

Cover Page

Milky Way Sensor: Device Validation for Non-Infiltrated Tissues

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ClinicalTrials.gov NCT number: NCT07228416

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Clinical Investigational Plan

Milky Way Sensor: Device Validation for Non-Infiltrated Tissues

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Version Date: September 15, 2025

Table of Contents

General Information	5
Identification of the Clinical Investigation Plan	5
Sponsor	5
Manufacturer of Investigational Device	5
Investigators and Investigation Site(s)	6
External Organizations	7
Synopsis of Clinical Investigation.....	7
Investigational Device Information	9
Technical and Functional Features of the Device	14
Clinical Investigation Design Justification	16
Stage of Clinical Investigation	16
Benefit and Risk Analysis of the Investigational Device, Clinical Procedure, and Clinical Investigation	18
Critical to Quality Factors.....	19
Study Purpose and Objectives	20
Study Design	21
General Information	21
Investigational Device(s) and Comparator(s)	22
Subjects.....	22
Procedures	24
Data Monitoring Plan	27
Site Team Roles and Responsibilities.....	29
Statistical Design and Data Analysis	30
Data Management	32
Deviations from the Clinical Investigation Plan	33
Device Accountability	34
Statements of Compliance and Regulations	34
Informed Consent Process	35
Adverse Events, Adverse Device Effects, and Device Deficiencies	35
Vulnerable Population	36
Suspension, Premature Termination, or End of Clinical Investigation	36

Publication Policy.....	36
Investigator Signatures	38
Bibliography	39
Appendix A - Clinical studies performed with the Fiber Optic Sensor	40
Appendix B - Clinical studies performed with SmartTouch Sensor	44
Appendix C – Electronic Case Report Form (eCRF)	50
Appendix D – Pre-Screening Form.....	58
Appendix E – Electronic Health History Form (eHHF)	64
Appendix F – Participant Activity Log.....	66
Appendix G – FDA Class Determination & Clearance Letters	67
Appendix H – Amendments.....	81
Proposed Amended Section	81
Amendment Description	81
Justification.....	81
Impact changes have on performance, effectiveness, safety, endpoints, and identification of affected documents.....	81
Updates to CRFs due to Amendment.....	81
Amendment Version Number and Date	81
Amendment Approval	81
Appendix I – Statistical Monte Carlo Analysis.....	82

Figures

Figure 1. ivWatch Model 400 Infiltration Monitoring System with Fiber Optic Sensor Cable	10
Figure 2. ivWatch Model 400 with Extension Module and SmartTouch Sensor.....	11
Figure 3. Milky Way Sensor Exploded View of Components	12
Figure 4. (Left) Milky Way Sensor Affixed Label, ML-1002119; (Right) Milky Way Sensor Pouch Label, ML-1002120	13
Figure 5. (Left) Model 400 S/N Label, ML-0000337; (Right) Model 400 Shipper Box Label, ML-1001000	13
Figure 6. (Left) Extension Module S/N Label, ML-1001018; (Right) Extension Module Shipper Box Label, ML-1001040	14
Figure 7. Investigational Device Label, ML-1000019	14
Figure 8. Effects of scattering (a) and absorption (b) of photons on the reflected energy on the surface	15
Figure 9. Schematic Diagram of the Clinical Investigation.	21
Figure 10. Statistical power analysis (left) and Monte Carlo simulation results from n=20 research subjects (right).	31

Tables

Table 1. Investigator Information	6
Table 2. MDCG 2024-3 Appendix A: Clinical Investigation Plan Synopsis	8
Table 3. Milky Way sensor algorithm development studies	18
Table 4. Anticipated Events.....	18
Table 5. List of study inclusion criteria.....	23
Table 6. List of study exclusion criteria.	23
Table 7. Medical equipment required for each case.....	25
Table 8. Example study timeline.....	26
Table 9. Site team roles and responsibilities	29

Note: The following terms may be used terms synonymously, as they may differ by the ISO 14155 and ICH E6 standards.

- Protocol and plan
- Clinical study, clinical investigation, and clinical trial
- Subject and participant
- Essential documents and essential records

General Information

Identification of the Clinical Investigation Plan

Clinical Investigation Plan (CIP) Title:

Milky Way Sensor: Device Validation for Non-Infiltrated Tissues

CIP Reference Number:

IVW-CLR-CS37-400 / Pro00089955

CIP Version and/or Date:

Rev. 02 – September 15, 2025

Summary of Revision History, if applicable:

Revision – Version Date	Details	Author
Rev. 01 – 09/15/2025	Initial Release	Marisa Brown
Rev. 02 – 09/15/2025	Added inadvertently missing header	Marisa Brown

Abbreviations and Acronyms:

BMI – Body Mass Index

IFU – Instructions for Use

IPM – ivWatch Patient Monitor

IRB – Institutional Review Board

IV – Intravenous

NIR – Near Infrared

PIV – Peripheral Intravenous

Sponsor

Name and Address:

ivWatch, LLC

700 Tech Center Parkway, Suite 300

Newport News, VA 23606

Funding Source:

ivWatch, LLC will cover all expenses related to this clinical investigation.

Investigator's Brochure Reference Number:

DR-1002145, Rev. 01

Manufacturer of Investigational Device

Name, address, and contact details:

ivWatch, LLC

700 Tech Center Parkway, Suite 300
Newport News, VA 23606

(855) 489-2824

Investigators and Investigation Site(s)

Principal Investigator – Jason Naramore, Chief Technology Officer, ivWatch

Investigator – Marisa Brown, Senior Biomedical Engineer, ivWatch

All investigators have the following address and contact information:

ivWatch, LLC – Headquarters
700 Tech Center Parkway, Suite 300
Newport News, VA 23606

(855) 489-2824

Investigation Site(s):

ivWatch – City Center
709 City Center Parkway, B-112
Newport News, VA 23606

(855) 489-2824

Roles, Responsibilities, Qualifications of investigators:

Table 1. Investigator Information

Role	Responsibilities / Authorizations	Qualifications
Principal Investigator (PI)	Ensures compliance with the regulations and protocol, and protects the rights, safety, and well-being of all subjects. May sign and make corrections to CRFs, following Good Documentation Practices (GDP), when needed and can accept or reject data. Authority over entire clinical trial. May act as other roles in the clinical study. Authorized to sign the protocol and amendments for the sponsor. May alter device accountability records.	- Bachelor of Science from the University of Virginia. - Chief Technology Officer. - Over 19 years of experience in research and development and clinical studies. A Principal Investigator on 12 studies and Investigator on 14 studies with ivWatch products and technology. - All studies, except one, described above have been conducted on healthy adult volunteers, which is the same subject population for this clinical study. - The Investigator has executed a similar protocol at ivWatch, where no adverse events or other issues that would threaten the life or wellbeing of the subject occurred.

Investigator	Assists the PI with managing the day-to-day conduct of the clinical trial. May sign and make corrections to CRFs, following GDP, when needed and can accept or reject data. May act as other roles in the clinical study. Authorized to sign the protocol and amendments for the sponsor. May alter device accountability records.	• Bachelor of Science from Virginia Polytechnic Institute and State University. • Association of Clinical Research Professionals – Certified Professional (ACRP-CP) since October 2021 • Eight years of experience in medical device research and development and clinical studies. A Principal Investigator on 7 studies and Investigator on 10 studies with ivWatch products and technology. • All studies, except one, the Investigator has worked with have been conducted on healthy adult volunteers, which is the same participant population for this clinical study. • The Investigator has executed a similar protocol at ivWatch, where no adverse events or other issues that would threaten the life or wellbeing of the subject occurred.
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Sponsor's Medical Expert:

Brian Clare, MD
Emergency Medicine Physician
700 Tech Center Parkway, Suite 300
Newport News, VA 23606

**Qualified Physician (if other than Investigator) for all trial-site related medical decisions:**

Brian Clare, MD
Emergency Medicine Physician
700 Tech Center Parkway, Suite 300
Newport News, VA 23606

**External Organizations**

Advarra IRB
6100 Merriweather Dr., Suite 600
Columbia, MD 21044
410.884.2900

Synopsis of Clinical Investigation

This is a randomized one-center trial of approximately 20 healthy adult volunteers to validate the performance of the ivWatch Milky Way Sensor on healthy human tissue. Inclusion and exclusion criteria are listed in Table 5 and Table 6, respectively. The entire study is expected to take less than one month to complete, with each subject's participation totaling approximately 24 hours. There is no anticipated need for follow-up. The primary endpoint is the rate of non-infiltration yellow and red notifications for the Milky Way Sensor. The secondary (safety) endpoint is the occurrence of skin irritation and/or allergic reaction at the Milky Way Sensor monitoring site, as assessed by the investigator during the study period.

