Clinical Research Protocol

Protocol Title:	TESTING THE EFFECTIVENESS OF A FALL PREVENTION SYSTEM
Version Date:	Version 4; 07/29/2019
Investigational Product:	PUP™ (Patient is Up) System
IND Number:	Not applicable
Study Design:	Single Arm intervention
Sponsor:	Tammy Moore, RN PhD
Funding Organization:	Palarum, LLC
Principal Investigator:	Tammy Moore, RN PhD Director, Nursing Neurological Institute The Ohio State University
Medical Monitor:	Not Applicable
Study Site:	Brain and Spine Hospital The Ohio State University

Approval:

_____ _____

PI or Sponsor Signature (Name and Title) *Date*

This confidential information about an investigational product is provided for the exclusive use of investigators of this product and is subject to recall at any time. The information in this document may not be disclosed unless federal or state law or regulations require such disclosure. Subject to the foregoing, this information may be disclosed only to those persons involved in the study who have a need to know, with the obligation not to further disseminate this information.

PROTOCOL AGREEMENT

I have read the protocol specified below. In my formal capacity as Investigator, my duties include ensuring the safety of the study subjects enrolled under my supervision and providing [Tammy Moore] with complete and timely information, as outlined in the protocol. It is understood that all information pertaining to the study will be held strictly confidential and that this confidentiality requirement applies to all study staff at this site. Furthermore, on behalf of the study staff and myself, I agree to maintain the procedures required to carry out the study in accordance with accepted GCP principles and to abide by the terms of this protocol.

Protocol Title: Testing and Effectiveness of a Fall Prevention System

Protocol Date: 29 JUNE 2019

Investigator Signature	*Date*

Tammy Moore, RN PhD Director of Nursing

Print Name and Title

Site Name	Brain and Spine Hospital, The Ohio State University
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Phone Number	614-293-7847

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LIST OF ABBREVIATIONS

AE	Adverse Event
BTLE	Blue Tooth Low Energy
CFR	Code of Federal Regulations
CRF	Case Report Form
DMC	Data Monitoring Committee
DSMB	Data Safety Monitoring Board
FDA	Food and Drug Administration
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act of 1996
HUC	Health Pod Coordinator/UCA Monitor
ICF	Informed Consent Form
IEC	Independent Ethics Committee
IRB	Institutional Review Board
IRL	In Room Locator
IRT	In Room Tablet
PI	Principal Investigator
PLS	Palarum Local Server
PUP™	Patient is Up Fall Prevention System
RSSI	Receive Signal Strength Indicator
RTLS	Real Time Location System
PCS	Palarum Cloud Service
SAE	Serious Adverse Experience
WIRB	Western Institutional Review Board

PROTOCOL SYNOPSIS

TITLE	Testing the Effectiveness of a Fall Prevention System
SPONSOR	Tammy Moore, RN PhD
FUNDING ORGANIZATION	Palarum, LLC
NUMBER OF SITES	1 Site on 3 floors of the Ohio State University Wexner Center Brain and Spine Hospital; (8 South, 9 South, 10 South, 8 East, 9 East & 10 East
RATIONALE	Each year, between 700,000 and 1,000,000 people in the United States fall in a healthcare environment (Agency for Healthcare Research and Quality, 2015). Falls can have a widespread and significant impact on health, can be deadly, and often result in high costs. Falls with serious injury are consistently among the Top 10 sentinel events reported to The Joint Commission's Sentinel Event database (The Joint Commission, 2015). The average 200-bed hospital might log 300 patient falls a year (based on 5 patient falls per 1000 patient days), which results in $10,200 per fall in medical costs annually – or more than $3 million. (Agency for Healthcare Research and Quality) The best way to reduce the number of falls is to prevent them. A whole marketplace of bed and chair alerts and other devices has been developed to address the need, yet the numbers increase. On a busy patient floor, nurses lose valuable seconds just figuring out which patient's bed alert is sounding. We expect research to show that the Palarum PUP™ System reduces the incidence of falls.
STUDY DESIGN	Single arm trial
PRIMARY OBJECTIVE	To determine if the fall rate (as measured by falls per 1000 patient days) for patients designated "fall risk" decreases with the use of the intervention (**P**atient is **UP** fall prevention technology [PUP™]) when compared to historical NDNQI data for the prior 12 months ("Benchmark Data") from nursing units where the intervention is being undertaken.

SECONDARY OBJECTIVES	1. To reduce the incidence of false alerts, <5%. Our goal is a high reliability notification system. 2. To provide positive alert reliability of 95%. Our goal is to reduce alert fatigue with nurses. To determine number of alerts sent out; what is the frequency of these patient safety events (i.e.), fall risk patient up, out of bed, unassisted 3. To gather compliance data and response times from alert to caregiver response.
NUMBER OF SUBJECTS	2500 patients
SUBJECT SELECTION CRITERIA	Inclusion Criteria: All risk fall patients, eighteen years of age or older, who are admitted to the OSU Brain and Spine Hospital on Floors 8 South, 9 South, 10 South, 8 East, 9 East or 10 East. Patients will undergo a pre-assessment as per OSUWMC procedure to determine if they are of fall risk. Exclusion Criteria: Patients whose medical condition as assessed by the PI prohibits their participation in the program, which would include among others the following: patients who lack the capacity to consent that do not have an Legally Authorized Representative (LAR), patients with an anatomy or wound issue on their feet or around their calves that would bar them from wearing socks on either foot, and/or patients for whom the sock would impede medical treatment.
TEST PRODUCT, DOSE, AND METHOD OF USE	**Test Product:** Palarum LLC's, PUP™ (Patient is Up) System **Dose:** N/A **Method of Use:** The Study site, the OSU Wexner Center Brain and Spine Hospital, is located on three contiguous floors with each floor being made up of two units or Pods designated East and South. Following commencement of the study, and throughout its duration, Pods assigned to the Study will only utilize the Palarum Fall Prevention System and a monitored PUP™ sock as the standard of care intervention for fall prevention in accordance with its operating instructions and procedures. The Implementation Team for the Study will consist of the PI, the Nurse Managers and Staff, allied health professionals as may be assigned to the Pods during the course of the Study. The Palarum Fall Prevention System is made up of seven tangible elements connected by Wi-Fi and/or BTLE: an inpatient room

