions honestly and to the best of your knowledge. The full questionnaire will take less than 10 minutes of your time. Your answers will help us understand your current experience of living with Stress Urinary Incontinence.

Thank you for your time and effort!

PGI-S: Patient Global Impression Scales
Check the one number that best describes how your urinary tract condition is now.

- □ 0 – normal
- □ 1 – mild
- □ 2 – moderate
- □ 3 – severe

Baseline measurement. No exclusion.

QUID Questionnaire

Q1: Do you leak urine (even small drops), wet yourself, or wet your pads or undergarments when you **cough** or **sneeze**?
A1: Rarely, once in a while, often, most of the time, all of the time, none of the time

Q2: Do you leak urine (even small drops), wet yourself, or wet your pads or undergarments when you **bend down** or **lift something up**?
A2: Rarely, once in a while, often, most of the time, all of the time, none of the time

Q3: Do you leak urine (even small drops), wet yourself, or wet your pads or undergarments when you **walk quickly, jog** or **exercise**?
A3: Rarely, once in a while, often, most of the time, all of the time, none of the time

Q4: Do you leak urine (even small drops), wet yourself, or wet your pads or undergarments while you are **undressing** in order to use the **toilet**?
A4: Rarely, once in a while, often, most of the time, all of the time, none of the time

Q5: Do you get such a **strong and uncomfortable need** to urinate that you leak urine (even small drops) or wet yourself before reaching the toilet?
A5: Rarely, once in a while, often, most of the time, all of the time, none of the time

Q6: Do you have to **rush to the bathroom** because you get a **sudden, strong need** to urinate?
A6: Rarely, once in a while, often, most of the time, all of the time, none of the time

Each item scores 0 (None of the time), 1 (Rarely), 2 (Once in a while), 3 (Often), 4 (Most of the time) or 5 (All of the time). Responses to items 1, 2 and 3 are summed for the Stress score; and responses to items 4, 5, and 6 are summed for the Urge score.

IIQ-7 Questionnaire

Q1: Has urine leakage affected your ability to do household chores (cooking, cleaning, laundry)?
A1: Not at all, a little bit, moderately, greatly

Q2: Has urine leakage affected your physical recreation such as walking, swimming, or other exercise?
A2: Not at all, a little bit, moderately, greatly

Q3: Has urine leakage affected your entertainment activities (movies, concerts, etc.)?
A3: Not at all, a little bit, moderately, greatly

Q4: Has urine leakage affected your ability to travel by car or bus more than 30 minutes from home?
A4: Not at all, a little bit, moderately, greatly

Q5: Has urine leakage affected your participation in social activities outside your home?
A5: Not at all, a little bit, moderately, greatly

Q6: Has urine leakage affected your emotional health (nervousness, depression, etc.)?
A6: Not at all, a little bit, moderately, greatly

Q7: Has urine leakage affected your feeling frustrated?
A7: Not at all, a little bit, moderately, greatly
Baseline measurement. No exclusion.

Pelvic Floor Disability Index (PFDI-20)
While answering these questions, please consider your symptoms over the last 3 months.
Symptom scale: 0 = not present ,1= not at all ,2 = somewhat, 3 = moderately, 4 = quite a bit

Pelvic Organ prolapse Distress Inventory 6 (POPDI-6)
Do You…

1. Usually experience pressure in the lower abdomen?
2. Usually experience heaviness or dullness in the pelvic area?
3. Usually have a bulge or something falling out that you can see or feel in your vaginal area?
4. Ever have to push on the vagina or around the rectum to have or complete a bowel movement?
5. Usually experience a feeling of incomplete bladder emptying?
6. Ever have to push up on a bulge in the vaginal area with your fingers to start or

complete urination?

Colorectal-Anal distress Inventory 8 (CRAD-8)
Do You…

7. Feel you need to strain too hard to have a bowel movement?
8. Feel you have not completely emptied your bowels at the end of a bowel movement?
9. Usually lose stool beyond your control if your stool is well formed?
10. Usually lose stool beyond your control if your stool is loose?
11. Usually lose gas from the rectum beyond your control?
12. Usually have pain when you pass your stool?
13. Experience a strong sense of urgency and have to rush to the bathroom to have abowel movement?
14. Does part of your bowel ever pass through the rectum and bulge outside during orafter a bowel movement?

Urinary distress Inventory 6 (UDI-6)
Do You…

15. Usually experience frequent urination?
16. Usually experience urine leakage associated with a feeling of urgency, that is, a strong sensation of needing to go to the bathroom?
17. Usually experience urine leakage related to coughing, sneezing or laughing?
18. Usually experience small amounts of urine leakage (that is, drops)?
19. Usually experience difficulty emptying your bladder?
20. Usually experience pain or discomfort in the lower abdomen or genital region?