Table 2. MDCG 2024-3 Appendix A: Clinical Investigation Plan Synopsis

Clinical Investigation Synopsis	
Title	Milky Way Sensor: Device Validation for Non-Infiltrated Tissues
Short title	N/A
Lay title, if applicable	Milky Way Motion Study Validation
CIP number, version, and date	IVW-CLR-CS37-400 / Pro00089955 Rev. 02 – September 15, 2025
EUDAMED Single Reference Number (SRN) or CIV-ID, if previously assigned	Study is only being conducted in USA, US-MF-000001531
CI modification number, if applicable	N/A
Sponsor name and address	ivWatch, LLC 700 Tech Center Parkway, Suite 300 Newport News, VA 23606
Participating Location(s) and country(ies)	ivWatch – City Center 709 City Center Boulevard, B-112 Newport News, VA 23606, USA
Name of Investigational Device	ivWatch Milky Way Sensor
Clinical investigation Purpose and Background - Rationale for CI - Background of device and condition - Current standard of care	Study Purpose and Objectives, and Investigational Device Information
Name of Comparator, if applicable	N/A
Clinical development stage	Validation – Confirmatory (Stage of Clinical Investigation)
Design of the clinical investigation	Study Design
Objectives	Study Purpose and Objectives
Primary endpoints	The rate of non-infiltration yellow and red notifications for the Milky Way Sensor.
Secondary endpoint	Occurrence of skin irritation and/or allergic reaction at the Milky Way Sensor monitoring site, as assessed by the investigator during the study period.
Safety endpoints /safety parameters	See secondary endpoint, above.
Exploratory / Other endpoints and outcomes	N/A
Description of participants / study population	Healthy adult volunteers (Subjects)
Inclusion criteria	Table 5. List of study inclusion criteria.
Exclusion criteria	Table 6. List of study exclusion criteria.
Sample size	A sample size of 20 accepted cases (Statistical Design and Data Analysis)
Duration and follow up of the clinical investigation	The entire study is expected to take less than one month to complete, with each subject's participation being approximately 24 hours. There is no expected follow up in this investigation.
Statistical considerations	Statistical Design and Data Analysis

Investigational Device Information

ivWatch, LLC, a medical device company located in Newport News, VA, has developed the ivWatch Model 400 – a Class II medical device that is FDA cleared and CE Marked for use on adults and pediatrics. The ivWatch Model 400 is indicated for the detection of subcutaneous infiltrations and extravasations of 10 cc or less of optically clear and iron* infusates, as an adjunctive device to the clinical evaluation in the healthcare setting of adults and pediatrics with PIVs.

*Note: Some markets specify iron sucrose infusates.

The ivWatch Model 400 Monitor (IPM) is already in the market with two sensor options:

1. Fiber Optic Sensor Cable, and
2. SmartTouch Sensor.

This protocol validates expansion to a third sensor option:

3. Milky Way Sensor (investigational device).

Figure 1 illustrates the Fiber Optic Sensor Cable applied to a PIV site. The sensor delivers visible and near-infrared light to the tissue and transmits reflected light back to the IPM. The IPM contains an optical system that generates light signals that are sent to the patient's skin (via the Fiber Optic Sensor Cable) and measures the light returning from the patient's skin (also via the Fiber Optic Sensor Cable). The sensor head of the Fiber Optic Sensor Cable is held in place and attached to the patient using the Sensor Receptacle. The IPM also contains the hardware for executing the proprietary ivWatch signal processing algorithm, and for displaying system status on a user interface, including audible and visual notifications indicating changes to the state of the PIV. When changes in the diffuse reflectance in the tissue near the peripheral IV insertion site are consistent with an infusate pooling in the subcutaneous tissue, the IPM emits audible and visual notifications intended to prompt the clinician to inspect the peripheral IV site for a possible infiltration event. Prompt identification of infiltrations reduces the risk of injury or severity of injury to patients undergoing peripheral IV therapy and improves the likelihood of receiving the correct dosage of medications delivered intravenously.

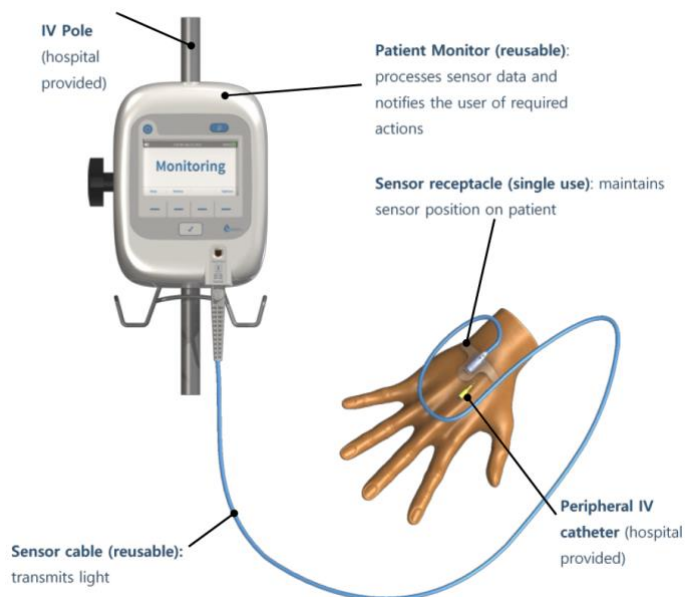


Figure 1. ivWatch Model 400 Infiltration Monitoring System with Fiber Optic Sensor Cable

The ivWatch Model 400 system was expanded in 2020 to support both the Fiber Optic Sensor Cable configuration and the SmartTouch electronic sensor cable configuration. The SmartTouch Sensor consists of low-cost optical components built into the sensor head, like disposable pulse oximeter sensors. This design allows the SmartTouch Sensor to be a more cost effective single-use sensor, as opposed to the costlier reusable fiber optic sensor. A Patient Cable and an Extension Module compatible with the existing ivWatch Model 400 were developed to support an electronic sensor cable configuration, (Figure 2). The Extension Module is connected to the IPM via USB and runs the SmartTouch Sensor algorithm. The SmartTouch Sensor was designed to be an electronic version of the Fiber Optic Sensor Cable configuration. The SmartTouch Sensor is placed on the skin of a patient near the PIV site, following the same protocol as the Fiber Optic Sensor Cable, and the same indications for use apply.



Figure 2. ivWatch Model 400 with Extension Module and SmartTouch Sensor

The Milky Way Sensor is considered an advanced version of the SmartTouch Sensor, capable of detecting infusates with lipids, in addition to the same infusates as SmartTouch. Lipid detection is done with a 3-wavelength LED system, where the Fiber Optic and SmartTouch sensors have 2-wavelength LED systems. The Milky Way Sensor has the same format and components as the SmartTouch Sensor (adhesive stack, cable, connector), except its flex PCB and plastic optical covers (seen in Figure 3). The Milky Way flex PCB contains a 3-wavelength LED and some necessary chips for driving the LEDs. The plastic optical covers are the same materials as those used in SmartTouch, but slightly modified in shape to fit the Milky Way LEDs. The skin-contacting adhesive is the same as that used on the SmartTouch Sensor. This is an acrylic-based adhesive which has been tested to the appropriate ISO 10993 biocompatibility standards.

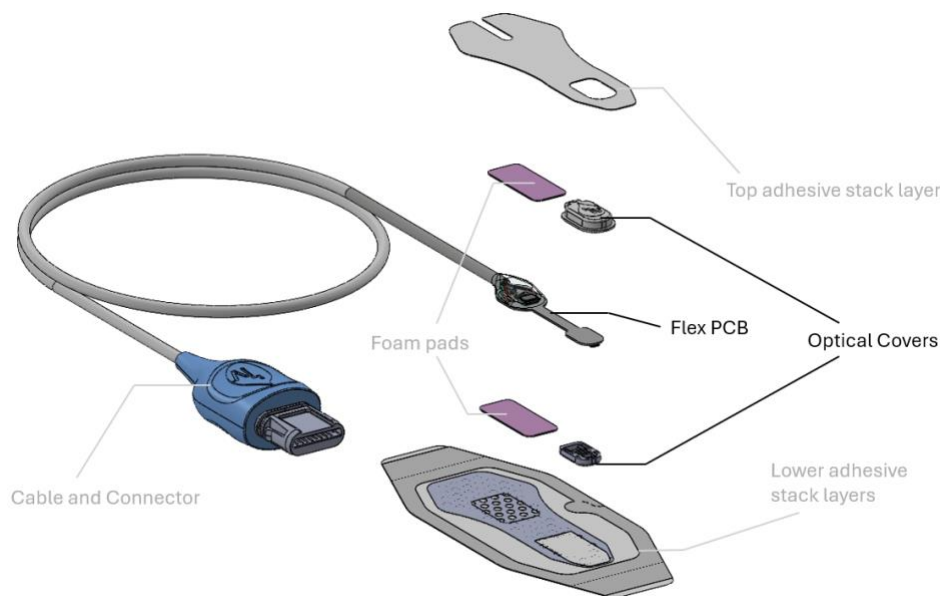


Figure 3. Milky Way Sensor Exploded View of Components

The Milky Way Sensor's intended purpose in this investigation is to gather normal tissue signals on healthy adult skin (>18 years) over a period of approximately 24-hours. The data gathered in this investigation will be used to calculate the non-infiltration notification rate of the Milky Way sensor.