	Android tablet (IRT), a nurse station Android monitor (HUC), a local server (PLS), a cloud server (PCS), a Bluetooth Low Energy beacon(s), an Android smart notification device, and an e-textile sock connected sensor transmitter (PUP™ sock). The PUP™ sock monitors and transmits pressure, force, acceleration and motion data to IRT and PLS, and HUC and PCS. This data is evaluated and validated by an Android application on the IRT to determine whether or not a fall risk patient is standing unaccompanied by a caregiver. If a monitored patient is standing unattended, the PLS locates and alerts the Smart Notification Devices of the five (5) closest healthcare providers and the HUC using the beacon technology. Alerts are terminated by the Smart Notification Device and PLS based on caregiver proximity to the patient. All data, alerts, suspensions, terminations and notifications are recorded by the PCS. On a daily basis, PCS reports are produced which contain data for each patient enrolled, number of alerts, excessive alerts, and caregiver response time, as well as summaries by Pod and entire facility. All Brain and Spine Hospital patients will be evaluated as to fall risk using the current fall risk assessment procedures employed by OSU Medical Center and administered in the usual and customary fashion upon evaluation on the floor and Pod. Any patient fall is to be reported and evaluated following current processes and procedures developed by the OSU Brain and Spine Institute as maintained with IHIS. If a fall risk patient is admitted to the unit and is not otherwise disqualified by the Study Exclusion Criteria, the patient and/or LAR in form of a Patient Consent document, will be given information about and the opportunity for the patient to participate in the Study. If the patient or legal surrogate declines participation, the patient will receive standard of care provided prior to the Study. Upon receiving a consent to participate, the patient will be fitted with a monitored PUP™ sock sized to the patient's foot from the Study inventory, and thereafter enrolled by a caregiver in the Palarum Fall Prevention System using an Android application on the IRT. The Palarum Fall Prevention System and PUP™ sock thereafter monitor the patient's activity 24x7 throughout the patient's entire length of stay. During the patient's stay, the PUP™ sock will be evaluated daily for proper fit, patient comfort, and patient safety. Upon discharge or transfer, the patient is un-enrolled from the system again

	utilizing the IRT. All patient relevant fall data, including system performance, is collected and stored in the PCS for future study and evaluation. Any patient fall is to be reported and evaluated following current OSU Medical Center processes and procedures independent of the Palarum Fall Prevention System. Technical support for the Palarum Fall Prevention system is available by phone at 844-PALARUM (844) 725-2786 and email, it@palarum.com, 24x7. If there is a Palarum Fall Prevention System outage each Intervention Group Pod should follow policies related to downtime procedures for fall risk patients.
CONTROL PRODUCT, DOSE AND ROUTE OF ADMINISTRATION	N/A
DURATION OF SUBJECT PARTICIPATION AND DURATION OF STUDY	Duration: Once a patient has been placed in the fall risk protocol, the patient will remain in the study until a nurse removes the patient from risk fall status or the participant has been discharged from the hospital.
CONCOMITANT MEDICATIONS	Allowed: YES Prohibited: NONE
EFFECTIVENESS EVALUATIONS	Effectiveness evaluation data will be collected by the Palarum Fall Risk System, and incorporated and integrated with patient diagnosis, co-morbidities, and other medical data within REDCap including: 1. Enrollment Data a. Patient Identifier/MRN b. Patient Weight c. Patient Sock Size (S-M-L-XL) d. Sex e. Pod and Room/Bed f. Date g. Time h. Sock Number i. Sensor Number 2. Event Logs 3. Time of stand alert 4. Time to clear 5. Who cleared stand 6. Manual or Automatic termination 7. Accelerator and Gyroscopic Data surrounding each stand event

	8. Pressure on foot 9. Motion of patient
PRIMARY ENDPOINT	Fall rate per patient days within the study sample population
SECONDARY ENDPOINTS	As collected by the Palarum Fall Prevention System, validated by manual audits of thereof, and integrated with REDCap, • Rate of false alerts • Rate of fall related patient safety events • Time to respond to alert • Pressure on foot • Motion of patient • Alert fatigue analyzed and measured by alert responded/alerts generated over time. • Notification system alerts only the closest five caregivers when a fall risk patient is up • Time to staff notification (latency) when a fall risk patient is up and unattended • Time to clear data • Identification of caregiver clearing alert • Determination of manual or automatic termination
OTHER EVALUATIONS	N/A
SAFETY EVALUATIONS	Incidence of adverse events arising use of device
PLANNED INTERIM ANALYSES	N/A
STATISTICS **Primary Analysis Plan**	The primary endpoint for this study is the number of patient falls. This will be expressed as a falls incidence rate, i.e., number of falls per patient days where patient days are counted from the initiation of the PUP™ System until discharge or removal from the fall risk protocol. Using a one-sided one-sample test for Poisson means, we will test whether the observed fall rate is less than the historical rate of 0.004. This test will be conducted at the alpha=0.1 level. Results will be presented as the fall rate and the corresponding one-sided 90% confidence interval which will provide an upper bound for the fall rate.

Rationale for Number of Subjects	The primary endpoint of the trial is the patient fall rate per patient days. Comparing to a historical rate of 0.004 using a one-sided test of Poisson means, we have at least 70% power to detect a 25% reduction in the fall rate at alpha level 0.1 with 2360. Assuming a dropout rate of 5%, we will enroll 2500 patients into the study.

1 BACKGROUND

The PUP™ System is designed to monitor patient activity in a hospital, clinic, nursing home, or other facility where a patient may be receiving care.

The System includes pressure sensors incorporated into the toe and heel of a sock using both pressure sensitive fibers and also a Bluetooth transmitter affixed to the exterior of the sock in the ankle region. After the caregiver assists the patient in putting on the PUP™ socks, the caregiver will enter the appropriate patient data into the dedicated in-room PUP™ tablet to associate the patient with the specific sensor. When the patient gets out of bed and steps on the floor, pressure is detected by the sock sensors which trigger an alert signal to the PUP™ tablet. This alert is displayed locally in the patient's room on the PUP™ tablet and can be dismissed by a caregiver present in the room with the patient, as appropriate. The in-room PUP™ tablet also relays the alert signal to a local Palarum server which sends the alert signal to both a monitoring device located at the nursing station as well as to notification devices being worn by select caregivers. The sock also includes a sensor for motion detection for power-saving purposes. If the patient is idle for a specified amount of time, the device enters a power-saving mode. Once motion is detected, the system 'wakes' in order to be able to detect whether pressure is applied to the sock indicating that the patient is standing or attempting to get out of bed.