Baseline measurement. No exclusion.

C. POST-STUDY QUESTIONNAIRES

Welcome back!

Thank you very much for participating in our study! We are almost at the end. Please answer the following questions honestly and to the best of your knowledge. The full questionnaire will take less than 10 minutes of your time. Your answers should refer to the period of time during which you wore the *Pippa Fitness Pessary*. Please respond to all questions honestly and to the best of your knowledge.

Thank you for your time and effort!

PGI-C: Patient Global Impression Scales

Q: Please choose the response below that best describes the overall change in your SUI **while wearing the device.**

A: Very much better, much better, a little better, no change, a little worse, much worse, very much worse

PGI-S: Patient Global Impression Scales

Check the one number that best describes how your urinary tract condition is **while wearing the device**.

- □ 0 – normal
- □ 1 – mild
- □ 2 – moderate
- □ 3 – severe

QUID Questionnaire

Please choose the responses below that best describes your SUI while wearing the device.

Q1: Do you leak urine (even small drops), wet yourself, or wet your pads or undergarments when you **cough** or **sneeze**?

A1: Rarely, once in a while, often, most of the time, all of the time, none of the time

Q2: Do you leak urine (even small drops), wet yourself, or wet your pads or undergarments when you **bend down** or **lift something up**?

A2: Rarely, once in a while, often, most of the time, all of the time, none of the time

Q3: Do you leak urine (even small drops), wet yourself, or wet your pads or undergarments when you **walk quickly, jog** or **exercise**?

A3: Rarely, once in a while, often, most of the time, all of the time, none of the time

Q4: Do you leak urine (even small drops), wet yourself, or wet your pads or undergarments while you are **undressing** in order to use the **toilet**?

A4: Rarely, once in a while, often, most of the time, all of the time, none of the time

Q5: Do you get such a **strong and uncomfortable need** to urinate that you leak urine (even small drops) or wet yourself before reaching the toilet?

A5: Rarely, once in a while, often, most of the time, all of the time, none of the time

Q6: Do you have to **rush to the bathroom** because you get a **sudden, strong need** to urinate?

A6: Rarely, once in a while, often, most of the time, all of the time, none of the time

Each item scores 0 (None of the time), 1 (Rarely), 2 (Once in a while), 3 (Often), 4 (Most of the time) or 5 (All of the time). Responses to items 1, 2 and 3 are summed for the Stress score; and responses to items 4, 5, and 6 are summed for the Urge score.

IIQ-7 Questionnaire

Q1: Has urine leakage affected your ability to do household chores (cooking, cleaning, laundry)?

A1: Not at all, a little bit, moderately, greatly

Q2: Has urine leakage affected your physical recreation such as walking, swimming, or other exercise?
A2: Not at all, a little bit, moderately, greatly

Q3: Has urine leakage affected your entertainment activities (movies, concerts, etc.)?
A3: Not at all, a little bit, moderately, greatly

Q4: Has urine leakage affected your ability to travel by car or bus more than 30 minutes from home?
A4: Not at all, a little bit, moderately, greatly

Q5: Has urine leakage affected your participation in social activities outside your home?
A5: Not at all, a little bit, moderately, greatly

Q6: Has urine leakage affected your emotional health (nervousness, depression, etc.)?
A6: Not at all, a little bit, moderately, greatly

Q7: Has urine leakage affected your feeling frustrated?
A7: Not at all, a little bit, moderately, greatly

Pelvic Floor Disability Index (PFDI-20)
While answering these questions, please consider your symptoms while you were wearing the Pippa Fitness Pessary.
Symptom scale: 0 = not present ,1= not at all ,2 = somewhat, 3 = moderately, 4 = quite a bit

Pelvic Organ prolapse Distress Inventory 6 (POPDI-6)
Do You…

7. Usually experience pressure in the lower abdomen?
8. Usually experience heaviness or dullness in the pelvic area?
9. Usually have a bulge or something falling out that you can see or feel in your vaginal area?
10. Ever have to push on the vagina or around the rectum to have or complete a bowel movement?
11. Usually experience a feeling of incomplete bladder emptying?
12. Ever have to push up on a bulge in the vaginal area with your fingers to start or complete urination?

Colorectal-Anal distress Inventory 8 (CRAD-8)
Do You…

7. Feel you need to strain too hard to have a bowel movement?
8. Feel you have not completely emptied your bowels at the end of a bowel movement?
9. Usually lose stool beyond your control if your stool is well formed?
10. Usually lose stool beyond your control if your stool is loose?
11. Usually lose gas from the rectum beyond your control?
12. Usually have pain when you pass your stool?
13. Experience a strong sense of urgency and have to rush to the bathroom to have abowel movement?
14. Does part of your bowel ever pass through the rectum and bulge outside during orafter a bowel movement?