Signal data will be collected from the Milky Way Sensor with the ivWatch Patient Monitor, Extension Module, and Patient cable mounted to an IV pole. Exactly like the SmartTouch Sensor, the Milky Way Sensor is plugged into the blue connector on the Patient Cable. The Patient Monitor/Extension Module will be running production-equivalent software including the Milky Way infiltration detection algorithm, which issues Check IV notifications. The signal data and device state (i.e. Check IV notification) are saved locally on the Patient Monitor, and can be downloaded through the USB port on the front of the Extension Module. For the purposes of this study, the investigational device system is defined as the investigational sensor (primary investigational device) plus the Patient Monitor/Extension Module (both FDA-cleared) running the following software versions, which are required to operate the sensor:

- Software version – 6.#.#;
- GUI version – 3.#.#;
- Extension Module version – 2.#.#.

Please note that the exact versions will be identified in the service records for the Patient Monitor/Extension Modules that are used in this clinical investigation.

The case report form (Appendix C – Electronic Case Report Form) and the Investigational Device Accountability Log (REC-0000220) will be used to trace devices during and after this clinical investigation. The software versions viewable on the System Information IPM screen will be the following:

Software version – 6.#.#; GUI version – 3.#.#; Extension Module version – 2.#.#

Based on the risk assessment for the investigational device, users will need to train on removal methods of the investigational device, which are described in the device's user manual, QL-1002011. Users should also receive a classroom training that includes how to start a monitoring run and conduct troubleshooting in the case of notifications.

There are no specific medical or surgical procedures involved in the use of the investigational device. Below are samples of labelling and packaging for the investigational system. The Milky Way Sensor is the primary investigational device while the Model 400 Patient Monitor and Extension Module have new software necessary to operate the sensor.

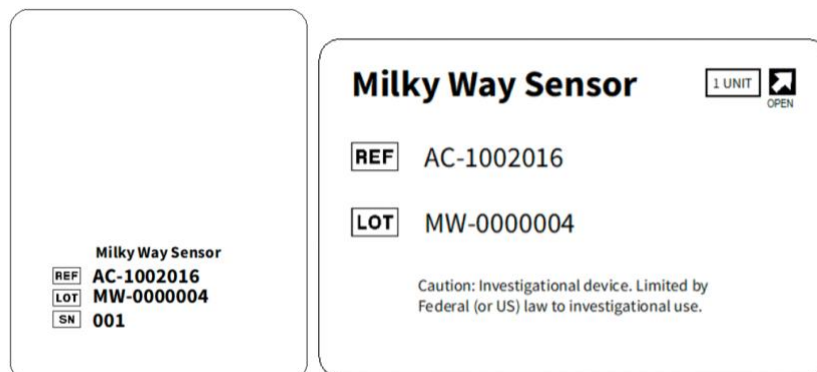


Figure 4. (Left) Milky Way Sensor Affixed Label, ML-1002119; (Right) Milky Way Sensor Pouch Label, ML-1002120

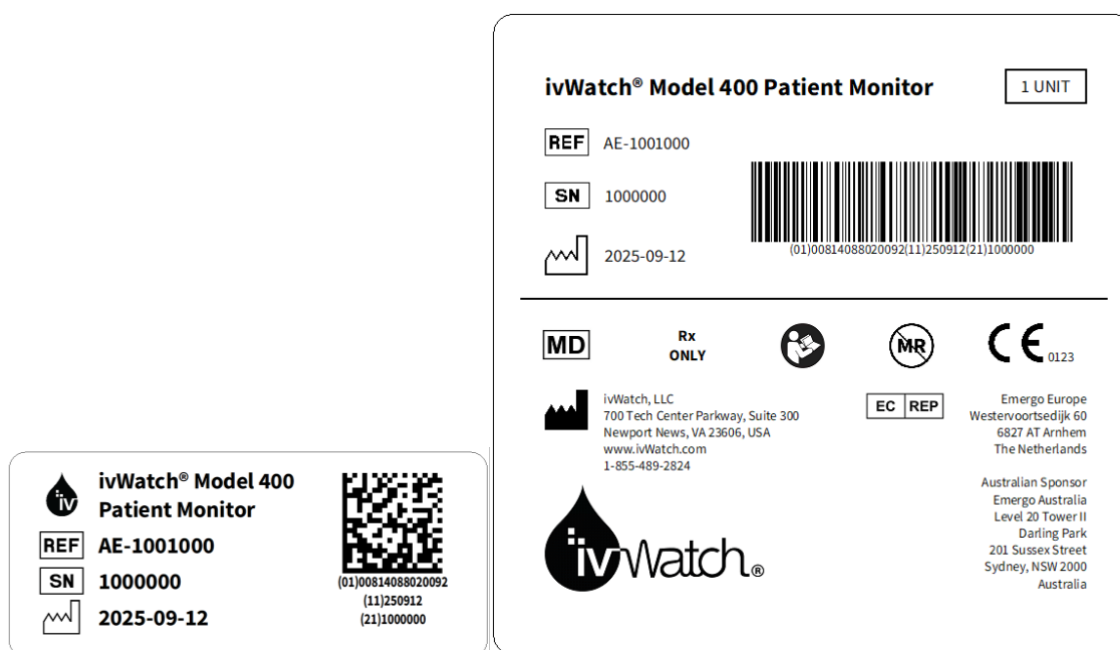


Figure 5. (Left) Model 400 S/N Label, ML-0000337; (Right) Model 400 Shipper Box Label, ML-1001000

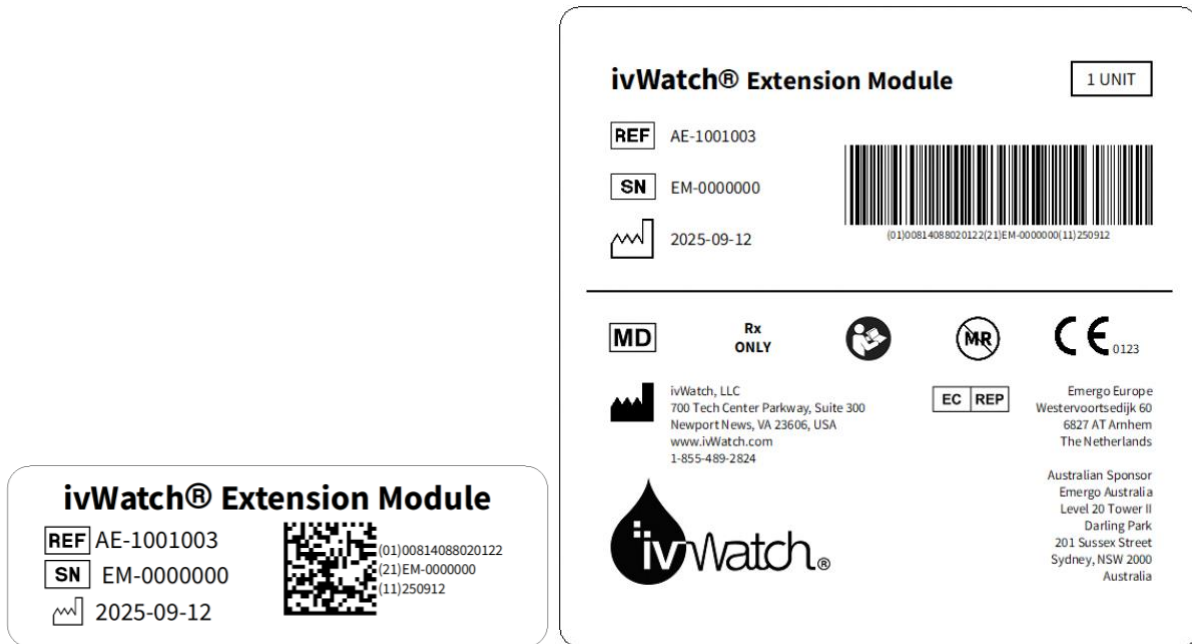


Figure 6. (Left) Extension Module S/N Label, ML-1001018; (Right) Extension Module Shipper Box Label, ML-1001040

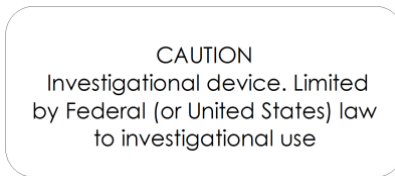


Figure 7. Investigational Device Label, ML-1000019

The Investigator's Brochure, DR-1002145 can be accessed through ivWatch's Quality Management System. There are two useful Instructions for Use in this study. The Milky Way Sensor's (investigational device) instructions for use are in QL-1002011, while the Model 400 system's instructions for use are in QL-1002009. These can both be accessed through ivWatch's Quality Management System.