The system can support monitoring of sensors for multiple patients, allowing display of sensor status for multiple patients on the tablet app.

1.1 Overview of Research

Each year between 700,000 and 1,000,000 people in the United States fall in a healthcare environment (Agency for Healthcare Research and Quality, 2015). Falls can have a widespread and significant impact on health, can be deadly, and often result in high costs. Falls with serious injury are consistently among the Top 10 sentinel events reported to The Joint Commission's Sentinel Event database (The Joint Commission, 2015). The average 200-bed hospital might log 300 patient falls a year (based on 5 patient falls per 1000 patient days), which results in $10,200 per fall in medical costs annually – or more than $3 million.

Falls are one metric that Medicare now uses to measure hospitals on patient safety. Not meeting the fall metric will trigger a reduction in the hospital's cost reimbursements.

While one in three hospitalized Americans, aged 65 and over falls every year, elderly patients are not the only ones vulnerable to falling in health care facilities. Any patient of any age or physical ability can be at risk for a fall due to medical condition, medications, surgical procedures or diagnostic testing. Falls increase the length of inpatient stays by 6.3 days and hospital charges by $14,000. (The Joint Commission, 2015).

Most facilities have tried to address falls with traditional motion detection systems, room sitters, and enhanced training, but falls continue to be a quality of care and cost issue. Traditional motion detectors can result in a false alert, which can lead to nurses or other

hospital workers tuning out alerts or turning them off. One hospital executive said they spent $4.2 million on patient sitters last year

2 STUDY RATIONALE

Palarum LLC ("Palarum") has designed and developed a wireless and "smart" fall prevention system and desires to have the effectiveness of the system evaluated by The Ohio State University Wexner Medical Center ("OSU") through a disciplined and structured product evaluation process.

Each year between 700,000 and 1,000,000 people in the United States fall in a healthcare environment (Agency for Healthcare Research and Quality, 2015). Falls can have a widespread and significant impact on health, can be deadly, and often result in high costs. Falls with serious injury are consistently among the Top 10 sentinel events reported to The Joint Commission's Sentinel Event database (The Joint Commission, 2015). The average 200-bed hospital might log 300 patient falls a year (based on 5 patient falls per 1000 patient days), which results in $10,200 per fall in medical costs annually – or more than $3 million. (Agency for Healthcare Research and Quality).

Falls are one metric that Medicare now uses to measure hospitals on patient safety. Not meeting the fall metric will trigger a reduction in the hospital's cost reimbursements.

While one in three hospitalized Americans aged 65 and over falls every year, elderly patients are not the only ones vulnerable to falling in health care facilities. Any patient of any age or physical ability can be at risk for a fall due to medical condition, medications, surgical procedures or diagnostic testing. Falls increase the length of inpatient stays by 6.3 days and hospital charges by $14,000. (The Joint Commission, 2015).

Falls represent both a patient safety priority and an economic priority for healthcare organizations. A fall may result in fractures, lacerations, or internal bleeding, leading to increased health care utilization. As of 2008, the Centers for Medicare & Medicaid Services (CMS) does not reimburse hospitals for the extra care associated with an inpatient fall and the trauma associated with it. (The Joint Commission, 2015).

The best way to reduce the number of falls is to prevent them. A whole marketplace of bed and chair alerts and other devices has been developed to address the need, yet the numbers creep up. On a busy patient floor, nurses lose valuable seconds just figuring out which patient's bed alert is sounding. We expect research to show that the Palarum PUP™ System takes back that critical time.

2.1 Risk / Benefit Assessment

Risks of Product

- Over-reliance on automation of technology decreasing hourly rounding presence
- System fails to notify staff of stand alert
- Possible skin impression from prolonged use of sock

Mitigation of Each Risk

- Education
- Patient Assessments
- Replacement of Socks
- Socks come with multiple locations with sock sensor placement

Benefits

- Improved patient safety by reducing the number of patient falls. A 25% reduction in patient falls will result in 90 less falls per year in a 200-bed hospital.
- Improved patient outcomes
- Staff is notified immediately when a patient safety event occurs (fall risk patient is up and unattended)
- Reduced alert fatigue. Improved accuracy of the stand detection with innovative pressure sensitive smart textiles. New notification system which alerts only the closest five caregivers, with an escalation protocol, when a fall risk patient is up and automatically terminates the alert when a caregiver enters the room.
- Data & Analytics. The PUP™ Fall Prevention System delivers critical new data to enhance patient care and improve hospital operations.
- Cost Savings. The Palarum LLC, alert system could save one 200 bed hospital approximately $744,600 dollars each year. Average 200 bed hospital is expected to have 5 patient falls per 1000 patient days. Therefore, an average 200 bed hospital will have 365 falls per year (20% reduction in patient falls (73)/year x $10,200/ fall).

3 STUDY OBJECTIVES

3.1 Primary Objective

The primary objective of this study is to determine if the fall incidence rate for patients with the intervention, Palarum LLC's, PUP™ (Patient is Up) System is less than the historical incidence rate of patient falls in the units under study.