Urinary distress Inventory 6 (UDI-6)

Do You…

15. Usually experience frequent urination?
16. Usually experience urine leakage associated with a feeling of urgency, that is, a strong sensation of needing to go to the bathroom?
17. Usually experience urine leakage related to coughing, sneezing or laughing?
18. Usually experience small amounts of urine leakage (that is, drops)?
19. Usually experience difficulty emptying your bladder?
20. Usually experience pain or discomfort in the lower abdomen or genital region?

Likelihood to Recommend

Q: How likely is it that you would recommend the *Pippa Fitness Pessary* to a friend or colleague?

NOT AT ALL LIKELY								EXTREMELY LIKELY	
1	2	3	4	5	6	7	8	9	10

A: Scale of 10, where “not at all likely” = 1 and “extremely likely” = 10

User Satisfaction Survey

Q: Overall, how satisfied or dissatisfied are you with the Pippa Fitness Pessary

A:

- Very satisfied
- Somewhat satisfied
- Neither satisfied nor dissatisfied
- Somewhat dissatisfied
- Very dissatisfied

User Experience Questions

Q1: Choose three words to describe the Pippa Fitness Pessary.

A1:

Q2: Please evaluate the following statement: “The Pippa Fitness Pessary was easy to use.”

A2:

- Strongly agree
- Agree
- Neither agree nor disagree
- Disagree
- Strongly disagree

Q3: Please evaluate the following statement: “The Pippa Fitness Pessary improved my confidence in social situations.”

A3:

- Strongly agree
- Agree
- Neither agree nor disagree
- Disagree
- Strongly disagree

Q4: Please evaluate the following statement: “The Pippa Fitness Pessary improved my confidence in physically active situations.”

A4:

- ○ Strongly agree
- ○ Agree
- ○ Neither agree nor disagree
- ○ Disagree
- ○ Strongly disagree

Q5: Please evaluate the following statement: “The Pippa Fitness Pessary was comfortable to wear.”

A5:

- ○ Strongly agree
- ○ Agree
- ○ Neither agree nor disagree
- ○ Disagree
- ○ Strongly disagree

Q6: Given the option, how likely are you to use the Pippa Fitness Pessary again?

A6:

- ○ Extremely likely
- ○ Very likely
- ○ Somewhat likely
- ○ Not so likely
- ○ Not at all likely

Q7: Please offer any suggestions or feedback for the makers of the Pippa Fitness Pessary.

A7:

Q8: Please share any additional comments.

A8:

Observational Study Interest

Q: We plan to conduct a new study of the *Pippa Fitness Pessary* that simply involves wearing it as one wishes for 6 months. Do you agree to be contacted to participate in this study?

A: Yes / no

Exit Interview Questions *(to be recorded for automated transcription)*

Q1: How would you describe this product and your experience to a friend?

Q2: Please describe any lifestyle changes you made while using the product?

Q3: Is there anything else you think we should know?

APPENDIX C – PAD WEIGHT TEST PREPARATIONS WORKSHEET

- Before each test session, complete all the preparations described here.
- Check every box in the right-hand column.

IMPORTANT: If you are enrolled in the formal study, you will complete a second 1-hour pad weight test during treatment. Keep this worksheet. The second test should be as similar as possible to the first test. **So make sure that you choose a location for the test, and for your 30-minute walk, that you can use again in future.**

Min.	**Test Session Activities**		**1st Test**	**2nd Test** (+ device)
5	Get ready for the call	• Make sure you have good internet access • Have the call-in instructions handy • Choose a private time and location. • Wear comfortable clothes, suitable for light exercise, including a supportive bra (sports bra).	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐
15	Drink water and rest	• Have access to a restroom. • Have access to drinking water.	☐ ☐	☐ ☐

30	Go for a walk and climb one flight of stairs	• Have a plan for where to walk.
		  • outdoors if the weather is good
		  • inside a large building
		  • on a treadmill
		  • up and down a hallway
		• Have a plan for where to climb one flight of stairs.
		• Have a change of clothes, if needed.
			☐
			☐
			☐
			☐
			☐
			☐
			☐
				☐
				☐
				☐
				☐
				☐
				☐
				☐

15	Perform several physical activities	• Set up your video call for easy visibility. • Get a side chair you can move around easily.	☐ ☐	☐ ☐
5	Prepare return shipping of Clinical Pak	• Have a mobile phone nearby. • Have ready the address from which you would like FedEx to pick up your study materials.	☐ ☐	☐ ☐

Instructions for joining the telehealth session:

- ☐ The time and date of your session is indicated on a sticker inside the box lid of the pad weight test materials that you received in the mail.
- ☐ The test facilitator will send you a tele-conference invitation and confirmation for each session.
- ☐ **Make sure to confirm the invitation.**

If you lose connection during the session, please dial back in with the same ID and passcode.