Technical and Functional Features of the Device

The Milky Way, SmartTouch, and Fiber Optic sensors all operate based on the same mechanism. They are sensors placed on the skin that emit visible and near-infrared light to measure changes in the optical properties of the tissue near a PIV insertion site.

Diffuse reflectance corresponds to the light that propagates through the tissue and is emitted at the tissue surface. The amount of light detected by any given sensor depends primarily on the scattering and absorption properties of the monitored tissue. Scattering occurs when a photon is redirected due to an interaction with some structure in the tissue. Scattering structures in the tissue can include cells (e.g. blood cells, keratinocytes), fibers (e.g. collagen and elastin fibers), and cellular components (e.g. mitochondria, nuclei). The degree of scattering in tissue is characterized by a reduced scattering coefficient, which describes the probability of a photon scattering for a given propagation distance within the tissue. When there are more scattering structures in the tissue, more energy

will be reflected from the surface and if there are fewer scattering structures in the tissue, less energy will be reflected from the surface, as shown in Figure 8(a).

Absorption occurs when the energy of the photon is absorbed by a structure in the tissue such as hemoglobin in blood or melanin in the epidermis. Similar to scattering principles, the absorption coefficient is used to characterize the degree of absorption and describes the probability of a photon being absorbed for a given propagation distance within the tissue. When there are more absorption structures in the tissue, less energy will be reflected from the surface and fewer absorption structures result in more energy reflected from the surface as shown in Figure 8(b).

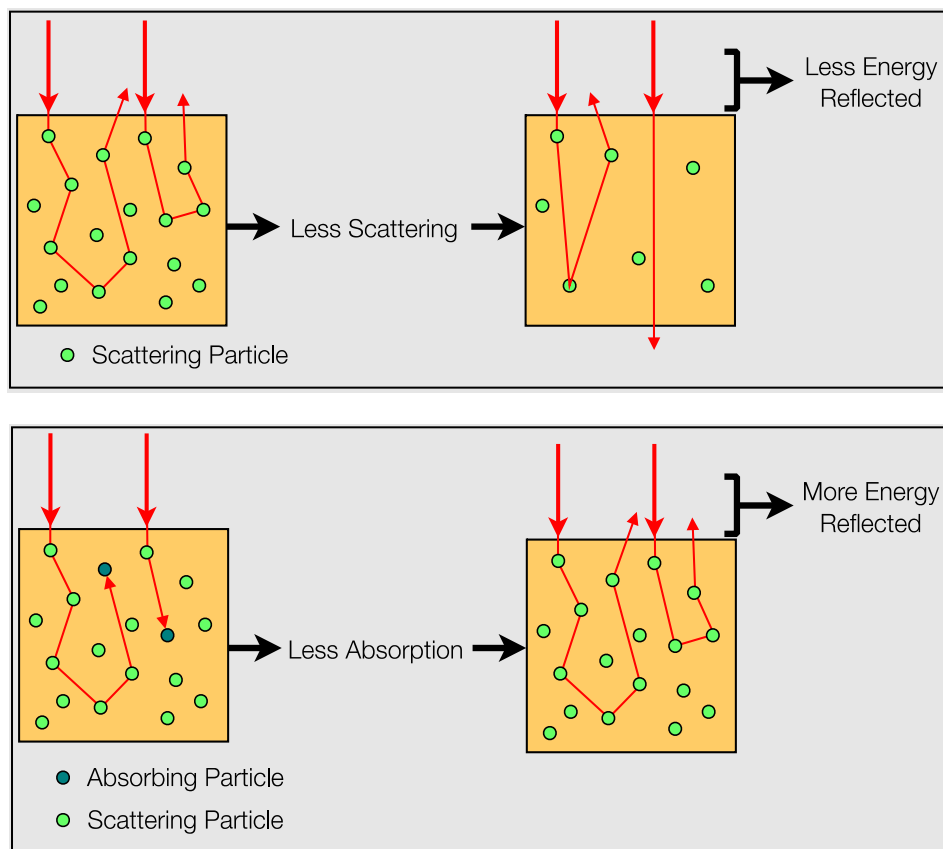


Figure 8. Effects of scattering (a) and absorption (b) of photons on the reflected energy on the surface

During an infiltration by a low scattering infusate such as normal saline, fluid accumulates in subcutaneous tissue, reducing the scattering coefficient in the monitored tissue volume. A highly absorbing fluid like Iron Sucrose is detected by an increase in absorption. For lipid-based infusates a combination of scattering and absorption effects are detected. The Milky Way Sensor's LEDs are selected to detect changes in water-lipid absorption profile of the tissue. And depending on the dilution of lipids to clear fluids, large swings in the tissue's scattering properties can also be detected.

In two previous Milky Way "Algorithm Development" studies, an algorithm was developed to differentiate between normal and infiltrated tissue with high sensitivity and low false-notification rate. The goal of this study is to validate the sensors performance in terms of false-notification rate, which will be quantified according to the first study objective.

Clinical Investigation Design Justification

Stage of Clinical Investigation

Check the applicable boxes to identify the stage of the Clinical Study

	Study Type	Study Design	510k/regulatory submission required?
Pre-Market Study (Design/Development)	☐ Feasibility Study ☐ Verification Study ☒ Validation Study	☐ Exploratory ☒ Confirmatory	☒ Yes ☐ No
Post-Market Study	☐ PMCF Study	☐ Exploratory ☐ Confirmatory	☐ Yes ☐ No

Summary of Previous Clinical Studies

This will be the first of two clinical studies performed with the Milky Way sensor for device validation. Two algorithm development studies have been performed with the Milky Way sensors. Previous studies with Fiber Optic and SmartTouch Sensors are also discussed below.

ivWatch Model 400 Clinical Studies

The ivWatch Model 400 was tested in a series of IRB-approved studies on healthy adult research subjects, as summarized in Appendix A - Clinical studies performed with the Fiber Optic Sensor. The Design Verification studies evaluated the performance of the device under different conditions. The NIR Detection of PIV Infiltration study evaluated two models of PIV infiltration as well as potential algorithm correction for changes in tissue blood volume. The Signal Variation of Normal Tissue study evaluated the sources and rates of non-infiltration alarms when monitoring normal, non-infiltrated tissues. In this protocol document, the terms ‘alarm’ and ‘notification’ are considered interchangeable, although the device does not comply with IEC 60601-1-8. Two clinical studies evaluated how the infiltration rate and catheter depth affected the diagnostic performance of the ivWatch Model 400. The device detected all 10mL infiltrations for common adult infusion rates ranging from 5 mL/hr to 150 mL/hr. The device detected all infiltrations with a catheter depth less than 5 mm deep although deeper infiltrations caused a reduced sensitivity by the device. The final study assessed the adhesion of the ivWatch receptacle over a 96-hour period. There were no adhesion issues with the receptacle when used with an occlusive dressing.

After completing the design verification studies, two additional studies were performed to validate the final design. The study, titled Device Validation for Non-Infiltrated Tissues, evaluated non-infiltrated sites over a 24-hour period. The device issued a false red notification once every 4.2 days and a false yellow notification once every 2.0 days. These notifications were often caused by compression of the IV site. The next study, titled Device Validation for Infiltrated Tissues, evaluated the performance of the ivWatch Model 400 for detecting 140 infiltrated IV sites. Of the 140 IV sites, the ivWatch device issued 135 red notifications (96% sensitivity) and 139 yellow notifications (99% sensitivity). These results demonstrated the ivWatch Model 400 is highly sensitive to infiltrated PIV sites on the hands and forearms of adults while having a false notification rate that should have negligible effects on clinical alarm fatigue.

Three additional IRB-approved studies were performed to (1) examine the infiltration detection performance as a function of the distance separating the catheter tip and ivWatch sensor, (2) examine the infiltration detection

performance when the sensor is placed above and below a transparent occlusive dressing, and (3) examine the false notification rate when the sensor is placed above a transparent occlusive dressing.