3.2 Secondary Objectives

Within the context of the Study

- Determine the rate of false alert delivered by the PUP™ System
- Determine the rate of fall related patient safety events
- Determine the average caregiver response time to an alert delivered by the PUP™ System

4 STUDY DESIGN

4.1 Study Overview

- **Problem -** Falls occur at a rate of 5.5 per 1000 patient days in US hospitals. In addition to the human morbidity and mortality costs, falls cost hospitals in excess of $8 billion in unreimbursed charges. No intervention to date has been shown to significantly reduce that rate.
- **Purpose -** To determine the effectiveness, if any, of the PUP™ Fall Prevention System. The hypothesis is that the System will reduce the fall rate by at least 25% of prior years' average fall rate.
- **Population to be studied** - All fall risk patients, eighteen years old or older, admitted to OSU Brain and Spine Hospital on Floors 8, 9, and 10 until the sample size is reached.
- **Research Design –** Single arm trial
- **Extent of Researcher Interference -** Minimal, only studying events as they normally occur. The PUP™ System will have been previously evaluated and approved for use as the standard of care at the OSU Medical Center Brain and Spine Hospital in accordance with the terms of an agreement between Palarum and OSU Medical Center dated March 28, 2018.
- **Time horizon** - Current.
- **Study setting** - Non-contrived. OSU Medical Center Brain and Spine Hospital.
- **Measurement and measures**
    - Patient fall rate (measured as number of falls/1000 patient days) data collection and reporting forms, criteria and protocols for the three calendar years preceding initiation of the research.
    - Patient fall rate data collection and reporting forms, criteria, and protocols for the research period calendar year.
    - Data collection standards and protocol for/of;
        - Positive stand detection alert
        - Negative stand detection alert
        - Participant inclusion, exclusion or exemption
        - Sampling methods of 1-3 above
        - Report form(s), structure and content
        - Participant or data exclusion standards, if any.
- **Data Collection Method** - Unobtrusive automated physical measurement using the PUP™ sock, sensors, wireless technology, and REDCap.

4.2 Research Procedures & Steps

- **Pre-Conditions**
  - All Nurses/applicable staff Trained on Palarum System
  - All Equipment Installed in Rooms
  - At Beginning of Shift Nurses Wearing Smart Notification Devices & Enrolled into Unit

- **Patient Admission**
  - Patient Admitted into Room with Palarum Technology

- **Fall Risk Screening**
  - Patient undergoes fall risk assessment.
  - If patient is determined to be fall risk, they proceed to next step

- **Determination of Inclusion/Exclusion Criteria**
  - Containment - Hospital Specific
  - Weight Limit – Hospital Specific
  - Mental Cognizance – Hospital Specific
  - Other Health Conditions – Hospital Specific

- **Registration into Study**
  - If patient is determined as candidate for study and patient and/or LAR has provided written informed consent, then that patient will be registered as a study participant.

- **Patient Education**
  - Patient and/or Patient family will be educated on admission using a video on the in-room tablets.

- **Fit with Sock**
  - Upon registration into study the patient will be fitted for a sock by the nursing staff.
  - Nursing staff utilizes sizing chart to correlate patient's foot size with Palarum Sock size.
  - Sock is placed on patient

- **Enroll Sock in Application**
  - Once sock is successfully fitted on patient the nurse proceeds to enroll the patient through Palarum Application.
  - The following categories must be completed before proceeding to a successful enrollment: Patient Name/Initials/MRN, Sex, Weight, Sock Size, Sensor.

- Upon successful sock pairing to IRT the enrollment process is complete and the patient is now being monitored.

- **Application Records/Data**
  - Enrollment Data

- **Event Logs**
  - Time of stand alert
  - Time to clear
  - Who cleared stand
  - Manual or Automatic termination
  - Accelerator and Gyroscopic Data surrounding each stand event

- **Report Generation**
  - At 12am each morning a report is generated detailing the previous day's activity on the system.
  - Two separate reports are sent each morning at 12am (filtered by audience): Nurse Manager, Site Executive.
  - The reports show: the Pod the patient is enrolled in, # of Alerts during their length of stay, whether a patient has alerted 3 or more times in less than 24 hours.

- **Alert Generation**
  - An alert is generated when a patient places their foot on the ground and takes a step.
  - False alerts are prevented through the use of a gyroscope and accelerometer.
  - Once an alert is generated it is sent to the IRT, HUC, and Smart Notification Devices.

- **How to respond to Alerts**
  - There are two ways to respond to an alert in the Palarum Fall Prevention System
    - Nurse proceeds into the room (wearing Palarum Smart Notification Device) and the system automatically turns off do to his/her proximity.
    - Nurse proceeds into the room and manually turns off the system on the IRT by touching the red alert Icon on the screen and proceeding to put in their initials.

5 CRITERIA FOR EVALUATION

5.1 Primary Effectiveness Endpoint

The primary endpoint is the fall rate per patient days within the study population. A fall is defined as "*an unplanned descent to the floor with or without injury to the patient. Include falls when a patient lands on a surface where you wouldn't expect to find a patient. All unassisted and assisted falls are to be included whether they result from physiological reasons (fainting) or environmental reasons (slippery floor). Also report patients that roll off a low bed onto a mat as a fall*."

5.2 Secondary Effectiveness Endpoints

- The rate of false alerts per patient days delivered by the PUP™ System. We define as false alert as an alert generated by other than a physical stand by the PUP™ System.
- The number of patient safety events. Fall related patient safety events include patient standing, walking, and otherwise moving without a caregiver present.
- We will assess the average time to respond to an alert delivered by the PUP™ System. This will be the time from the initiation of an alert until it is silenced automatically by RSSI proximity of a caregiver or manually by the caregiver.

5.3 Safety Evaluations

Falls are inherent in healthcare settings and cannot be entirely eliminated. As such they are not an adverse event arising from or related to the use of the Palarum PUP™ System.

6 SUBJECT SELECTION

6.1 Study Population

- All fall risk patients, eighteen years old or older, admitted to the OSU Medical Center Brain and Spine Institute on Floors 8, 9 and 10. "Fall risk" will be defined by OSUWMC standard of care criteria.

6.2 Inclusion Criteria

- Written informed consent obtained from subject (and/or LAR) and ability for subject to comply with the requirements of the study.
- All fall risk patients, eighteen years old and older, on Floors 8, 9 and 10 of the OSUWMC Brain and Spine Hospital, with "fall risk" as defined by OSU criteria, for whom no medical condition prohibits their participation in the program, (see Exclusion Criteria).

6.3 Exclusion Criteria

- Presence of a condition or abnormality that in the opinion of the Investigator would compromise the safety of the patient or the quality of the data.
- Patients whose medical condition prohibits their participation in the program, which would include among others, patients with an anatomy or wound issue on their feet or around their calves that would bar them from wearing socks on either foot, and/or patients for whom the sock would impede medical treatment.