Instructions for return shipping:

Please return ship within 24 hours. You may either schedule a pick up, or drop off the package at a FedEx Express location.

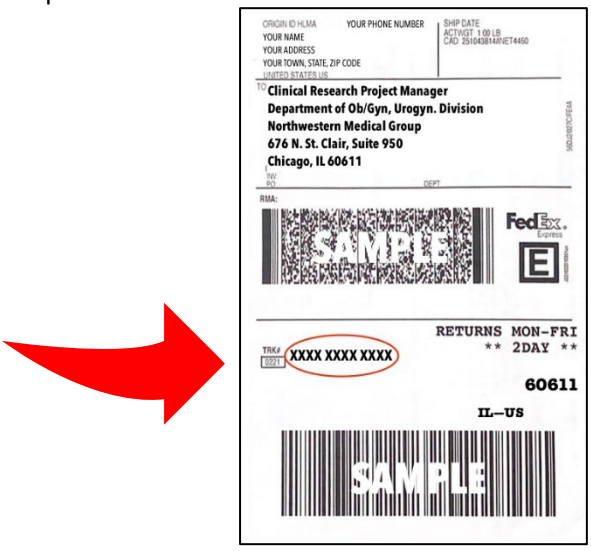
Drop off at FedEx location:

You may drop off your Clinical Pak at any FedEx Express Drop Box near you.
You can look up the nearest drop box here: **fedex.com/locate.** Or you can call 1.800.463.3339.

Schedule a FedEx pick up:

1. Have the pick-up address and your phone number ready
2. If needed, have instructions ready for the pick-up driver (example: porch, lobby, doorbell etc.)
3. Call FedEx at 1-800-463-3339
4. FedEx uses automation to schedule the pick up. It can be confusing to answer the questions. Here are the answers you need to provide:
    a. Ask for “Express Return”
    b. Answer: There is no stamp on the label
    c. Answer: Provide tracking number
    d. Answer: Provide pick up address
    e. Answer: Provide pick up phone number
    f. Answer: Provide earliest/latest pick up time (example: “after 4 pm same day”)
    g. Answer: Provide optional pick up instructions

Tracking Number



APPENDIX D – PRE-ENROLLMENT CLINIC VISIT INVITATION

To: [Study Candidate]

- You are invited for a clinical assessment based on your recent 1-hour Pad Weight Test.
- The clinic visit will determine if you meet all of the many requirements for our study.
- You will be paid $25 at the end of your visit.

Assessment Activities (approximately 40 minutes)
The visit includes three types of assessments. If you pass each assessment, you will have the opportunity to enroll in the full study.

The three assessments are:

1. Clinical Exam (~5 minutes)
   The clinician will conduct a vaginal exam, similar to a yearly gynecological checkup.

2. Cough Stress Test (~10-15 minutes)
   This test involves drinking water and then coughing vigorously, while a clinician monitors for visible leakage.

3. Device Fit Assessment (~20 minutes)
   This assessment will determine if the investigational device fits you. The device is a vaginal pessary to be worn in the vagina to help control involuntary urine leakage. You will be asked to use the device as you would at home, based on package labeling and instructions. Then the clinician will check to see if the device fits you.

Enrollment (approximately 10 minutes)
If you are confirmed eligible for the study and enrolled as a study participant, then you will complete a short survey about your current incontinence symptoms. The researcher will also explain the home phase of the study and provide all necessary materials.

APPENDIX E – STUDY PARTICIPANT GUIDE

Hello!

Dear Participant,

You have passed the clinical assessment and have been invited to enroll in the full study.

Thank you for taking part in the Clinical Trial of the self-administered *Pippa Fitness Pessary* ("the Pessary") for adult women with stress urinary incontinence (SUI), hereafter referred to as "the study" or "the user experience study." This study plan has been cleared as safe and ethical by an Institutional Review Board (IRB) comprised of medical study experts.

I will be the Study Coordinator and look forward to supporting you with any questions or issues you may have.

[Key Contact Name]
[Key Contact Job Title]
[Key Contact Employer Address][
Key Contact Email Address]
[Key Contact Phone Number]

What are we looking for from you?
We are asking you to wear the Pippa Fitness Pessary ("the Pessary") on a particular schedule, and track leaking episodes on paper.. Most of all, we ask that you give us your honest feedback on surveys and in the exit interview.

