CLINICAL STUDY PROTOCOL

Study evaluating efficacy of a non-invasive pelvic floor muscle trainer for treatment of stress urinary incontinence

Protocol #: PLX-001

jeremy@pelex-med.com

19-Feb-2021

PROTOCOL VERSION HISTORY

Version	Date (01-Feb-2021)
Initial	19-Feb-2021
Amendment	21-Feb-2021

ETHICS AND REGULATORY COMPLIANCE STATEMENT

The procedures set forth in this protocol are designed to ensure that the sponsor(s) and principal investigator(s) abide by the International Conference on Harmonization (ICH) current Good Clinical Practice (cGCP) guidelines, current Good Laboratory Practice (cGLP) guidelines, the Declaration of Helsinki, and applicable local regulatory requirements and laws in the conduct, evaluation, and documentation of this study.

Protocol Name	Study evaluating efficacy of a non-invasive pelvic floor muscle trainer for treatment of stress urinary incontinence
Protocol Number	PLX-001
Investigational Product Name	Pelex Upp
Date: (dd-mmm-yyyy)	19-Feb-2021
Author	Jeremy Wiygul, MD

PROTOCOL HISTORY

Version	**Date** (dd-mmm-yyyy)	**Description**
V1	19-Feb-2021	Initial Release
V2	21-Feb-2021	

PROTOCOL APPROVALS

Name	**Signature**	**Date** (dd-mmm-yyyy)	**Department**
	eSignature	eDate	
	eSignature	eDate	
	eSignature	eDate	

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Coordinating Investigator and Principal Investigators An updated list of Principal Investigators (PI), investigation sites, and institutions will be maintained separately. The definitive list will be provided in the clinical study report.	

PROTOCOL SIGNATURE PAGE

Protocol #: PLX-001

Study evaluating efficacy of a non-invasive pelvic floor muscle trainer for treatment of stress urinary incontinence

As an Investigator for this Study, I have read the Clinical Trial Protocol. I agree to make available to the Sponsor, Pelex, Inc. (or its designee), original source documents and all regulatory documents pertaining to this Study. I agree to cooperate fully with the Sponsor with the conduct of study-related audits.

By my signature below, I agree to conduct this Study in accordance with the Clinical Trial Protocol, current Good Clinical Practice (cGCP) and Good Laboratory Practice (cGLP) guidelines, obligations as set forth in Title 21 CFR Parts 812, 54, 56 and 11 (as applicable), and any applicable regulatory laws. I will make no changes to protocol-defined procedures without written permission from the Sponsor.

I understand that Investigational Use Products may be used **only** for the purposes explicitly described in this protocol.

I further agree to treat the results of this Study as confidential information and will not submit the results of the Study for publication without prior written authorization from the Sponsor.

Jeremy Wiygul		02/19/2021
PRINTED NAME	SIGNATURE	DATE

SYNOPSIS

Title of Study	Study evaluating efficacy of a non-invasive pelvic floor muscle trainer for treatment of stress urinary incontinence.
Objectives	Evaluate efficacy of Pelex Upp in treatment of patients with stress urinary incontinence.
Planned Number of Subjects and Duration of Involvement	5 study subjects will be enrolled for a total of 4 weeks.
Patient Population	Women > 18 years of age with symptoms of stress urinary incontinence
Investigational Product Name	Pelex Upp
Methodology Overview	This will be a prospective cohort study of women > 18 years of age with symptoms of stress urinary incontinence, recruited via an online recruitment tool. After screening, patients meeting inclusion criteria will be given a study brochure, and then given instructions on how to indicate desire to participate in the study. The patient will then be contacted for study participation, including explanation of study and details and completion of Informed Consent. Participants will then complete a pre-treatment urinary incontinence symptom questionnaire(ICIQ). After completion of the above, the participants will then be given a Pelex Upp study, in addition to educational materials on use of the device, and a treatment schedule. Participants will perform a standardized biofeedback-mediated pelvic floor muscle training program with the study device 10 minutes a day, five times a week for 4 weeks. There will be a mid-study check in to assure all devices are functioning appropriately. At the end of the study, participants will complete a post-treatment urinary incontinence symptom questionnaire(ICIQ). Endpoint of the study will be change in stress urinary incontinence symptoms as measured by the ICIQ. The ICIQ will be collected at 2 time points: before study entry, and at study close.

ABBREVIATIONS

PFMT	Pelvic floor muscle training
SUI	Stress urinary incontinence
OAB	Overactive bladder
UI	Urinary incontinence
PFM	Pelvic floor muscles
US/USA	United States of America

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1 INTRODUCTION

Pelex, Inc. is a medical device company that is dedicated to addressing pelvic health disorders. The company is developing a non-invasive medical device that uses electromyography and neurostimulation to treat incontinence and other pelvic floor disorders. In support of its research and development efforts, Pelex is conducting a clinical study to assess the efficacy and usability of the electromyography component of the company's pelvic health product. Five patients suffering from stress urinary incontinence, a form of pelvic floor disorder, will be recruited to participate and the duration of participation is expected to be four weeks. The result of this study will be used to verify that the underlying technology functions as expected, identify subject preferences for device form factor and other design decisions, and capture other patient feedback.