7 STUDY TREATMENTS

7.1 Method of Assigning Subjects to Placebo or Test Evaluation Groups

Eligible patients will be enrolled in the PUP™ System treatment. Pod staff will assess fall risk and study team will determine eligibility.

7.2 Formulation of Test and Control Products

Palarum, LLC manufactures the socks and provides the equipment.

7.3 Packaging and Labeling

The PUP™ System socks will be provided individually wrapped in a plastic package.

Each pair of socks will be labeled with a unique number and each package will be labeled with the name of the sponsors, and directions for patient use and storage. (Appendix A)

7.4 Supply of Study Socks and Equipment at the Site

All socks for patients admitted to study will be stocked in the respective floors supply closet with their existing socks. All equipment for the study patients will be in place and tested before the study begins.

7.5 Regimen

Each patient will be fitted with a sized pair of PUP™ socks and enrolled in the system. Socks will be worn continuously throughout the stay unless soiled or identified as defective by the self-testing of the PUP™ System. If soiled or defective, the socks will be replaced from the supply.

7.6 Dispensing

All fall risk candidates who provide consent will be enrolled by the caregiver or CRC into the PUP™ Fall Risk Solution upon enrollment.

7.7 Administration Instructions

- Nurse will enroll the patient.
- Sock is fitted to patient.
- Patient anatomy and foot size will determine the selection of appropriate sock size.

- Series of 5-7 dots (size dependent) on top of sock will be aligned with center of foot.

7.8 Supply of Study Inventory at the Site

- Appropriate sizes will be stored in a supply cart on the unit.
- Sock inventory will be maintained

7.9 Storage

Storage of the PUP™ S equipment will be within the Brain and Spine Hospital.

7.10 Study Accountability

- Upon discharge, the patient will be un-enrolled from the PUP™ Fall Prevention Solution.
- Socks will be put in a special recyclable bin that will be returned to the vendor to be laundered and inspected for quality assurance.
- An accurate and current accounting of the dispensing and return of PUP™ socks for each subject will be maintained on an ongoing basis by a member of the study site staff.

7.11 Measures of Treatment Compliance

- Each morning at 12am a report will be generated detailing the previous day's activity on the system.
- Two separate reports will be sent each morning at 12am (filtered by audience): Nurse Manager, Site Executive.
- The reports will show:
    - The Pod where the patient is enrolled
    - # of alerts during their length of stay
    - Whether a patient has alerted 3 or more times in less than 24 hours.

8 STUDY PROCEDURES AND GUIDELINES

- A Schedule of Events representing the required testing procedures to be performed for the duration of the study is diagrammed in (Appendix B).
- Prior to conducting any study-related activities, Pod staff will identify eligible patients and notify study staff to consent and enroll. Written informed consent and the Health Insurance Portability and Accountability Act (HIPAA) authorization must be signed and dated by the subject or subject's legal representative.

8.1 Clinical Assessments

Clinical assessment of foot and ankle

8.2 Concomitant Medications

All concomitant medication and concurrent therapies will be documented at Baseline/Screening, at early termination when applicable and at discharge. Dose, route, frequency of administration, and indication for administration and dates of medication will be captured.

8.3 Demographics

Demographic information (date of birth, sex, race) will be recorded at Baseline Screening and again at enrollment in the PUP™ System.

8.4 Medical History

Relevant medical history, including history of current disease, other pertinent history, and information regarding underlying diseases will be recorded at Baseline Screening.

8.5 Physical Examination

Clinical assessment of foot and ankle

8.6 Adverse Events

Information regarding occurrence of adverse events will be captured throughout the study. Duration (start and stop dates and times), severity/grade, outcome, treatment and relation to study will be recorded on the case report form (CRF – Appendix C).

9 EVALUATIONS BY VISIT

9.1 Pre-Conditions

- All nurses/applicable staff trained on Palarum PUP™ System
- All equipment installed in rooms
- At beginning of shift nurses wearing smart notification devices & enrolled into unit.

9.2 Day 1 – Admission

- Patient Admission
    - Patient admitted into a room with the Palarum PUP™ technology
- Fall Risk Screening
    - Patient undergoes fall risk assessment.
    - If patient is determined to be fall risk they proceed to next step
- Registration into Study
    - Dedicated trained staff will be notified and will enroll the Patient into the Study as soon as medically feasible and reasonable.
    - If patient is determined as candidate for study, they are registered as a study participant.

  - Review the study with the subject and obtain written informed consent and HIPAA authorization and assent, if appropriate.
  - Assign the subject a unique screening number.
  - Record demographics data.
  - Record concomitant medications.
- Patient Education
  - As noted in "Pre-Conditions" all nursing and related staff are trained on how to use the Palarum Fall Prevention Technology before the study starts.
  - Continuous training will be available for new staff through Buckeye Learn.
- Fit with Sock
  - Upon registration into this study, the patient will be fitted for a PUP™ sock by the nursing staff.
  - Nursing staff utilizes a sizing chart to correlate patient's foot size with PUP™ Sock size.
  - Sock is placed on patient
- Enroll Sock in Application
  - Once sock is successfully fitted on patient the nurse proceeds to enroll the patient through Palarum Application.
  - The following categories must be completed before proceeding to a successful enrollment: Patient Name/Initials/MRN, Sex, Weight, Sock Size, and Sensor.
  - Upon successful sock paring to IRT the enrollment process is completed, and the patient is now being monitored.

9.3 Day 1 through length of stay

- **S**ystem will electronically monitor patient compliance
- Report Generation
  - Each morning at 12am a report is generated detailing the previous day's activity on the system.
  - Two separate reports are sent each morning at 12am (filtered by audience): Nurse Manager, Site Executive.
  - The reports show: the Pod the patient is enrolled in, # of Alerts during their length of stay, whether a patient has alerted 3 or more times in less than 24 hours
- Alert Generation
  - An alert is generated when a patient places their foot on the ground and takes a step.
  - False alerts are prevented through the use of a gyroscope and accelerometer.
  - Once an alert is generated it is sent to the IRT, HUC, and Smart Notification Devices.
- How to respond to Alerts
  - There are two ways to respond to an alert with Palarum's Fall Prevention System

  - Nurse proceeds into the room (wearing Palarum Smart Notification Device) and the system automatically turns off due to his/her proximity.
  - Nurse proceeds into the room and manually turns off the system on the IRT by touching the red alert icon on the screen and then entering their initials.
- Documentation of exceptions.
- Record any Adverse Experiences and/or Review subject diary for adverse experiences and compliance.
- Perform clinical examination of foot and ankle.