What can you expect from us?
This Study Participant Guide walks you through the study phases and tasks and provides a checklist for all the activities. You have also been provided with the Pessary and applicator and *Instructions for Use*, which includes information on routine product care, possible side effects, and medical warnings.

Can I stop using the product if I want to?
Yes, you can stop using the product at any time without asking for permission. However, you must inform the Study Coordinator of any changes or pauses in the study schedule.

What if something goes wrong?
If you feel you are experiencing a medical emergency, seek medical treatment immediately or call 911. Should you experience any pain, discomfort, abnormal bleeding, fever or other side effects – regardless of their cause, you must let the Study Coordinator know immediately.

Our primary request during the study, and for any survey you complete, is that you be honest and forthcoming.

Study Overview & Schedule

The study takes places at home and includes daily digital reminders from the research team.

Week 1	Week 2	Week 3	Week 4	
7 days of leakage tracking without use of the Pessary	14 days of Pessary use during waking hours, with ongoing urinary leakage tracking		1-hour pad weight test with Pessary use	Follow-up clinic visit and materials return

Summary of Activities

The study consists of multiple activities over 4 weeks of time.

- **Week 1:** urinary leakage and symptom tracking **without** the Pessary
- **Weeks 2 & 3:** urinary leakage and symptom tracking with the Pessary
- **Week 4:** a 1-hour pad weight test with Pessary use, followed by a final clinic visit

You will confirm with the Study Coordinator on what day you wish to start the study. You must sign up to receive text messages one day prior to your desired start date. During the study, you will follow your regular daily routines, including any type of work and leisure activities.

Scheduling and Menstruation

The Pessary may be worn during menstruation, in combination with menstrual pads. (You ***may not*** wear tampons or a menstrual cup together with the Pessary. Having multiple devices in the vagina may increase the risk of toxic shock syndrome during menses.) However, if you prefer, the study can be scheduled to avoid your period, or put on hold during that time if it starts unexpectedly. Although the Pessary may impede menstrual flow, it does not stop it or collect it (like a menstrual cup). So, during your period, be mindful that removal of the pessary might be messy.

The 1-hour pad weight study must take place between periods, as menstrual flow will prevent an accurate assessment of urinary leakage.

Study Communications

Throughout the study you will receive twice-daily text messages with reminders. You will also be contacted by telephone at least twice. At the end of the home use phase, the Study Coordinator will reach out to confirm appointments for the 1-Hour Pad Weight Test with Pessary use and the final clinic visit.

Study Materials

The research team will provide you with all materials needed to complete the home study. It is imperative that you protect these materials, as they must be returned to the clinic at the follow-up clinic visit in exchange for final study compensation.

Pippa Fitness Pessary Kit

- Instructions for Use
- Pessaries (2)
- Reusable applicator
- Water-based lubricant
- Water-based cleanser

Paperwork

- This participant guide
- Paper records to track leakage and pessary use

Pad Weight Testing Kit

- Instructions
- Incontinence pads (2)
- Water bottle (if needed)
- Activity tracker
- FedEx return mailer

At Home Study Details

WEEK 1 – **Leakage Tracking**

DAYS	ACTIVITY	Check
1-7	Follow your regular daily routines	
	Track leaking episodes and known causes in the paper record	

During the first seven days of the study, you **will not** be using the Pessary.

You will **record your leakage episodes** in the paper record**.** This part of the study will help us understand how much you leak ordinarily. If you usually wear incontinence pads during the day, or for specific activities, you should continue to do so.

Leakage information is very, very important for this study. Please create a habit of recording every leak during this at-home phase.

WEEKS 2 & 3 – **Leakage Tracking with Pessary Use**

DAYS	ACTIVITY	Check
8-21	Wear the Pessary daily (and keep a record of insertion and removal)	
	Follow your regular daily routines	
	Track leaking episodes and known causes in the paper record	
	Track any other noticeable symptoms	

During the subsequent fourteen days, you **will** wear the *Pippa Fitness Pessary* every day during waking hours.

You will continue to **record your leakage episodes** just as you did in the first week of the study. This phase of the study will help us understand if the Pessary works as intended for you, by helping to reduce or eliminate urine leakage. If you usually wear incontinence pads during the day, or for specific activities, you may continue to do so.

You will be expected to report on leakage episodes throughout the day, noting if the leak occurred with or without pessary use. You will record pessary insertion and removal times, days of menstruation and any side effects or concerning symptoms.

It is essential that you fill out the paper record every day of the study and ***bring it to the clinic*** when you return!

Preparation for Weeks 2 and 3

- Carefully read this guide.
- Determine where you will store the Pessary for air-drying overnight.
- Re-read the Pessary *Instructions for Use* carefully. (Make sure, always make sure, that you wash your hands properly before inserting or removing the Pessary.)