After the FDA clearance for ages 18 and up, an IRB-approved clinical study was conducted to measure the performance of the ivWatch Model 400 device for detecting early-stage infiltrations on pediatric patients at Cincinnati Children's Hospital Medical Center. Hospitalized pediatric patients who were 2 weeks to 17 years old who received continuous IV therapy were monitored with the device. The study was broken into two groups, 156 subjects in a blinded non-alarming group, and 57 subjects in an alarming group. The objectives of the study were to determine the amount of time between infiltration detection by the clinician and the device as well as the device sensitivity and specificity. Each site was continuously monitored during IV therapy and the IV was terminated if an infiltration was detected or other complications were identified. In the nonalarming group, the device issued red "Check IV" notifications a median time of 15.2 hours before clinician detection. The device issued notifications for 18 out of 23 clinician-confirmed infiltrations in the non-alarming group, for a sensitivity of 78.3%. In the alarming group, the device issued notifications for 12 out of 15 clinician-confirmed infiltrations. The results from this study were used to support the FDA clearance for all age groups including pediatrics in December of 2016.

Results of previous studies are listed in Appendix A - Clinical studies performed with the Fiber Optic Sensor.

ivWatch SmartTouch Sensor Clinical Studies

A series of clinical studies then took place with the SmartTouch Sensor to test feasibility then verify and validate the sensor in a similar way to the original Model 400 studies. Two feasibility studies were completed to examine the 'alpha' design of the SmartTouch Sensor in terms of (1) infiltration signal performance and (2) false notification rate of the SmartTouch Sensor (Appendix B - Clinical studies performed with SmartTouch Sensor). These studies have indicated the optical design of the alpha SmartTouch Sensor performs equivalently to the Model 400 fiber optic sensor. Four verification studies were performed to test the 'beta' SmartTouch design and show equivalence to the Model 400 in terms of (1) device sensitivity and (2) false notification rate. The beta SmartTouch design contains the same optical sensor as alpha, but improvements were made to the sensor for increased durability and manufacturability. Signal data from these verification studies were used to improve signal processing algorithms prior to final software design. Finally, two validation studies were performed to demonstrate statistical equivalence to the Model 400 in (1) infiltration detection volume, (2) infiltration sensitivity, and (3) false notification rate. After these validation studies were conducted, six long-term wear clinical investigations took place to confirm that shelf life (expiration date) did not affect sensor adhesive performance.

Results of previous studies are listed in Appendix B - Clinical studies performed with SmartTouch Sensor.

Milky Way Algorithm Development Studies

The first algorithm development study was collecting long-term motion data, which is used to develop the specificity side of the Milky Way algorithm. Signal data was collected on simulated (no injection) peripheral IV sites of 40 accepted case studies for about 24 hours each, with the goal of measuring typical variability in the Milky Way optical signals. The second study involved collected data on 84 IV sites that were intentionally infiltrated with saline, to aid in the development of the clear-fluid sensitivity side of the Milky Way algorithm. Study results are listed in Table 3.

Table 3. Milky Way sensor algorithm development studies

Study	Purpose	Outcome	Key Performance Metrics
Milky Way Sensor: Non-Infiltrated Tissues Algorithm Development <i>ivWatch Study ID: IVW-CLR-CS35-400</i> <i>Advarra IRB ID: 00082496</i> <i>Number of Subjects: 40</i> <i>Dates: Nov 2024 to Jan 2025</i>	- Quantify the non-infiltration notification rates for the Milky Way Sensor. - Identify conditions that may cause a non-infiltration notification.	- The Milky Way Sensor has a similar false-notification performance to the SmartTouch Sensor. - An analysis of the notifications indicated many were associated with patient activities that applied a force to the site, either distorting the tissue or affecting the skin-sensor coupling efficiency.	Red Notification Rate: 0.052 notifications / day 1 notification every 19.2 days 95% confidence interval: 0.015 to 0.210 notifications / day
Milky Way Sensor: Non-Infiltrated Tissues Algorithm Development <i>ivWatch Study ID: IVW-CLR-CS36-400</i> <i>Advarra IRB ID: 00086485</i> <i>Number of Subjects: 42</i> <i>Dates: June 2025</i>	Determine if infiltration signals measured with the Milky Way Sensor are equivalent to those measured with the SmartTouch Sensor	The mean MW sensor signal in this study was 0.36, which was considered not less than the previous SmartTouch signal mean of 0.33 using this t-test ($p=0.9974$).	Red Notification Sensitivity: 100% Sensitivity - Red notification on 84/84 cases 95.7 to 100.0% for 95% Conf. Interval Red Detection Volume: - Average red Check IV detection volume was 2.08 ml - Minimum and maximum of 0.27 ml and 9.46 ml, respectively

Benefit and Risk Analysis of the Investigational Device, Clinical Procedure, and Clinical Investigation

There are no anticipated clinical benefits for research participants. Future hospital patients who are monitored with ivWatch technology may benefit from this study while ivWatch technology is continuously monitoring their IV site(s). Hospitals and health care staff may also benefit from this study as the data collected in this investigation will validate ivWatch's algorithm. There are no other devices on the market that continuously monitor an IV site for infiltration and extravasation.

Table 4. Anticipated Events

Anticipated Event Type	Description
Adverse Event	- Allergic reaction (e.g., food, bedding, cleaning products, etc.). - Minor injury from unfamiliar environment (e.g., slip, trip, fall). - Poor sleep quality leading to headache, fatigue, or irritability. - GI upset, mild food intolerance, or illness from provided meals. - Anxiety or homesickness.

	• Skin irritation or inflammation. • Razor bumps or cut. • Seasonal or other illness from sharing space with others.
Adverse Device Effect	• Allergic reaction due to investigational device. • Local skin irritation (redness, itching, rash) or inflammation. • Minor injury from equipment (e.g., tangled in cables, fall from cables) • Poor sleep quality leading to headache, fatigue, or irritability.
Serious Adverse Event	None
Serious Adverse Device Effect	None
Device Deficiency with Serious Adverse Device Effect Potential	None

The study design is considered to have non-significant risk to the healthy adult volunteers participating in this study, and the risks associated with participation and risk mitigations are listed in Form-0000182, Medical Device and Clinical Trial Protocol Risk Determination Form. The benefit-risk analysis for the investigational device, Milky Way Sensor, is favorable since the benefits outweigh the risks as described in Form-0000182. While some risks exist like allergic reaction to medical supplies or the investigational device and data privacy leak, many risks pre-mitigation were already at an “acceptable” level. Post-mitigation, there are no residual risks as all risks are “acceptable”. Additionally, many of these risks are comparable to what volunteers might experience in a typical hospital visit or a typical public space.

The risk threshold establishes the upper limit of acceptable risk, considering potential adverse events or device-related complications. For the investigational device, the risk threshold is set using ivWatch’s Milky Way Risk Management Plan, DP-1002132, while for the protocol and procedure, the risk threshold is set using ivWatch’s Risk Management procedure, QP-1001020. Risks are continuously evaluated throughout the investigation using the risk section of the case report form. If new risks are identified or a risk differs from what’s expected, the analysis will be updated using a subsequent risk analysis.

The degree of distress refers to any discomfort or psychological impact experienced by participants, whether physical (e.g., pain, irritation) or mental (e.g., anxiety). It is assessed using clinical observations and objective measures, like subject withdrawal. Any significant increase in distress is evaluated to determine if adjustments to the trial protocol or additional support are required. If a participant feels uncomfortable or experiences undue mental or emotional stress, they are free to withdraw from study participation and leave the study center at any time.

Over the last seven years of post-market surveillance, there continue to be no early warning signs of any quality issues, and no corrective and preventative actions have been needed. The devices continue to meet the intended use, be high quality, safe, and effective.

Given the absence of technology to continuously monitor lipid-based peripheral IV infusions and the significant harm caused by lipid-based extravasations, the benefit to future patients outweighs the minimal risks associated with the investigational device and this protocol, leading to a favorable benefit-risk ratio.

Critical to Quality Factors

Critical to quality (CtQ) factors and their elements for this investigation include:

- Patient safety and rights

- Informed consent that clearly explains the study procedures, device function, risks, and alternatives.
 - Monitoring and reporting of device-related adverse events.
 - Protection of participant privacy.
- Trial design
 - Appropriateness of participant population.
 - Appropriately powered sample size.
- Data integrity
 - Data capture that is attributable, legible, contemporaneous, original, and accurate.
 - Secure electronic data transfer.
 - Validation of electronic systems (21 CFR Part 11 compliance).
 - Appropriate handling of missing or corrupted device data.
- Device reliability and performance
 - Software version controls and hardware consistency.
 - Device traceability and accountability.
 - SOPs for device use and updates.
- Operator and site consistency
 - Training of staff in device operation.
 - Monitoring for protocol deviations related to device operation.
 - Documentation of training/experience and adherence to SOPs.
- Ethical oversight
 - IRB approval
 - Timely adverse event reporting
 - Data monitoring

Based on these CtQ factors and elements, the risks that threaten these factors were evaluated. There were several risks that were scored ‘medium (planned mitigation and monitoring)’ and after planned mitigation, all risks from the risk matrix were scored as ‘acceptable.’