9.4 Discharge

- Upon discharge from the hospital, the nurse will log patient out of the Palarum PUP™ System. The PUP™ socks will be placed in the Palarum laundry receptacles located on each hospital floor.

10 ADVERSE EXPERIENCE REPORTING AND DOCUMENTATION

10.1 Adverse Events

An Adverse Event has to meet three basic criteria to be reportable; an AE has occurred, the device is associated with the AE and the AE led to 1 of 4 outcomes: decline in state of health of patient, threat to public health, could lead to death or serious injury if it occurs.

The Investigator will probe, via discussion with the subject, for the occurrence of AEs during each subject visit and record the information in the site's source documents. Adverse events will be recorded in the patient CRF. Adverse events will be described by duration (start and stop dates and times), severity, outcome, treatment and relation to study, or if unrelated, the cause.

10.2 Serious Adverse Experience Reporting

Study sites will document all SAEs that occur (whether or not related to study protocol) per UCSF CHR Guidelines. The collection period for all SAEs will begin after informed consent is obtained and end after procedures for the final study visit has been completed.

In accordance with the standard operating procedures and policies of the local Institutional Review Board (IRB)/Independent Ethics Committee (IEC), and OSU's CH Guidelines, the site investigator will report SAEs to the IRB/IEC.

10.3 Medical Monitoring

Medical monitoring will be provided by the research team. If further medical assistance is determined necessary, then medical assistance will occur through standard of care per OSU Brain and Spine Hospital standard operating processing.

11 DISCONTINUATION AND REPLACEMENT OF SUBJECTS

11.1 Early Discontinuation of Study

A subject may be discontinued from study treatment at any time if the subject, the LAR, the investigator, or the Sponsor feels that it is not in the subject's best interest to continue. The following is a list of possible reasons for study treatment discontinuation.

- Subject or LAR withdrawal of consent
- Subject is not compliant with study procedures including but not limited to intermittent wearing of the sock, refusal after enrollment to wear the socks, or repeatedly engaging in activity which defeats the integrity of the electronic circuitry of the sock.
- Adverse event that in the opinion of the investigator would be in the best interest of the subject to discontinue study treatment
- Protocol violation requiring discontinuation of study treatment
- Sponsor request for early termination of study
- All subjects are free to withdraw from participation at any time, for any reason, specified or unspecified, and without prejudice.
- Reasonable attempts will be made by the investigator to provide a reason for subject withdrawals. The reason for the subject's withdrawal from the study will be specified in the subject's source documents. Refer to Section 10 for early termination procedures.

11.2 Withdrawal of Subjects from the Study

- A subject may be withdrawn from the study at any time if the subject, the investigator, or the Sponsor feels that it is not in the subject's best interest to continue.
- All subjects are free to withdraw from participation at any time, for any reason, specified or unspecified, and without prejudice.
- Reasonable attempts will be made by the investigator to provide a reason for subject withdrawals.
    - The reason for the subject's withdrawal from the study will be specified in the subject's source documents.
    - As noted above, subjects who discontinue study treatment early should have an early discontinuation visit. Refer to Section 10 for early termination procedures.

12 PROTOCOL VIOLATIONS

- A protocol violation occurs when the subject or investigator fails to adhere to significant protocol requirements affecting the inclusion, exclusion, subject safety and

primary endpoint criteria. Protocol violations for this study include, but are not limited to, the following:

- Failure to meet inclusion/exclusion criteria
- Failure to comply with Good Clinical Practice (GCP) guidelines will also result in a protocol violation. The Sponsor will determine if a protocol violation will result in withdrawal of a subject.
- When a protocol violation occurs, it will be discussed with the investigator and a Protocol Violation Form detailing the violation will be generated. This form will be signed by a Sponsor representative and the Investigator. A copy of the form will be filed in the site's regulatory binder and in the Sponsor's files.

13 STATISTICAL METHODS AND CONSIDERATIONS

Prior to the analysis of the final study data, a detailed Statistical Analysis Plan (SAP) will be written describing all analyses that will be performed. The SAP will contain any modifications to the analysis plan described below.

13.1 Demographic and Baseline Characteristics

Demographic and baseline characteristics will be summarized using appropriate descriptive statistics including the mean and standard deviation for continuous values and counts and proportions for discrete variables.

13.2 Analysis of Primary Endpoint

The primary endpoint for this study is the number of patient falls. This will be expressed as a rate per patient days where patient days are counted from the initiations of the PUP™ System until discharge or removal from the fall risk protocol. Using a one-sided one-sample test for Poisson means, we will test whether the observed fall rate is less than the historical rate of 0.004. This test will be conducted at the alpha=0.1 level. Results will be presented as the fall rate and the corresponding one-sided 90% confidence interval which will provide an upper bound for the fall rate.

13.3 Analysis of Secondary Endpoints

Secondary outcomes include estimating the incidence of false alerts, the rate of alerts sent out per patient days, characteristics of the patient safety events, and time to response. The analyses of the secondary endpoints will be descriptive and exploratory with the goal of further characterizing the properties of the PUP™ System. Rates and means will be calculated as appropriate. Confidence intervals will be computed to accompany each estimate. No formal statistical testing will be conducted.

We will also examine how fall rates may be associated with patient characteristics. We may also explore data related to the activity level of fall risk patients that are collected by the PUP™ System. These descriptive analyses could help to further characterize the fall risk patient population.

13.4 Sample Size

The primary endpoint of the trial is the patient fall rate per patient days. Comparing to a historical rate of 0.004 using a one-sided test of Poisson means, we have at least 70% power to detect a 25% reduction in the fall rate at alpha level 0.1 with 2360. Assuming a dropout rate of 5%, we will enroll 2500 patients into the study.

14 DATA COLLECTION, RETENTION AND MONITORING

14.1 Data Collection Instruments

The Investigator will prepare and maintain adequate and accurate source documents designed to record all observations and other pertinent data for each subject treated with the study drug.