2 DESCRIPTION OF THE INVESTIGATIONAL PRODUCT

2.1 Overview

The Pelex Upp is a non-invasive device that is designed to guide a user through personalized pelvic floor strengthening exercises. The device consists of a patient contact interface approximately 12" x 6" whose upper surface is embedded with disposable electrodes which by a short cable is linked to an enclosed circuit board component. When a patient interacts with the patient contact interface by sitting upon it, the electrodes of the sensor array are able to detect and measure the patient's muscle contractions. The circuit board component analyzes the collected data and provides feedback to the patient on sensor array placement and strength of muscle contractions via a user interface panel consisting of LEDs that is located on a handheld piece that is connected to the hardware component by a fixed cable. The handheld component also houses a cadence LED, which prompts the user through a series of standardized pelvic floor contraction and relaxation exercises.

2.2 Proposed Intended Use Statement

The Pelex Upp is a non-invasive electromyography device designed to treat stress urinary incontinence in adults.

3 STUDY OBJECTIVES

The principal objective of this study is to demonstrate efficacy of the Pelex Upp in treatment of stress urinary incontinence. The secondary objective will be to determine ease of use of the Pelex Upp by patients at home.

4 STUDY OVERVIEW

4.1 Study Approach

Urinary incontinence (UI), as defined by the International Continence Society as any involuntary loss of urine, is among the most prevalent of all medical conditions, affecting one in four adult women and increasing in incidence with age (1). Stress urinary incontinence (SUI), which is the involuntary loss of urine during exertion, sneezing or coughing, is the most common form of UI (2) and is estimated to be responsible for over $12 Billion in health care expenditures annually (3). SUI is typically the result of weakening of the pelvic floor muscles and atrophy of vaginal tissues, both of which occur increasingly with age and after childbirth(4).

Therapies for SUI primarily revolve around restoring the strength and function of the pelvic floor muscles (PFM), and can be understood as lying on a spectrum between more conservative and more invasive options. First line (conservative) therapy for SUI typically consists of behavioral modification, such as more frequent urinating to avoid larger bladder volumes, in addition to some form of pelvic floor muscle training (PFMT)(2), while more invasive options, such as surgery to reconstruct the pelvic floor, are reserved for patients who have failed first line therapy.

The goal of PFMT is to increase the strength, coordination and endurance of PFM, which allows for stabilization of the urethra and pelvic organs during rises in intra-abdominal pressure(5), thereby avoiding loss of urine during these pressure rises. PFMT in the form of Kegel exercises is a well-established form of treatment for urinary incontinence (6), and success rates with PFMT for UI approach 84% in selected patients (7; 8), which, combined with their relative simplicity, make them a highly desirable and often-used treatment option. Most simply, PFMT is performed in the form of daily timed contractions and relaxations of the pelvic floor, typically after being coached about appropriate muscle use by a trained professional during a clinic visit (9). While this has been proven to improve SUI symptoms over behavioral therapy alone, PFMT with biofeedback, where a device is used to record the biological signal of contraction of the PFM and then present that signal to the user in audio or visual form, has been proven to offer even greater benefit that PFMT alone(10). Biofeedback in the setting of PFMT is accomplished by placement of surface electrodes on the skin overlying the pelvic floor muscles, or an intravaginal device sensitive to pressure changes, both of which can detect contraction and relaxation of the pelvic floor muscles and allows the user to then gain greater awareness of their PFM. Patients undergoing PFMT plus biofeedback typically do so under the guidance of weekly visits to a physical therapist, usually over the course of four to six weeks.

There is a robust body of evidence supporting use of biofeedback during PFMT in the treatment of all forms of urinary incontinence. In a systematic review in 2011, Herdershee et al(10) evaluated all randomized controlled trials (RCT) that compared PFMT alone to PFMT plus various types of feedback, including biofeedback, in treatment of urinary incontinence in women, and found across all studies, patients treated with PFMT plus biofeedback were significantly more likely to report improvement or resolution of their urinary incontinence,

though the authors pointed out that the results also could be partially attributable to more contact with health care providers (10). In another recent analysis, Glazer et al (11), using more inclusive inclusion criteria, also found a general benefit to biofeedback for treatment of urinary incontinence when compared not only to PFMT alone, but also medications and electrical stimulation. However, a more recent meta-analysis was more equivocal in its findings, with significantly better objective results, such as pad tests, in patients undergoing PFMT plus biofeedback, but with not as clear a difference in subjective quality of life (QoL) measures as compared to PFMT alone (12).