Study Purpose and Objectives

The purpose of this study is to validate the non-infiltration notification rate performance of the Milky Way Sensor using healthy adult volunteers under controlled conditions. Within the state of art of clinical practice, false alarms remain a well-documented challenge contributing to alarm fatigue, workflow inefficiencies, and potential delays in clinical response, underscoring the relevance and necessity of this study.

The primary objective is to quantify the non-infiltration notification rate for the Milky Way Sensor. A secondary objective is to identify conditions that may cause a non-infiltration notification.

Risks and anticipated adverse device effects to be assessed are listed in Form-0000182 and Table 4, respectively. Overall, the investigation is clinically relevant as it addresses a persistent need for improved notification accuracy, supporting the safe and effective integration of the Milky Way Sensor into clinical practice.

Study Design

General Information

This clinical trial is a single-arm, one-center trial without a control group. As ivWatch's technology is the first and only device currently on the market capable of continuous monitoring to detect IV infiltrations and extravasations, there will be no control group in this study. Any potential comparative technologies have already been evaluated in previous ivWatch studies using similar designs. If a comparator group becomes necessary, ivWatch may utilize previously collected data from IRB-approved clinical studies involving the Fiber Optic Sensor or SmartTouch Sensor.

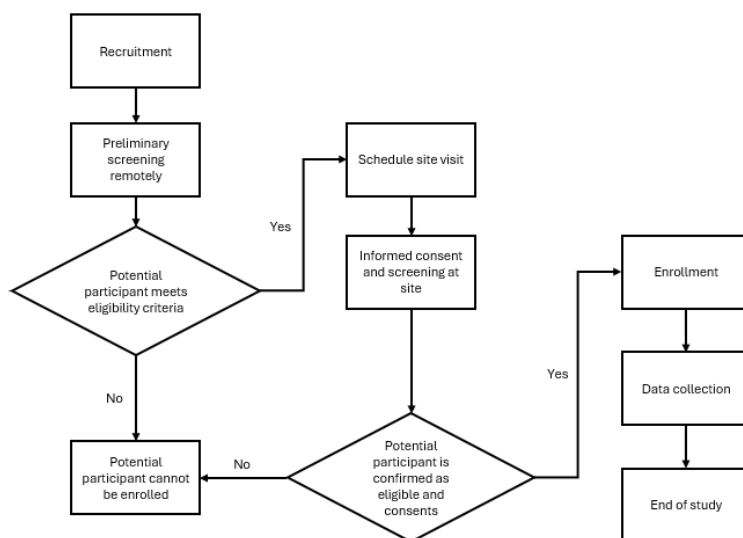


Figure 9. Schematic Diagram of the Clinical Investigation.

To minimize bias, the simulated IV site configurations are selected at random for each research volunteer by a pre-study research assistant (non-salaried contractor of ivWatch). The possible configurations are (1) non-dominant hand, (2) dominant hand, (3) non-dominant forearm, and (4) dominant forearm.

Primary and secondary endpoints are as follows:

1. Primary endpoint – The rate of non-infiltration notifications for the Milky Way Sensor.
1. Secondary endpoint and safety endpoint – Occurrence of skin irritation and allergic reaction at the Milky Way Sensor monitoring site.

Endpoints will be measured after data collection for all participants is complete. The primary endpoint was chosen as a measure of specificity of the device, in other words, the probability of a false positive per unit time. The secondary endpoint was chosen to continue to evaluate the comfort and safety of the device and will be evaluated through the occurrence and severity of adverse events.

Since this study is expected to take less than one month to complete, each piece of equipment that is used to assess the clinical investigation variables, such as the physician's scale to measure height and weight as well as

the Model 400 Patient Monitors, will be assessed for calibration and maintenance needs prior to the start of the study. If needed, calibration and maintenance needs will be assessed annually following this initial check.

Research participants will be replaced after SF-1001041, Case Study Rejection Request Form, is approved by an Investigator. Replacement cases will be assigned the same simulated IV site configuration as the rejected case.

This is a one-center clinical study, and the study center is located at 709 City Center Parkway, B-112, Newport News, VA 23606. The ivWatch Model 400 is intended to be used in hospitals and similar medical care facilities; therefore, the study center will be set up to resemble a general hospital environment and rooms. Each room will include at least a hospital bed, a recliner, medical equipment (an IV pole with an attached ivWatch Model 400 Monitor and an over-bed table), a TV for entertainment, and personal Wi-Fi access. The study center will also have shared restrooms, a communal relaxation space, and a communal kitchen. Actual hospital environments may have more medical equipment and supplies stored in a patient's room; however, these additional supplies and equipment are not expected to impact the collection of data and therefore will not be staged.

The completion of a clinical investigation shall be deemed to coincide with the completion of the visit with last participant, whether the clinical investigation concluded according to the pre-specified clinical investigation plan or was terminated prematurely. Follow-up is not expected to be necessary for this clinical investigation.

Investigational Device(s) and Comparator(s)

Research volunteers will have a Milky Way Sensor (Investigational Device) applied to the randomly selected simulated IV site. The sensor will be connected to a Patient Cable, which is plugged into the Patient Monitor and Extension Module that is mounted to an IV pole. The Extension Module and Patient Monitor will be running production equivalent software, and issuing Check IV notifications for signals that deviate significantly from normal tissue. Both the Milky Way Sensor and the Patient Cable are patient-contacting, and the materials used to make these products have been tested to the appropriate ISO 10993 biocompatibility standards, through a predicate product (SmartTouch Sensor) in the case of the Milky Way Sensor. There are no other medical devices used to record ivWatch monitoring data in this clinical investigation.

Each Milky Way Sensor is single use, therefore, the number of Investigational Devices will be approximately equal to the number of enrolled research participants. Occasionally, a sensor may have a manufacturing defect, the adhesive may be disturbed, or another issue may exist where the sensor needs to be replaced. Therefore, there may be additional investigational devices when compared to research participants, with flexibility for 25% over. So, if there are 20 participants, there may be 25 investigational devices used. There will be approximately six systems to support the Milky Way Sensor, meaning Patient Monitor / Extension Module / Patient Cable.

Subjects

For this protocol, the terms “subject” and “participant” are synonymous. Inclusion criteria and exclusion criteria are listed in Table 5 and Table 6 below, respectively. Subjects may withdraw from the study at any time and for any reason. All subject withdrawals will be documented by the study staff. Additionally, an investigator may withdraw a subject for various reasons, such as safety concerns or non-compliance with the study protocol. Any data collected up to the point of withdrawal will remain part of the study. Since there is no follow-up period in this study, subjects are not expected to be lost to follow-up. Subjects who withdraw may be replaced until a total of 20 accepted case studies are reached. If a subject withdraws due to safety concerns related to the study procedure or investigational device, an investigator or the qualified physician will contact the subject within two weeks of withdrawal for a safety follow-up.

Subjects are enrolled in the study after they sign the informed consent form and are deemed eligible by the health history form. Subjects are randomly assigned a simulated IV site configuration immediately following enrollment. The entire study is expected to take less than one month to complete, with each subject's participation totaling approximately 24 hours. Approximately 25 subjects may be enrolled in the study with the goal of achieving 20 accepted case studies. The time needed to select this number (enrollment period) is approximately one month. Investigation population will not include children or those under 18 years of age. However, ivWatch technology (Model 400) has been FDA cleared for all age groups, skin tones, and body sizes.

Twenty (20) accepted case studies is the ultimate determination for whether the study is complete since previous clinical studies have shown no difference in the technology when considering age, skin tone, or body size; however, the study has the following enrollment goals:

1. For BMI, at least 3 participants in the healthy weight (18.5 to less than 25) and overweight categories (25 to less than 30) and at least 3 in the obese category (30 or greater).
2. For skin type, at least 3 participants in color bar survey categories 1 and 2, at least 3 participants in categories 3 and 4, and at least 1 participant in categories 5 and 6. These distribution numbers are based on what's expected in the population based on the original study to validate this color bar survey tool.¹
3. For sex, at least 5 male participants and at least 5 female participants.
4. For age, at least 5 participants over 50 years of age.

Vulnerable populations will not be specifically targeted and pregnant women will not be enrolled. Please see the Vulnerable Population section for additional information.

Table 5. List of study inclusion criteria.

1	18 years of age or older
2	Healthy individual, verified by an eligible designation on the Health History Form

Table 6. List of study exclusion criteria.

1	Currently enrolled in another clinical trial
2	Currently pregnant or trying to become pregnant
3	Serious and uncontrolled medical condition
4	Tattoo(s), scarring, or bruising that severely limits vein visualization at a sensor monitoring location
5	Medical adhesive allergy
6	Sleepwalking occurrence in the last year
7	Current drug/alcohol dependence
8	Sick or had an infection in the last 14 days
9	Hospitalized in the last 14 days
10	Fever at the time of study visit ($\geq 100.4^{\circ}\text{F}$)

Patients will not be involved in different phases of the clinical investigation like designing objectives or disseminating results.