Study personnel at each site will enter data from source documents corresponding to a subject's visit into the protocol-specific electronic Case Report Form (eCRF) OR paper CRF when the information corresponding to that visit is available. Subjects will not be identified by name in the study database or on any study documents to be collected by the Sponsor (or designee) but will be identified by a site number, subject number, and initials.

If a correction is required for an eCRF, the time and date stamps track the person entering or updating eCRF data and create an electronic audit trail.

The Investigator is responsible for all information collected on subjects enrolled in this study. All data collected during the course of this study must be reviewed and verified for completeness and accuracy by the Investigator. A copy of the CRF will remain at the Investigator's site at the completion of the study.

14.2 Data Management Procedures

The data will be entered into a validated database. The Data Management group will be responsible for data processing, in accordance with procedural documentation. Database lock will occur once quality assurance procedures have been completed.

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.

14.3 Data Quality Control and Reporting

After data have been entered into the study database, a system of computerized data validation checks will be implemented and applied to the database on a regular basis. Queries are entered, tracked, and resolved through the EDC system directly. The study database will be updated in accordance with the resolved queries. All changes to the study database will be documented.

14.4 Archival of Data

The database is safeguarded against unauthorized access by established security procedures; appropriate backup copies of the database and related software files will be

maintained. Databases are backed up by the database administrator in conjunction with any updates or changes to the database.

At critical junctures of the protocol (e.g., production of interim reports and final reports), data for analysis is locked and cleaned per established procedures.

14.5 Availability and Retention of Investigational Records

The Investigator must make study data accessible to the monitor, other authorized representatives of the Sponsor (or designee), IRB/IEC, and Regulatory Agency (e.g., FDA) inspectors upon request. A file for each subject must be maintained that includes the signed Informed Consent/HIPAA Authorization Form and copies of all source documentation related to that subject. The Investigator must ensure the reliability and availability of source documents from which the information on the CRF was derived.

All study documents (patient files, signed informed consent forms, copies of CRFs, Study File Notebook, etc.) must be kept secure for a period of two years following marketing of the investigational product or for two years after centers have been notified that the IND has been discontinued. There may be other circumstances for which the Sponsor is required to maintain study records and, therefore, the Sponsor should be contacted prior to removing study records for any reason.

14.6 Monitoring

Monitoring visits will be conducted by representatives of the Sponsor according to the U.S. CFR Title 21 Parts 50, 56, and 312 and ICH Guidelines for GCP (E6). By signing this protocol, the Investigator grants permission to the Sponsor (or designee), and appropriate regulatory authorities to conduct on-site monitoring and/or auditing of all appropriate study documentation.

14.7 Subject Confidentiality

In order to maintain subject confidentiality, only a site number, subject number, and subject initials will identify all study subjects on CRFs and other documentation submitted to the Sponsor. Additional subject confidentiality issues (if applicable) are covered in the Clinical Study Agreement.

15 ADMINISTRATIVE, ETHICAL, REGULATORY CONSIDERATIONS

The study will be conducted according to the Declaration of Helsinki, Protection of Human Volunteers (21 CFR 50), Institutional Review Boards (21 CFR 56), and Obligations of Clinical Investigators (21 CFR 312).

To maintain confidentiality, all laboratory specimens, evaluation forms, reports and other records will be identified by a coded number and initials only. All study records will be kept in a locked file cabinet and code sheets linking a patient's name to a patient identification number will be stored separately in another locked file cabinet. Clinical information will not be released without written permission of the subject, except as necessary for monitoring by the FDA. The Investigator must also comply with all applicable privacy regulations (e.g., Health Insurance Portability and Accountability Act of 1996, EU Data Protection Directive 95/46/EC).

15.1 Protocol Amendments

Protocol amendments cannot be implemented without prior written IRB/IEC approval except as necessary to eliminate immediate safety hazards to patients. A protocol amendment intended to eliminate an apparent immediate hazard to patients may be implemented immediately, provided the IRBs are notified within five working days.

15.2 Institutional Review Boards and Independent Ethics Committees

The protocol and consent form will be reviewed and approved by the IRB/IEC of each participating center prior to study initiation. Serious adverse experiences regardless of causality will be reported to the IRB/IEC in accordance with the standard operating procedures and policies of the IRB/IEC, and the Investigator will keep the IRB/IEC informed as to the progress of the study. The Investigator will obtain assurance of IRB/IEC compliance with regulations.

Any documents that the IRB/IEC may need to fulfill its responsibilities (such as protocol, protocol amendments, Investigator's Brochure, consent forms, information concerning patient recruitment, payment or compensation procedures, or other pertinent information) will be submitted to the IRB/IEC. The IRB/IECs written unconditional approval of the study protocol and the informed consent form will be in the possession of the Investigator before the study is initiated. The IRB/IECs unconditional approval statement will be transmitted by the Investigator to the Sponsor or designee prior to the shipment of study supplies to the site. This approval must refer to the study by exact protocol title and number and should identify the documents reviewed and the date of review.

Protocol and/or informed consent modifications or changes may not be initiated without prior written IRB/IEC approval except when necessary to eliminate immediate hazards to the patients or when the change(s) involves only logistical or administrative aspects of the study. Such modifications will be submitted to the IRB/IEC and written verification that the modification was submitted and subsequently approved should be obtained.

The IRB/IEC must be informed of revisions to other documents originally submitted for review; serious and/or unexpected adverse experiences occurring during the study in accordance with the standard operating procedures and policies of the IRB; new information that may affect adversely the safety of the patients of the conduct of the study; an annual update and/or request for re-approval; and when the study has been completed.

15.3 Informed Consent Form

Informed consent will be obtained in accordance with the Declaration of Helsinki, ICH GCP, US Code of Federal Regulations for Protection of Human Subjects (21 CFR 50.25[a,b], CFR 50.27, and CFR Part 56, Subpart A), the Health Insurance Portability and Accountability Act (HIPAA, if applicable), and local regulations.