While PFMT plus biofeedback has traditionally been performed in a medical facility, whether it be a clinician's office or physical therapist's, more recent research has looked to leverage the ability to perform biofeedback at home to improve outcomes. This movement has been aided by the development in recent years of several medical devices designed to help patients perform biofeedback for PFM exercises at home, and thus avoid the need for recurrent trips to the physical therapist or physician's office. In a recent study, use of a home biofeedback device was found to be as efficacious as a standard twelve week PFMT program with four weekly visits to a physical therapist in treating women with predominantly SUI symptoms (13). In pilot studies, other devices have also shown promising rates of improvement in urinary incontinence when used at home and without other PFMT training (14). The use of medical devices to perform biofeedback at home is not only much more convenient than typical PFMT plus biofeedback, it has the potential to increase access to treatment overall. In a study by Washington et al, over one third of patients referred to a physical therapist for PFMT did not ultimately undergo treatment, with lack of insurance being the variable most associated with non-participation in treatment (15). Considering that the out-of-pocket cost of an initial physical therapist visit for PFMT is $500 (15), while most of the devices designed for home biofeedback use are priced several hundred dollars less (13), these devices could greatly expand treatment capability.

However, despite the advantages these devices provide, there are still significant barriers to use. Due to the way biofeedback in conjunction with PFMT must be performed, specifically capture of the contraction and relaxation of the PFM, devices designed for use in these setting are either invasive (inserted into the vagina or rectum) or require placement by a trained professional (surface EMG electrodes). This presents a barrier to use for patients, and an opportunity for innovation. Specifically, the product under investigation, the Pelex Upp is designed for use at home for biofeedback plus PFMT sessions. It has a non-invasive patient interface that takes advantage of the unique anatomical properties of the perineum, the skin between the anus and vagina or scrotum, allowing the patient to perform PFMT plus biofeedback without the need for invasive devices or professionally placed electrodes.

The aim of the present pilot study is to determine efficacy of our product in the treatment of SUI in a home setting. Since PFMT plus biofeedback is considered standard of care in patients with SUI who are therapy-naïve, the study subjects will be exposed to no greater than normal risk associated with treatment. Study subjects will undergo evaluation by a treating physician and will have prescribed a treatment regimen typical for the disease process.

4.3 Study Duration

The study will last approximately a total of four weeks.

5 STUDY POPULATION

5.1 Sample Size and Target Study Population

5.1.1 Sample size

The total number of individual subjects is expected to reach approximately 5. This estimate is based on this being a pilot study, with the primary goal of determining efficacy of the Pelex Upp in treatment of stress urinary incontinence in adult women.

5.1.2 Study population

The study population will be representative of adults at least 18 years of age with symptoms of stress urinary incontinence. It is anticipated that Pelex will enroll approximately 5 qualifying adults in total.

5.1.3 Alignment with intended study population

The study population includes patients likely to benefit from pelvic floor muscle training plus biofeedback. It may also include other patients who may provide controls.

5.1.4 Alignment with intended use of the device

The device under investigation is intended as a biofeedback device to be used during PFMT.

5.2 Recruitment Methods

5.2.1 Recruitment for Study

Eligible patients will be invited to participate in the study on a first-come, first-serve basis, subject to Pelex weekly recruitment goals. They will be informed of the possible risks of the procedure and will be required to give informed consent before study-specific procedures can proceed. A minimal financial inducement will not be offered, and subject recruitment materials will be used. Each subject will be informed that no personally relevant clinical information will be derived from the collected data, and that the only possible benefit to the subject is the improvement in their stress urinary incontinence. Medications will be documented. Each subject's involvement in the study will be limited to the period between signing of the informed consent form (ICF) and the end of the study, which is expected to be four weeks after study initiation.

5.2.2 Duration of study activities

The study is anticipated to continue for approximately four weeks, excluding study enrollment period. In the event that additional studies are going to be conducted, new protocols will be developed specifically for those studies.

5.3 Patient Selection

The eligibility criteria for prospective enrollment of subjects are shown in **Table 1**.

Table 1. Inclusion/Exclusion Criteria for Enrollment of Subjects

Inclusion criteria	Female 18 years of age or older Documented symptoms of predominantly stress urinary incontinence as determined by the ICIQ questionnaire
Exclusion criteria	History of pelvic or lower back surgery Pregnancy or less than 12 months post partum History of physician-supervised PFMT History of Kegel exercises greater than once a month History of prior operative delivery Self-reported history of pelvic organ prolapse stage II or greater
Participant Withdrawal Criteria	Inability to demonstrate correct use of product Inability to devote sufficient time necessary to fulfill study goals Worsening of stress urinary incontinence symptoms