Daily Study Compliance

- Wear the Pessary during waking hours.
- Keep track of leakage episodes and their causes on the paper record.
- Keep track of Pessary use on the paper record.
- Disclose any noticeable symptoms of a possible side effect.
- Care for the Pessary as required by the *Instructions for Use.*
- Respond to any additional communications from the research team.

Possible Side Effects or Adverse Events

During the weeks of Pessary use, there is a possibility you may experience side effects and/or adverse events. Potential side effects may include excess vaginal discharge, discomfort, dislodging, spotting or pain. Potential adverse events could include vaginal irritation, infection, or erosion and/or Toxic Shock Syndrome.

WEEK 4 – **Final Pad Weight Test & Follow-up Clinic Visit**

DAY	ACTIVITY	Check
22-23	1-hour pad weight study performed while wearing the *Pippa Fitness Pessary*	
	Return to clinic for follow-up exam, survey, interview, and materials return	

For the final week of the study you will perform a second 1-hour pad weight test with a Pessary, and then return to the clinic for the follow-up clinical assessment. The Study Coordinator will contact you to confirm both appointments:

- You will need to use the Pessary one more time for the second 1-Hour Pad Weight Test, and
- You must bring the *21-Day Leakage Episodes Record* and the *Pippa Fitness Pessary* kit back for the follow-up Clinic Visit.

1-Hour Pad Weight Test with Pessary

When the time comes, follow the provided instructions to prepare by collecting your materials and setting up your space. Dial into the telehealth appointment and perform the same set of activities you

did for the first test, this time with the pessary. *Reminder:* This test *may not* be performed during a menstrual cycle. At the end of the test, you will return the provided incontinence pads and activity monitor via FedEx, just as you did after the pre-enrollment test.

Follow-up Clinic Visit

Your follow-up clinic visit will be scheduled after the in-home study phase is complete. You must return the *21-Day Leakage Episodes Record* and the *Pippa Fitness Pessary* kit to the clinic in order to complete the study and receive payment. The clinic visit will include a physical exam, a survey, a brief interview, materials return, and confirmation of payment.

Final Note

Our primary request during the study, and for any survey you complete, is that you be honest and forthcoming.

APPENDIX F – 21-DAY LEAKAGE EPISODES RECORD

Pippa Pessary Study Leakage Episodes Record

Subject ID#:			
Week #:	(No pessary in week 1)		
Today's Date:			
Pessary in:	AM		
Pessary out:	PM		
Pessary in:	AM		
Pessary out:	PM		
Pessary in:	AM		
Pessary out:	PM		
	When did you leak?	**What were you doing at the time of the leak?**	**Were you wearing the pessary when you leaked?**
	Time (AM/PM)	*For Example: exercising, laughing, coughing, sneezing, lifting, running, walking, stumbling, sitting down, bending over, sudden urge, nothing, or other*	yes • no (circle one)
1			yes • no
2			yes • no
3			yes • no
4			yes • no
5			yes • no
6			yes • no
7			yes • no
8			yes • no
9			yes • no
10			yes • no
11			yes • no
12			yes • no
13			yes • no
14			yes • no
15			yes • no
16			yes • no
17			yes • no
18			yes • no
Notes (optional):			

Pippa Pessary Study Leakage Episodes Record

Subject ID#:			
Week #:	(No pessary in week 1)		
Today's Date:			
Pessary in:	AM		
Pessary out:	PM		
Pessary in:	AM		
Pessary out:	PM		
Pessary in:	AM		
Pessary out:	PM		
	When did you leak?	**What were you doing at the time of the leak?**	**Were you wearing the pessary when you leaked?**
	Time (AM/PM)	*For Example: exercising, laughing, coughing, sneezing, lifting, running, walking, stumbling, sitting down, bending over, sudden urge, nothing, or other*	yes • no (circle one)
1			yes • no
2			yes • no
3			yes • no
4			yes • no
5			yes • no
6			yes • no
7			yes • no
8			yes • no
9			yes • no
10			yes • no
11			yes • no
12			yes • no
13			yes • no
14			yes • no
15			yes • no
16			yes • no
17			yes • no
18			yes • no
Notes (optional):			

APPENDIX G – DAILY COMMUNICATIONS

Daily communications will be facilitated by a third-party mobile text messaging service called SlickText, provided by Slick Innovations, LLC and carefully configured for the study needs by the research team.

Participant-facing communications *will* include A) instructions to participants sent automatically on a daily schedule, and *may* include B) tailored versions of automated messages that are sent upon possible user behaviors like opting out or seeking help with the mobile text messaging service.