The Investigator will prepare a combined informed consent form and HIPAA authorization, and provide the document to the Sponsor or designee for approval prior to submission to the IRB/IEC. The consent form generated by the Investigator must be acceptable to the Sponsor and be approved by the IRB/IEC. The written consent document will embody the elements of informed consent as described in the International Conference on Harmonization and will also comply with local regulations. The

Investigator will send an IRB/IEC-approved copy of the Informed Consent Form to the Sponsor (or designee) for the study file.

A properly executed, written, informed consent will be obtained from each subject and/or LAR prior to entering the subject into the trial. Information should be given in both oral and written form and subjects must be given ample opportunity to inquire about details of the study. A copy of the signed consent form will be given to the subject and the original will be maintained with the subject's records.

15.4 Publications

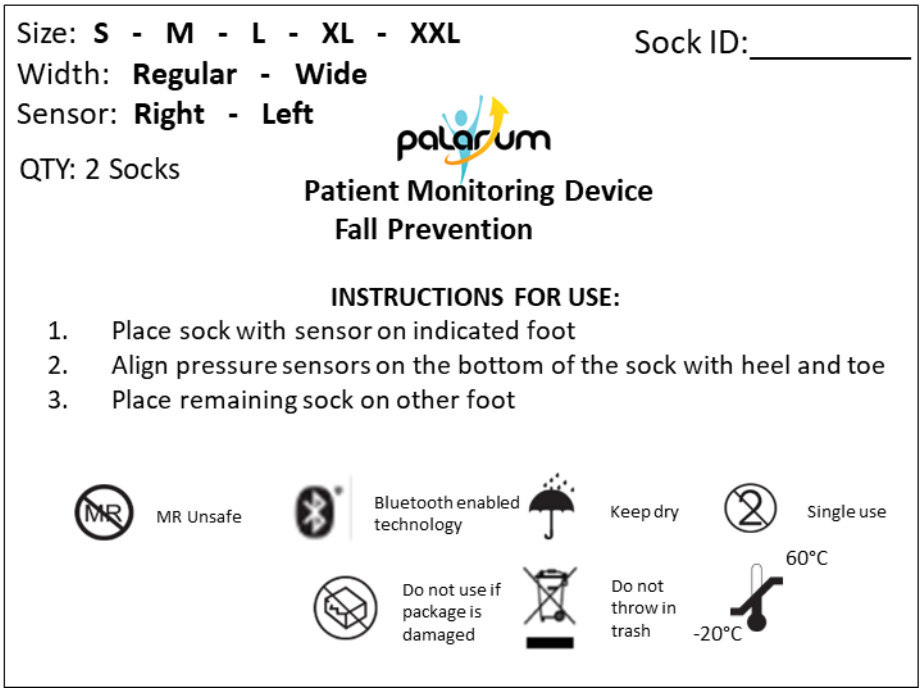
The preparation and submittal for publication of manuscripts containing the study results shall be in accordance with a process determined by mutual written agreement among the study Sponsor and participating institutions. The publication or presentation of any study results shall comply with all applicable privacy laws, including, but not limited to, the Health Insurance Portability and Accountability Act of 1996.

15.5 Investigator Responsibilities

By signing the Agreement of Investigator form, the Investigator agrees to:

1. Conduct the study in accordance with the protocol and only make changes after notifying the Sponsor (or designee), except when to protect the safety, rights or welfare of subjects.
2. Personally, conduct or supervise the study (or investigation).
3. Ensure that the requirements relating to obtaining informed consent and IRB review and approval meet federal guidelines, as stated in § 21 CFR, parts 50 and 56.
4. Report to the Sponsor or designee any AEs that occur in the course of the study, in accordance with §21 CFR 312.64.
5. Ensure that all associates, colleagues and employees assisting in the conduct of the study are informed about their obligations in meeting the above commitments.
6. Maintain adequate and accurate records in accordance with §21 CFR 312.62 and to make those records available for inspection with the Sponsor (or designee).
7. Ensure that an IRB that complies with the requirements of §21 CFR part 56 will be responsible for initial and continuing review and approval of the clinical study.
8. Promptly report to the IRB and the Sponsor (or designee) all changes in the research activity and all unanticipated problems involving risks to subjects or others (to include amendments and IND safety reports).
9. Seek IRB approval before any changes are made in the research study, except when necessary to eliminate hazards to the patients/subjects.
10. Comply with all other requirements regarding the obligations of clinical investigators and all other pertinent requirements listed in § 21 CFR part 312.

APPENDIX A –PUP™ SOCK LABEL



APPENDIX B - SCHEDULE OF STUDY VISITS

	DAY 1 ADMISSION (Day/Week/Month #)[a]	VISITS ON DAY 1 & EVERY DAY THROUGH LENGTH OF STAY	VISIT ON PATIENT EARLY WITHDRAWAL	VISIT ON PATIENT DISCHARGE
Informed Consent	**X**			
Medical History	**X**			
Complete Physical Exam	**X**			
Abbreviated Physical Exam		**X**	**X**	**X**
Weight	**X**	**X**	**X**	**X**
Administration of PUP™ Fall Prevention System	**X**			
Counting of Returned PUP™ socks		**X**	**X**	**X**
Initiate Subject Diary	**X**			
Subject Diary Review		**X**		**X**
Adverse Experiences		**X**	**X**	

[a] ±2 days

APPENDIX C - PUP (PATIENT IS UP) SYSTEM
CASE REPORT FORM – OHIO STATE UNIVERSITY

PARTICIPANT INFORMATION		
Participant ID		
Inclusion/exclusion criteria *Patient must meet all fall risk criteria to be eligible for the study	Met all ☐	Not met* ☐
Date of Informed IRB Consent		
Gender	☐ Male ☐ Female	
Date of Enrollment into Fall Prevention System		

EARLY DISCONTINUATION OF STUDY	
Date of discontinuation from study	
Reason for discontinuation	☐ Subject withdrawal ☐ Subject not compliant ☐ Intermittent wearing of the sock ☐ Refusal after enrollment to wear the sock ☐ Repeatedly engaging in activity which defeats the integrity of the electronic circuitry of the sock ☐ Sponsor request for early termination of study ☐ Protocol Violation:_____ _____

FINAL STUDY OUTCOME

Investigator's Statement: I have reviewed the data recorded in this CRF and confirm that the data are complete and accurate

Investigator (Full name): _____

Investigator Signed? ☐ **Signature Date:_____**