6 STUDY MATERIALS

6.1 Investigational Product

6.1.1 Identity of the investigational product and accessories

The Pelex Upp is intended to allow a patient to perform biofeedback-augmented PFMT non-invasively and at home. It is comprised of a patient contact interface, a connected handheld device, and disposable sensor arrays. The sensor array is a flexible circuit array holding a pair of sensing electrodes and a reference electrode which are connected to a male connector at one end. The patient contact interface, upon which the user sits after disrobing, has the sensor array embedded along the upper surface. A housing compartment within the patient contact interface will hold signal processing equipment, which will be connected to the sensor array externally via a female connector in the front of the patient contact interface. The signal processing equipment will also be separately connected via a cord on the side of the patient contact interface to the handheld device. The handheld device will have two LED systems, a power switch and battery compartment for housing of the power source. The two LED systems will include a “cadence” LED, which flashes in a pre-set pattern for the user to follow with contractions of their own pelvic floor muscles. It will also include a “response” LED, which allows the user to visualized the contraction of their pelvic floor muscles. The sensor array is disposable, and several replacement sensor arrays will be included, and can be changed at the user’s discretion.

The Pelex Upp is completely non-invasive and made of hypoallergenic, non-latex materials.

6.1.2 Safety issues

The device under investigation is completely non-invasive, and qualifies as a non-significant risk device based on Title 21 CFR 812.2 (c). Safety issues would include skin abrasions and contact allergic reactions from contact of bare skin with the flexible circuit array, which has a mild adhesive applied to it

6.1.3 Handling, storage, accountability

The Sponsor will provide the Investigator with a supply of study devices for conduct of the study. All devices will be logged into the device accountability log. If a device is used in the investigation it will be documented in the device accountability log. Devices returned to the Sponsor will be noted as such in the device accountability log. A final accounting of devices will be being presented in the final clinical study report.

The Investigator shall permit an investigational device to be used only in subjects enrolled in the study. The Investigator shall not supply an investigational device to any person not authorized to receive it.

The Investigator or designee shall document receipt, use, and disposition of the device as it relates to:

- The quantity of the device, dates of receipt, catalogue and lot numbers;
- The names of all persons who received each device; and
- Why and how many units of the device have been returned to Sponsor or otherwise have left the possession of the Investigator.

The devices must be stored separately from other clinical supplies. Opened, unused devices must be returned to the Sponsor or destroyed on site as directed by the Sponsor.

The use of the study device outside of this protocol is prohibited. Each investigational site will identify a designee who will be held responsible for controlling the devices and ensuring that a device is dispensed only for the purposes of this study. This designee will be expected to retain all unused study supplies until the completion of the study and/or until a representative of the Sponsor has inventoried and made arrangements to return the supplies to the Sponsor. Upon completion or termination of this investigation or the Investigator's part of this investigation, or at the request of the Sponsor, the Investigator shall return any remaining supply of the device or otherwise dispose of the device as directed by the Sponsor.

6.1.4 Required training

Each study participant will be given instruction materials to guide use of the investigational device.

6.1.5 External studies

In the event that plans are made to conduct additional studies, new protocols describing the relevant handling, storage, accountability, and training procedures will be prepared specifically for those studies.

6.2 Other Study Materials

6.2.1 Materials to be provided by study site

- Study notebooks to maintain study documents, including signed ICFs, all applicable information, and additional forms to be collected and retained by the study institution during the course of the study.
- Example spreadsheets for tracking patient information.

6.2.2 Materials to be provided by external testing facilities

No materials from external testing facilities will be given.

7 STUDY PROCEDURES

7.1 Workflow

The study design is a prospective cohort that enrolls adult female patients identified as having stress urinary incontinence via an online enrollment form to evaluate the effectiveness of the Pelex Upp in treatment of stress urinary incontinence. The treatment group will enroll 5 subjects. Following the granting of Informed Consent, subjects will be enrolled in the study within the prospective cohort and will complete a four-week course of biofeedback augmented PFMT using the Pelex Upp. Patients will complete a pre- and post-study urinary incontinence quality of life evaluation tool to assess response to the investigational device.

Subsequent treatment and work up will be dictated by the reported persistence of symptoms. Follow-up with care providers will be as needed, as determined by the patient.