A. Scheduled and Automated Instructional Messages

STUDY DAY	MESSAGING	PURPOSE
Communications Preparation		
0 (text opt-in)	Hello study participant! Your phone number is now ready to receive reminder messages from the research team at [clinic name]. Messages will be sent daily for three weeks, starting tomorrow morning. If at any time you need to pause or withdraw from the study, you must contact [name of Study Coordinator] for assistance. Upon study completion, text **STOP** and your phone number will be deleted from the mobile text messaging service. You can reply **HELP** for help or **STOP** to opt out of text messages. Message & data rates apply. Terms and privacy policy can be found at getapessary.com/communications.	Opt-in to use text message service
MORNINGS		
Daily Report Summary for "Yesterday" (w/o pessary)		
1	Good Morning! For the next three weeks you will track any leaking episodes and noticeable symptoms in your paper record. SAVE THE PAPER RECORD. IT MUST BE RETURNED TO THE CLINIC WHEN YOU RETURN. If you have any questions or concerns, please call the Study Coordinator at XXX-XXX-XXXX.	Assign journal use
2-7	Good Morning! Please remember to track any leaking episodes in your paper record.	Reminder
8	Good morning! Today you will start wearing the Pippa Fitness Pessary. You must track pessary use and any leaking episodes in your paper record. Be sure to record every pessary insertion and removal. If you have any questions or concerns, please call the Study Coordinator at XXX-XXX-XXXX.	Set up pessary use Reminder for tracking
Daily Report Summary for "Yesterday" *with* Pessary		
9-20	Good morning! Today you will wear the Pippa Fitness Pessary again and track any leaking episodes. If you have any questions or concerns, please call the Study Coordinator at XXX-XXX-XXXX.	Reminder to wear Confirm leak tracking

STUDY DAY	MESSAGING	PURPOSE
21	Good morning! Today is the final day for using the Pippa Fitness Pessary.	
22	Good morning! If you are not already scheduled for your second 1-hour Pad Weight Test and final clinic visit, please contact the Study Coordinator at XXX-XXX-XXXX. We look forward to seeing you at the clinic soon!	Confirm Session
EVENINGS		
Nightly Reminders for Leak Logging		
1-6	Good evening! Remember to complete your leakage tracking record tonight. If you have any questions or concerns, please call the Study Coordinator at XXX-XXX-XXXX.	Tracking reminder Catch issues
7	Good evening! Week one is almost over. Tomorrow you will start using the Pippa Fitness Pessary. If for any reason you cannot start as planned, please contact the Study Coordinator at XXX-XXX-XXXX. Over the next two weeks, continue to track any leaking episodes or noticeable symptoms while wearing the Pippa Fitness Pessary.	
Nightly Reminders for Leak Logging and Pessary Use Tracking		
8-13 & 15-20	Good evening! Don't forget to record your leakage and pessary use information. If you have any questions or concerns, please call the Study Coordinator at XXX-XXX-XXXX.	Tracking reminder Catch issues
14	Good evening! One more week to go. You will continue using the Pippa Fitness Pessary next week. Remember to track any leakage episodes and record details of pessary use. If you have any questions or concerns, please call the Study Coordinator at XXX-XXX-XXXX.	
21	Congratulations! You have nearly completed the at-home phase of the Pippa Fitness Pessary study.	

B. Standard (Non-Editable) SlickText Service Messages

Reply message for "STOP"	NETWORK MSG: You replied with the word "stop" which blocks all texts sent from this number. Text back "unstop" to receive messages again.

Reply message for "UNSTOP"	NETWORK MSG: You replied with the word "unstop" and will begin receiving messages again from this number.
Reply message for "HELP"	Pippa Fitness Pessary Study SMS Alerts: Help: getapessary.com or [research team email]. 5msg/mth. Reply STOP to cancel. Msg&data rates may apply.
Reply message for "CANCEL"	You are now opted out of Pippa Fitness Pessary Study SMS Alerts. No more messages will be sent. Reply HELP for help. Report spam to spam@slicktext.com." (Study team can create a "spam@emailaddress" in order to be alerted to this action.)
Rejoining the Service after a Pause	You have rejoined [TEXTWORD]! Thanks for coming back! Msg&data rates may apply. Reply STOP to cancel, HELP for help. Msg&data rates may apply. Terms & privacy: [link to Terms & Privacy]

Terms & Privacy
To be posted at getapessary.com/communications

MOBILE TEXT MESSAGING TERMS & CONDITIONS

Who operates this mobile text messaging service?
This mobile text messaging service, known as "SlickText," is operated by a technology company called Slick Innovations, LLC. The service has been carefully configured for the Pippa Fitness Pessary Study by the clinical research team. The service will provide automated communications to make study participation easier. You will receive no promotional messaging.