Procedures

Before Arrival to Study Site (Recruitment)

A brief description of the study will be sent via email to individuals who have previously expressed interest or participated in a Virginia-based ivWatch study and provided their email address. The email will include a link to an interest survey for potential participants to complete. Once a survey response is received, a study staff member will review and contact the individual to discuss their eligibility for the study. Potential eligible participants will then choose an appointment slot to visit the study center. The formal consent and screening process will be performed on the day of the study, prior to enrollment.

Preliminary Information and Consent (Enrollment)

Upon arrival at the study center, the potential participant will sign in at the reception desk. Staff will confirm the participant's identity and ensure they are over 18 by checking a government-issued ID.

The participant will then meet privately with a non-conflicted staff member (if not an Investigator, the staff member must be delegated informed consent duties). They will review the informed consent form and authorization to disclose protected health information. For the remainder of the protocol, this will be referred to collectively as the informed consent form.

Before signing the informed consent form, the potential research participant will have the opportunity to ask questions and receive clear, satisfactory answers from the Investigator or a staff member delegated informed consent duties. If the potential participant does not consent to the study by signing the form, they cannot be enrolled and will be asked to leave the study center.

If the participant agrees to join the study by signing the informed consent form, the pre-study research assistant will then update the participant's health history form as necessary (page 64). Any new questions where answers were not transferred from the pre-screening survey will also be completed at this time. The purpose of this form is to screen for any potentially infectious or unhealthy subjects who should not participate in the trial or those at an unnecessarily higher risk of complications from participation.

Next, the investigator or pre-study research assistant will determine if the potential participant meets the criteria for the study. Inclusion and exclusion criteria are provided in Table 5 and Table 6, respectively. If there are any uncertainties about the participant's eligibility related to health, a qualified physician is available by phone for consultation.

Once the informed consent form is signed and the health history form is approved, the participant will be enrolled in the clinical study. The Investigator or pre-study research assistant will then fill out the Subject Identification List. At this point, a copy of the complete informed consent form should be made and given to the participant for the participant's records.

A brief health screening will follow, where the subject's height and weight are measured. Additionally, age, sex, and skin tone will be participant-reported. These demographics have enrollment goals, as described previously in the Subjects section.

A pre-study research assistant will randomly select a simulated IV site configuration. Each participant will receive one simulated IV site, either on the hand or the forearm.

Finally, with preliminary information collected, the pre-study research assistant will provide a tour of the facilities, including the restrooms, kitchen, and common area. Participants are free to use these facilities as needed. Once finished, the participant will be taken to their designated observation room.

Data Collection

The data collection consists of three processes: (1) participant preparation, (2) data collection, and (3) study closeout.

Participant Preparation

Each observation room is designed to be similar to a hospital room and will include at least a bed and television. The study center will have a video camera in each observation room as well as in common areas to record the activities of participants throughout the 24-hour case studies. This is so researchers may review the video footage leading to any false notification and determine the cause. Each observation area contains the components required for the study, as listed in Table 7. Each item in the table also includes a letter designating whether the item is reusable or disposable. Reusable equipment will be cleaned with cleaning/disinfecting wipes according to their labeling in between participants.

Table 7. Medical equipment required for each case.

Item #	Description: (R: reusable, D: disposable)	Expected Number of Devices per Participant
1	IV pole (R)	1
2	Patient Monitor and Extension Module (R)	1
3	ivWatch Patient Cable (R)	1
4	ivWatch Milky Way Sensor (investigational device) (D)	1
5	IV tubing (R as it is a simulated IV site)	1
6	Catheter hub, with tube removed (D)	1
7	Statlock (D)	1
8	Alcohol wipes (D)	4
9	Adhesive remover wipes (D)	2
10	Medical tape (D)	1
11	Ultrasound gel (D)	1
12	Gauze (D)	6
13	Video cameras (R – cleaning not necessary)	1 or 2 per room plus common area cameras

In the observation room, the Investigator or data collection research assistant will explain how to complete the participant activity log (Appendix F – Participant Activity Log), which may be needed to understand activities when the participant is away from their observation room. For example, “At 7:33 AM I went to the restroom to brush my teeth.”

The Investigator or data collection research assistant will perform hand hygiene. If necessary, they or the participant may shave the monitoring area with a single-use razor to help the ivWatch sensor stick to the skin. A vein commonly used for IV therapy will then be chosen at the assigned monitoring site. Photos of this area will be

taken, both with and without NIR vein viewer illumination. The monitoring site will then be cleaned with alcohol wipes.

After the area dries, the ivWatch sensor is adhered next to the vein typically used for IV therapy. A catheter hub and IV tubing are secured to simulate an IV line, though no injections will be done in this study. The IV tubing and ivWatch cables are arranged for proper cable management. A photo is taken of the monitoring site to document its location and to assess the dressing throughout the study.

A staff member will ensure the video equipment is recording. A data collection research assistant will then start the ivWatch monitoring equipment, and the participant will be free to make themselves comfortable and move around the authorized areas of study center with their IV pole.

At this point, the Investigational Device Accountability Log, REC-0000220, should be updated, and the eCRF Demographics and Pre-Study pages in the electronic clinical trial management system (eCTMS) should be filled in as much as possible.

Data Collection

Wi-Fi is available to the participant, and they may entertain themselves using the provided television or personal belongings, such as a computer, tablet, cell phone, or video gaming system. Subjects are free to communicate with other participants, ivWatch staff, and other parties using their cell phone at any point during the study. The participant is not allowed to leave the facility, unless withdrawing from the study early. At least one staff member will always be at the study center and available throughout to supervise participant compliance and in case any unanticipated needs arise.

An example timeline of study activities is included in Table 8. The timeline serves as a guide for scheduling the activities, although deviations from this timeline may occur without jeopardizing the data integrity. Each routine assessment will include a visual check of the simulated IV site, photograph(s), an equipment check, and documenting the routine check in the eCRF.

Table 8. Example study timeline.

Time	Activity
9 AM	Informed consent process, health history and screening
10 AM	Start study – data collection begins
12 PM	Routine assessment & lunch
2 PM	Routine assessment
4 PM	Routine assessment
6 PM	Routine assessment & dinner
8 PM	Routine assessment
10 PM	Routine assessment
10 PM – 8 AM	Sleep
8 AM	Routine assessment & breakfast
9 AM	End study – participant receives payment

Study Closeout

At the end of the observation period, the monitoring run is stopped, and a photo is taken of the monitoring site. In analysis, this image may be compared with the image captured at the start of the study to assess the adhesion

of the sensor. The sensor and IV tubing are then disconnected and removed from the participant. The approximate location of the sensor head is marked on the participant so ultrasound images can be taken of this area. A photo is captured of the bare site to assess the skin integrity of the monitoring site, which includes signs of allergic reaction and skin removal. Ultrasound images are acquired from the monitoring site to measure the tissue microstructure (skin thickness, subcutaneous fat thickness). The Post-Study page in the eCRF is filled out as much as possible and the participant is asked any clarifying questions about the completed participant activity log. Then, the participant gathers their belongings and is taken to the front reception desk and given participation payment of \$298, which is Virginia's current minimum wage (\$12.41) multiplied by 24 hours. Should the participant withdraw from the study, the participation payment will be pro-rated based on time. The participant is asked to sign and date a check-out sheet to verify receipt of payment. The participant is reminded that contact information is listed on their copy of the informed consent form should they have any questions or concerns after departing the study center. There is no anticipated need for follow-up during this study.

After the participant departs from the study center, the research assistant is responsible for ending the video recording and cleaning the observation area. Data saved outside of the eCRF is then removed from the corresponding equipment and transferred to the eCRF. This data may include the monitoring data and ultrasound images. At this point, the remaining sections of the eCRF may be completed. All paper-based forms containing private health information are given to the HIPAA officer for separate and secure storage.

Investigators evaluate protocol deviations, device deficiencies and malfunctions, adverse events, participant withdrawal, and newly identified risks with each eCRF to ensure these events are tracked.

Source Data

All study data will be recorded directly by study staff into the eCTMS, which will serve as the source record for all clinical and participant-reported data unless otherwise specified. To protect personal information, the eCTMS is organized into two distinct areas. The first is the participant health history segment (eHHF), which supports eligibility determination. Information in this section will be captured directly in the eHHF, either through subject-completed forms linked to the system or via direct entry by study staff at the time of screening; when subject-completed forms are used, they will be retained as source documents. The second area is the case report form segment (eCRF), which contains study-specific data with identifiers such as name, email, and phone number removed. For data generated by external equipment (e.g., ultrasound machines), the original file will be considered the source document. In these cases, the image creation time (embedded in the ultrasound file name) will be documented contemporaneously in the eCRF at the time of assessment to ensure traceability, with the full file uploaded once it becomes available. This structure minimizes unnecessary transcription and maintains a clear and compliant data flow.