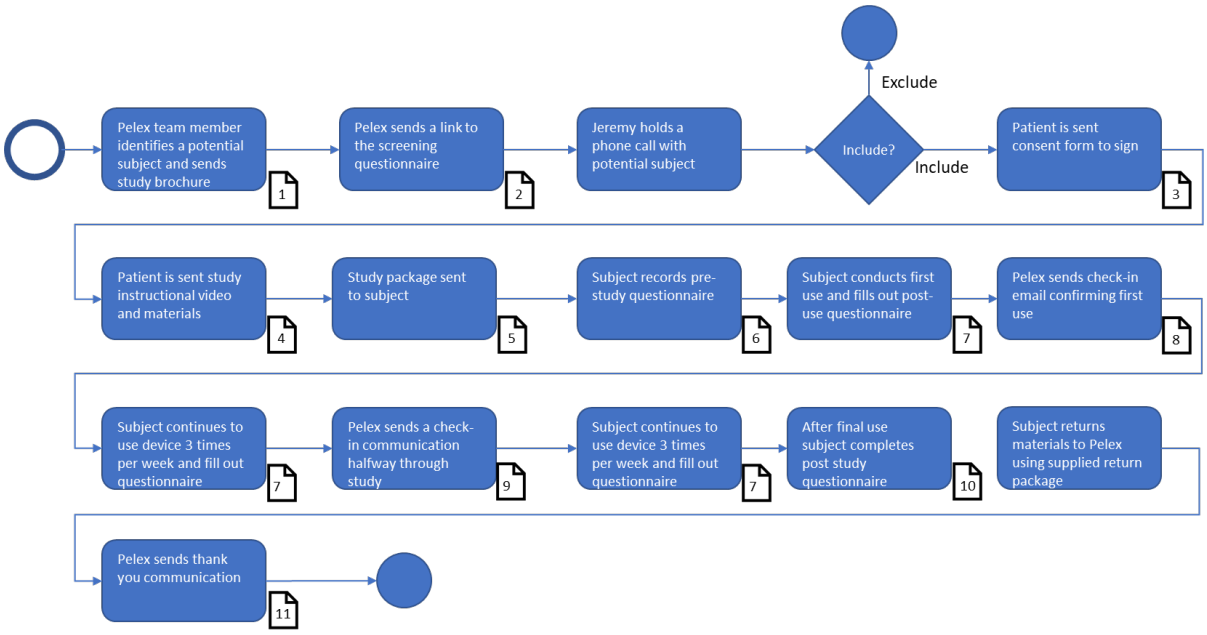

Figure 1: Study Workflow

Item
1. Study Brochure
2. Prospective Subject Screening Questionnaire
3. Subject Consent Form
4. Instructional Materials
5. Study Package with Study Materials
6. Pre-Study Questionnaire
7. Post-Use Questionnaire
8. Study Initiation Check-in Communication
9. Mid-Study Check-in Communication
10. Post-Study Questionnaire
11. Thank You Communication

Table 1: Study Materials

7.2 Study Data

Eligible subjects will be invited to participate in the study on a first-come, first-serve basis. Potential donors must provide informed consent to participate. To be eligible for participation, subjects must be at least 18 years of age.

At the discretion of the Investigator and subject to Pelex requirements, urinary incontinence data will be collected from each eligible subject providing signed informed consent.

7.2.1 Collection of data

Source data is all information, original records of clinical findings, observations or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents. Examples of source documents in this study include medical records, memoranda, evaluation checklists, CRF worksheets, and Data Capture

An Electronic Data Capture (EDC) system using an electronic Case Report Form (eCRF) that is compliant with 21 CFR part 11 is the primary data collection instrument for the study. All data requested on the eCRF should be recorded. The EDC system will only allow for data to be collected based on specified fields. The EDC system also generates an audit trail for any corrected data. All data entered on an eCRF must be traceable to a source document.

eCRFs will be completed for each subject enrolled into the clinical study. The Investigator will review, approve, and electronically sign the completed eCRF for each subject; the Investigator's electronic signature will serve as a testament of the Investigator's responsibility for ensuring that all clinical data entered on the eCRFs are complete, accurate, and authentic.

Subjects will be identified in the EDC by a numeric code used for study purposes. Subjects are not identified by name. Data entry staff are expected to follow data protection practices. All procedures for the handling and analysis of data will be conducted using good computing practices meeting FDA guidelines for the handling and analysis of data for clinical trials.

Information about study subjects will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). Those regulations require a signed subject authorization informing the subject of the following:

1. What protected health information (PHI) will be collected from subjects in this study;
2. Who will have access to that information and why;
3. Who will use or disclose that information; and
4. The rights of a research subject to revoke their authorization for use of their PHI.

In the event that a subject revokes authorization to collect or use PHI, the Investigator, by regulation, retains the ability to use all information collected prior to the revocation of subject authorization. For subjects that have revoked authorization to collect or use PHI, attempts should be made to obtain permission to collect at least vital status (i.e., that the subject is alive) at the end of their scheduled study period.

The accountability procedure will consist of Pelex, Inc., the principal investigator and project team lead, respectively, being responsible for upkeep of the secured database and the only people with access, except for the IRB. The IRB will be allowed to access site, records, etc.

7.3 Randomization and Blinding

No randomization nor blinding will occur.