What does SlickText do with my information?
SlickText is a 100% opt-in service. They do not provide lists of phone numbers nor do they access or share their users' contact lists. To can access their privacy policy here [hyperlink to https://www.slicktext.com/privacypolicy.php].

What are your mobile terms?
When you provide us with your mobile phone number, you agree that our research team may send you text messages (including SMS and MMS) to that phone number. Our research team may send you up to 50 study-related messages over the course of the study.

You will receive a confirmation text message, and you may need to reply as instructed to complete registration. Message and data rates apply. Reply **STOP** to cancel, **HELP** for help. You agree to receive a final text message confirming your opt-out. You may opt-out at any time by texting the word **STOP** to shortcode 31996. For help, send a text message with the keyword **HELP** to shortcode 31996.

Texts may be sent through an automatic telephone dialing system. You agree to notify us of any changes to your mobile number. Your carrier may prohibit or restrict certain mobile features and certain mobile features may be incompatible with your carrier or mobile device. Contact your carrier with questions regarding these issues.

How do I sign up for these text messages?
All you have to do is text **"[TEXTWORD]"** to **31996**. When you opt-in to the service, we will send you an SMS message to confirm your signup.

If at any time you forget what keywords are supported, just text **HELP** to **31996**. After you send the SMS message **HELP** to us, we will respond with instructions on how to use the service as well as how to unsubscribe.

How do I opt out of these text messages?
You can cancel the SMS service at any time. Just text **STOP** to **31996**. After you send the SMS message **STOP** to us, we will send you an SMS message to confirm that you have been unsubscribed.

Opting out of text messages will not automatically withdraw you from the study. If you wish to withdraw from the study, you must directly contact the Study Coordinator.

Will I be charged for the text messages I receive?
Our research team will never charge you for the text messages you receive. However standard message and data rates may apply for any messages sent to you from us and to us from you.

You will receive up to 50 messages over the course of the study. If you have any questions about your text plan or data plan, it is best to contact your wireless provider.

For all questions about the services provided through the number 31996, you can send an email to info@slicktext.com.

Supported wireless carriers

United States
We are able to deliver messages to the following mobile phone carriers: Major carriers: AT&T, Verizon Wireless, Sprint, T-Mobile, MetroPCS, U.S. Cellular, Alltel, Boost Mobile, Nextel, and Virgin Mobile. Minor carriers: Alaska Communications Systems (ACS), Appalachian Wireless (EKN), Bluegrass Cellular, Cellular One of East Central IL (ECIT), Cellular One of Northeast Pennsylvania, Cincinnati Bell Wireless, Cricket, Coral Wireless (Mobi PCS), COX, Cross, Element Mobile (Flat Wireless), Epic Touch (Elkhart Telephone), GCI, Golden State, Hawkeye (Chat Mobility), Hawkeye (NW Missouri), Illinois Valley Cellular, Inland Cellular, iWireless (Iowa Wireless), Keystone Wireless (Immix Wireless/PC Man), Mosaic (Consolidated or CTC Telecom), Nex-Tech Wireless, NTelos, Panhandle Communications, Pioneer, Plateau (Texas RSA 3 Ltd), Revol, RINA, Simmetry (TMP Corporation), Thumb Cellular, Union Wireless, United Wireless, Viaero Wireless, and West Central (WCC or 5 Star Wireless).

Canada
Bell (including NorthernTel, Solo Mobile, and Telebec), Fido, MTS, Rogers, SaskTel, Telus (including Koodo Mobile and Public Mobile), Videotron, Virgin Mobile, and Wind.

This service and the carriers are not liable for delayed or undelivered messages

MOBILE TEXT MESSAGING PRIVACY POLICY

Our research team is dedicated to protecting your privacy and works hard to ensure our study tools are both safe and secure.

Protection of Information
Any information communicated to our research team for text messaging and or storage will remain in the ownership of the user, which will be stored securely in accordance with our security policy and the law. Our research team will take the necessary steps to secure your personal information with safeguards appropriate for this study, as outlined in the Informed Consent document you signed.

Subscribing and Unsubscribing
It is policy that, just as a user must opt into a text messaging service, they have the right to opt out of a particular text messaging service as well. When a user opts out of a text messaging service, they will no longer receive any texts unless they, themselves, re-subscribe.

Opting out of text messages will not automatically withdraw you from the study. If you wish to withdraw from the study, you must directly contact the Study Coordinator.

About Policy Changes

Our research team will notify you of any change to this privacy policy. Your continued use of this service after you have been notified of changes to terms and conditions or our privacy policy is taken as acceptance of those changes. This privacy policy is subject to and applicable to all privacy laws.

You acknowledge that accepting this policy is a condition of your participation in our study and you agree to be bound by all of its terms and conditions.