7.4 Procedures for Study Closure

7.4.1 Routine study close-out

The study will end when Pelex has obtained all data necessary to complete its studies of the test product. Study close-out will follow Pelex standard procedures and may include, but is not limited to, review of regulatory documents, collection of completed case report forms, reconciliation of study records, removal or destruction of ancillary study supplies, and informing the Investigator of remaining obligations (e.g., record retention, final report submission to the IRB, financial disclosure updates, etc.).

7.4.2 Suspension or premature termination of the study

This study may prematurely terminate at any time because of a regulatory authority decision, a change in opinion of the IRB, or at the discretion of the Investigator or Sponsor. If this trial is temporarily suspended or prematurely discontinued, Pelex will promptly notify the Investigator(s) and provide instructions. If the study is temporarily suspended, Pelex will provide guidance on timing and procedures for resuming the study. If the study is prematurely discontinued, all study materials must be collected and all study forms completed to the extent possible. All such materials must be returned to Pelex upon request. Reasons for termination of the study or a study site may include, but are not limited to, the following:

- The risks and benefits of continuing the study have been reassessed, and the risks outweigh any potential benefits.
- The incidence of AEs constitutes a potential health hazard to the subjects.
- New scientific data do not justify a continuation of the study.
- The investigator or study site exhibit serious and/or persistent non-adherence to the clinical study protocol and/or applicable regulatory requirements.
- The Sponsor decides to terminate the study at any time for any other reason.

8 DATA QUALITY ASSURANCE

The study screening questionnaire, pre-study survey, post-use survey, and post-study survey are all forms requiring input from subjects. Pelex will endeavor to use electronic forms of data capture whenever possible. Possible forms of electronic data capture include Google

forms and SurveyMonkey. These forms will be configured such that only Dr. Wiygul has access to the raw information in order to protect patient health information.

While obtaining the informed consent, Dr. Wiygul will ask the subject whether she is able to use electronic data forms. In the event that the subject indicates that she is unable to use electronic data forms, then the study team will include a paper journal in the study package. The study package will be returned to Dr. Wiygul who will be responsible for converting the paper form to an electronic format, anonymizing the electronic version, and archiving or destroying the paper form.

Beyond subject input, the study device are intended to collect physiological parameters and store this data on the device. The data will be salvaged when the study materials are returned to the study team. The device data will only be stored using the anonymous subject identifier. Data stored on the device hardware that is returned to the study team will be recovered by Dr. Wiygul following a protocol that has been established with the primary device manufacturer, Arduino. Anonymized recovered data will be collectively stored in a password protected data server or database. The raw data will be backed up at least once to local storage.

The data will be processed through reproducible measures, such as by writing start-to-finish code. When data processing is complete, this code will be applied to a copy of backed-up raw data to confirm the reproducibility of the analysis and integrity of the raw data.

9 STATISTICAL METHODS

9.1 Determination of Sample Size

This study is exploratory and not designed to establish non-inferiority or superiority. Therefore, determining a sample size for the purposes of statistical significance is not necessary.

9.2 Bias Minimization

All subjects meeting the specified eligibility criteria will be enrolled on a first-come, first-serve basis.

9.3 Planned Analyses

Specific study parameters to be analyzed will be the maximum pelvic floor contraction at study entry and exit, as well as maximum sustained contraction at study entry and exit. Objective clinical response to use of device in improving SUI symptoms will also be captured per the symptom questionnaires, which will be entered into an electronic record, and then all responses will be aggregated.

10 ADVERSE EVENT REPORTING

10.1 Non-Device-Associated Adverse Events

Adverse events occurring during the enrollment period should be documented by the Investigator in progress notes, but will not be collected or analyzed by Pelex unless considered serious by the Investigator.

Serious adverse events (SAEs) encountered during study enrollment will be documented by the Investigator and reported to Pelex immediately upon discovery. SAEs are defined under current Good Clinical Practice (cGCP) guidelines as events that result in one or more of the following:

- life-threatening illness or injury;
- permanent impairment of a body structure or a body function;
- medically necessary in-patient hospitalization;
- medical or surgical intervention necessary to prevent permanent impairment to body structure or function; or
- fetal distress, fetal death, or congenital abnormality.

10.2 Device-Associated Adverse Events

10.2.1 Definition of an unanticipated adverse device effect (UADE) event

A UADE event, as defined by cGCP guidelines, is any SAE, life-threatening problem, or death caused by or associated with a device (or with the process of evaluating a device) if that SAE, 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, device-associated problem that relates to the rights, safety, or welfare of subjects or operators using the investigational product system or the comparator product system.

10.2.2 Reporting of device-associated adverse events

Any adverse event that results in serious injury or death and any type of unanticipated adverse device effect, regardless of seriousness or severity, must be reported to the Investigator once when site becomes aware of the event. Initial reports may be partial and should be updated as additional information becomes available. All unanticipated adverse device effects and all serious adverse events should be reported to the Investigator's IRB in accordance with the IRB reporting requirements.

SAEs will be reported using an Unanticipated Adverse Device Effects (UADE) form, which serves the dual role of capturing pertinent SAE information per industry guidelines and capturing device information pertinent to medical device standards. Other serious events that affect the rights, safety, or welfare of subjects must also be documented on the UADE form and must be reported immediately to Pelex and to the Investigator's IRB according to that IRB's policies.

All SAEs that occur during the study period, whether considered to be related to the investigational product or not, will be reported within 24 hours of knowledge of the event to the sponsor contact below via an EDC notification.

Although all information required for completion of an SAE report form may not be available within the specified time period, the following minimal initial information should be reported: Subject ID #, Site #, an identifiable reporting source name and contact information (e.g. investigator/study coordinator), which of the 6 SAE criteria identified above resulted in the event being deemed "serious". IRB reporting requirements may also apply for SAEs.

10.3 Sponsor Contact for Serious Adverse Event Reporting

Rohit Joshi
718-404-7152
rohit@pelex-med.com

11 RISK ANALYSIS

11.1 Potential Risks of the Investigational Product and Clinical Investigation

Study device is currently seeking 510(k) approval with the FDA and has been identified as a non-significant risk medical device under FDA regulations and guidance documents, specifically Title 21 CFR 812.2(c). Importantly, subjects will experience no greater risk than that associated with standard pelvic floor muscle training plus biofeedback treatment.

The types of risk associated with Pelex Upp align with those associated with biofeedback devices used for PFMT. These risks are all stated in the consent form.

11.2 Potential Benefits of the Investigational Product and Clinical Investigation

Subjects may benefit from this study through the possible improvement in their stress urinary incontinence symptoms. The benefits of the study will also be to the larger population of patients with stress urinary incontinence who would potentially benefit from a non-invasive device for usage at home in treatment of stress urinary incontinence.

The studies made possible by the data collected in this study are expected to lead to confirmation of the clinical efficacy of biofeedback-augmented PFMT performed at home.

11.3 Minimization of Risks

Although the risk to subjects participating in the study is anticipated to be minimal, the clinician, at his/her discretion, will not collect data from those individuals for whom collection is judged to pose an unusually high risk of physical or mental harm or discomfort.

Participation in this study poses no risk to study personnel other than that normally encountered during standard practice. These risks will be minimized by adherence to the following guidelines:

- Personnel should wear appropriate personal protective equipment to avoid contact of the eyes or skin with hazardous materials or products derived from biological sources.

12 INVESTIGATOR RESPONSIBILITIES

12.1 Site Qualification and Study Oversight

The PI is responsible for general administration of the study.
Before the study, the PI must:

- Obtain approval to conduct the study from the study site's IRB;
- Sign the Protocol PLX-001 Signature Page him/herself and have all sub-investigators sign the Protocol PLX-001 Signature Page and return it to Pelex;
- Provide financial disclosures to Pelex for themselves and all sub-investigators participating in study conduct, per Title 21CFR 54 (see **Section 12.4** below).

During the study, the PI must ensure that:

- The study is conducted ethically;
- Case report forms (CRFs), including Subject ICFs, are provided with each transfer of data requiring informed consent; and
- All other study forms are completed as instructed by Pelex.

In the case of completion or termination of the study or an Investigator's role in the study, or at Pelex request, all study materials must be returned to Pelex.

12.2 Case Report Forms/Electronic Data Records

As used in this protocol, the term CRF should be understood to refer to either a paper form or an electronic data record or both, depending on the data collection method(s) used.

Original CRFs are the sole property of Pelex and should not be made available in any form to third parties, except for authorized representatives of Pelex or appropriate regulatory authorities, without written permission from Pelex.

It is the PI's responsibility to ensure completion, review, and approval of all CRFs. CRFs must be signed by the PI or by an authorized staff member. These signatures serve to attest

that the information contained on the CRFs is true. At all times, the PI has final personal responsibility for the accuracy and authenticity of all clinical and laboratory data entered on the CRFs.

12.3 Access to Source Documents

Pelex or its agents and appropriate regulatory authorities shall be granted direct access to all study-related documents to perform verification that the protocol and all applicable current Good Laboratory Practices (cGLPs), Good Clinical Practices (GCPs), and regulations are being followed and to confirm that study documents are complete and accurate. It is important that Investigator(s) and their relevant personnel be made available during monitoring visits and any audits or inspections, and that sufficient time is allotted for the process.

12.4 Financial Disclosure

Investigators must provide Pelex with sufficient, accurate financial information in accordance with local regulations to allow Pelex to submit complete and accurate financial certification or disclosure statements to the appropriate health authorities. Investigators are responsible for providing information to Pelex concerning their relevant financial interests during the course of the study and for 1 year after completion of the study. Conflicts of interest should be disclosed as required by law.

Financial support for this project is provided by Pelex, Inc. Specifically, Pelex, Inc. is providing all investigational devices and device-associated materials, including instructional material. Pelex, Inc will also provide all documentation for the study.

12.5 Deviations from the Study Protocol

An Investigator may not deviate from the study protocol without prior approval by Pelex unless the deviations are necessary under emergency circumstances to protect the rights, safety, or well-being of human subjects or the scientific integrity of the clinical investigation. These deviations must be documented and promptly reported to Pelex and, if applicable, to the IRB providing oversight of the study. Protocol deviations may result in corrective and preventive actions and/or disqualification of the Investigator.

12.6 Record Retention

To enable evaluations and/or audits from regulatory authorities or Pelex, the PI and all sub-investigators agrees to retain all study records, including copies of all CRFs, UADE forms, and source documents, for 3 years following completion of the project dependent upon the study data. The Investigator must obtain the Pelex written permission before disposing of any records, even if retention requirements have been met.

If an Investigator relocates, retires, or for any other reason withdraws from the trial, Pelex must be notified in advance, and study records must be transferred to a designee acceptable to Pelex. This designee might be another Investigator, another institution, or Pelex itself.

12.7 Publication Policy

The results of this study may be submitted for publication to a medical journal. The PI agrees that any publication of data from this study will comply with Pelex publication policy, the instructions to authors outlined by the editor of the journal or conference proceedings where the data is to be published, and the spirit of recommendations made in the good publication practice guidelines (GPP3) of the International Society of Medical Publication Professionals. Pelex has the right to review any manuscripts, presentations, or abstracts that originate from this study or that utilize these data before they are submitted for publication or other means of communication.

13 ETHICS AND COMPLIANCE

13.1 Investigational Device Exemption

Although exempt from IDE regulations as noted in Title 21 CFR 812.2(c), the conduct and performance of this study will be in accordance with applicable Sponsor and Investigator responsibilities as described in Title 21 CFR 809 and Title 21 CFR 812.

13.2Informed Consent and De-Identification

Informed consent will be obtained in accordance with the Declaration of Helsinki, International Council for Harmonisation (ICH) guidelines for GCP, US Code of Federal Regulations (CFR) for Protection of Human Subjects (21 CFR 50.25[a,b], CFR 50.27, and CFR Part 56, Subpart A), and General Data Protection Regulation if applicable, and local regulations. All subjects for this study will be provided an informed consent form (ICF) describing this study and providing sufficient information for subjects to make an informed decision about their participation in this study. The consent form will be submitted with the protocol for review and approval by the IRB/EC for the study. A blank copy of the IRB/EC-approved form must be kept on-site and by the Sponsor and Investigator (see Attachment – Informed Consent Form).

The ICF will be reviewed with the prospective study subject by the Investigator or qualified designee who will be available to answer questions about procedures, risks, and alternatives. Appropriate essential information will be provided, and the procedure fully explained, to allow the subject's legal guardian to make an informed decision about study participation. The subject will be informed that study participation is voluntary and the decision not to participate will not result in penalty and they can still receive standard of care. If the subject consents, he/she and the qualified designee reviewing the consent will sign and date the IRB-approved paper ICF. The subject will receive a copy of the signed ICF. The original signed and dated ICF will be kept in the site's regulatory file. Documentation of informed consent for participation in this trial will be noted in the subject's medical record at the site.

13.2.1 Prospectively collected data

All subjects will be given a copy of the IRB-approved ICF to review before their study participation begins. The Investigator will explain all aspects of the study in lay language and answer all of the potential participant's questions regarding the study. If the participant decides to participate in the study, s/he will be asked to sign and date the ICF. Subjects who refuse to participate or who withdraw from the study will be treated without prejudice.

13.3IRB Review

The PI is required to obtain IRB oversight of the research study. The IRB must be provided with the Pelex-approved study protocol. Performance of the study may not begin until written evidence of IRB approval has been provided to Pelex.

The conduct and performance of this study will be in accordance with applicable Sponsor and Investigator responsibilities as described in Title 21 CFR 812 and other Good Clinical Practice guidance.

IRB/Ethics Committee oversight will be required as human subjects or data from humans are being used. This protocol and the associated informed consent document(s) (if applicable) must be submitted to the IRB for review and approval. Performance of the study at a given site may not begin until written evidence of IRB oversight has been provided to Pelex study manager. IRB Review and approval must comply with Title 21 CFR 812 Subpart D.

13.4Confidentiality of Data and Patient Records

The study institution shall keep all records associated with this study for at least 3 years, as specified in **Section 12.6**. Investigators will keep all records associated with this study for at least 3 years.

13.4.1 Provisions to Protect the Privacy Interests of Participants

The PI and/or study institution shall provide sufficient information to allow the IRB to evaluate the researcher's provisions to maintain the confidentiality of data.

Privacy data will be maintained in accordance with HIPAA and other applicable policies and local law.

14 REFERENCES

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