Data Monitoring Plan

The primary focus of monitoring will be to ensure participant safety and reliable capture of critical data. Given the limited study size and low-risk qualities, monitoring activities will emphasize verification of critical-to-quality factors, including informed consent documentation, eligibility confirmation, investigational device use, and adverse event reporting. Monitoring will be conducted in accordance with ivWatch policies and SOPs.

An independent data monitor, not otherwise involved in the conduct of the study, will be appointed by ivWatch to oversee the integrity of study conduct and data. The monitor will be trained on the clinical investigational plan, applicable regulations, and ivWatch SOPs. The monitor's role will be to ensure that the rights, safety, and well-

being of participants are protected, and that the trial data are complete, accurate, and verifiable against source documentation.

The Principal Investigator shall permit trial-related monitoring, audits, IRB review, and regulatory inspections. The PI shall provide direct access to source data and documents to applicable individuals/entities to perform these trial-related activities. The monitor will perform source data verification on 100% of informed consent forms, participant eligibility documentation (health history forms), and adverse event forms. Other less critical data (e.g., routine check case report form entries) will undergo targeted source data verification according to a pre-determined sampling plan, focusing on areas that could significantly affect data quality or trial conclusions.

Monitoring may be conducted with both on-site and remote methods. On-site monitoring will occur at initiation, during study, and end of study conduct to ensure protocol compliance, device accountability, and data verification. Remote monitoring may be used for timely review of case report forms.

Quality tolerance limits (QTLs) have been established to identify potential systemic risks to participant safety or data reliability. QTLs will be such that:

- Informed consent missing or signatures missing: 0% (must be 100% complete)
- Protocol deviations impacting endpoint assessments must not exceed 5% of enrolled participants.
- Device mismatch (e.g. IPM or EM serial numbers not matching eCRF): 0 occurrences for cases with non-infiltration notifications; any occurrence triggers review.
- Unauthorized software/firmware version in use: 0 occurrences.

If deviations beyond these limits are detected, an evaluation must be performed to determine whether corrective and preventative actions are required.

As there are no central laboratories or imaging facilities, oversight of external processes is not required. The Data Monitor will document issues and findings from each monitoring activity in written reports (Form-0000183 and SF-1001020) and significant issues will be communicated promptly to the principal investigator and IRB, as appropriate.

Conflicts of Interest

The PI of this study has a financial interest in the company sponsoring this study and owns stock options (0.15% ownership in ivWatch). As a result, the PI may benefit financially from a successful study. The stock options have not been awarded because of the results of any clinical study. The Investigator in this study has Class B Unit Appreciation Rights at ivWatch, currently valued at \$0. These also have not been awarded because of the results of any clinical study. Both the PI and Investigator are employees of ivWatch and have worked closely on device creation.

To manage the above conflict of interest (COI), these COI have been disclosed in the informed consent form. Conflict of Interest training through the CITI Program has been completed by both the PI and Investigator, and the valid certificates are viewable upon request. Undue influence on subjects will be avoided as only non-conflicted study members will obtain informed consent and determine participant eligibility. Finally, if the results of this study are submitted to a peer-reviewed publication, the PI and Investigator COIs will be disclosed.

Quality Assurance / Quality Control

As the research sponsor, ivWatch, LLC will continually monitor the research studies to ensure subject safety and data validity. Unlike multicenter studies, all aspects of the study are performed with ivWatch personnel facilitating the quality assurance process.

The first component of the quality assurance program is ensuring the research personnel have the correct training to perform the studies. All study personnel (investigators, research staff, data monitors) will have the proper training (HIPAA and CIT) for conducting clinical trials prior to the start of the study. The subject screening will be performed by the study staff.

The second component of the quality assurance program is the monitoring of studies as part of Quality Control activities to ensure the procedures outlined in this document are followed. This includes the procedures for data collection (ivWatch research system operation), data storage, and data validation.

The third component of the quality assurance program is monitoring the security of study data. As described in the data management section, study data stored in the database are password protected and restricted to authorized users. Any changes to the database are tracked. The case report forms do not contain subject identifiers. All paper forms with personally identifiable information will be stored in a locked filing cabinet. Data Management processes also serve as Quality Control.

Site Team Roles and Responsibilities

Table 9. Site team roles and responsibilities

Role/Function	Responsibilities/Authorizations
Principal Investigator (PI)	- Ensures compliance with the regulations and protocol, and protects the rights, safety, and well-being of all subjects. - May sign and make corrections in the clinical trial database, following Good Documentation Practices (GDP), when needed and can accept or reject data. - Authority over entire clinical trial. - May perform duties of other roles in the clinical study. - Authorized to sign the protocol and amendments for the sponsor. - May alter device accountability records.
Investigator	- Assists the PI with managing the day-to-day conduct of the clinical trial. - May sign and make corrections in the clinical trial database, following GDP, when needed and can accept or reject data. - May perform duties of other roles in the clinical study. - Authorized to sign the protocol and amendments for the sponsor. - May alter device accountability records.
Data Monitor	Conducts initial site assessment and periodic monitoring to verify compliance and documentation. Note: The Data Monitor cannot make corrections to the clinical trial database or source data.
Medical Expert / Qualified Physician	- Answers medical and enrollment questions. - May make trial-related medical decisions.
Ultrasound (US) Technician	Oversees or performs activities that require use of ultrasound equipment.

Pre-Study Research Assistant	- Non-conflicted research assistants can execute the informed consent process with subjects. - Those with a valid medical license or certificate to practice basic medicine may determine eligibility and perform a health screening.
Data Collection Research Assistant	- Assists with calling out, documenting, and/or executing the protocol steps. - Captures photographs of IV sites and configures data monitoring runs. - Ensures documentation of attendance and distribution of compensation to subjects.
HIPAA Officer	Ensures privacy policies to protect the integrity of protected health information are followed.
Note: personnel trained in the use of and creation of entries in the eCTMS may make corrections before the eCTMS is locked. All changes are captured by the audit trail in the database. After the eCTMS is locked, however, only the PI/I can make subsequent changes once form QF-1002003 is completed.	

Statistical Design and Data Analysis

The goal of this study is to measure the non-infiltration notification rate for the Milky Way sensor monitoring non-infiltrated tissues. Although non-infiltration notifications may not indicate an infiltration, the conditions generating these notifications are often situations clinicians would like to resolve. For example, previous studies indicated that significant tissue deformation at the monitored site, such as laying on the site, could generate a notification. Clinicians have indicated they should be alerted to these situations as significant deformations near the site are currently thought to increase the risk for PIV complications such as infiltrations, occlusions, and phlebitis (inflammation of the vein). Although potentially beneficial, these non-infiltration notifications have to occur at a relatively low rate in order to prevent clinical notification fatigue. Discussions with clinicians have suggested that a non-infiltration notification rate less than 1 notification per day would be ideal. The goal of the non-infiltrated tissue study is to demonstrate a non-infiltration notification rate less than 1 notification per day.

Statistical Power

Monte Carlo simulations were performed for the statistical power analysis of the non-infiltrated tissue study. Separate simulations for $n=8$ to $n=40$ research subjects were performed with one million trials each in MATLAB. The null hypothesis for this statistical test was a device generating a non-infiltration notification one time per day – this corresponds to the probability of a non-infiltration notification in any given hour to be 0.042, assuming each hour has the same probability of experiencing a non-infiltration notification. The alternative hypothesis assumes a rate of 0.25 notifications per day, which is slightly higher than those observed in IVW-CLR-CS35-400. Each trial consisted of ‘ n ’ subjects (8 to 40) with 23 hours of data for a total of 920 hours of monitoring. One hour was removed to accommodate for the time required for the informed consent process, initial setup, and final close-out.

For the simulation at each sample size (n), the statistical power is found using the count threshold that achieves an $\alpha \leq 0.05$ from the null hypothesis trials. Alpha cannot equal exactly 0.05 because of the discrete nature of count data, so the threshold is chosen at an alpha as close to 0.05 as possible, without exceeding 0.05. The left side of Figure 10 shows the statistical power at each sample size from $n=8$ to $n=40$. A sample size of $n=20$ research subjects provides sufficient statistical power (0.99) for this study. Results of the Monte Carlo simulation for $n=20$

subjects is shown on the right side of Figure 10. The red vertical line is the $\alpha \leq 0.05$ threshold for the null hypothesis, which is used to calculate power from the alternative hypothesis trials.

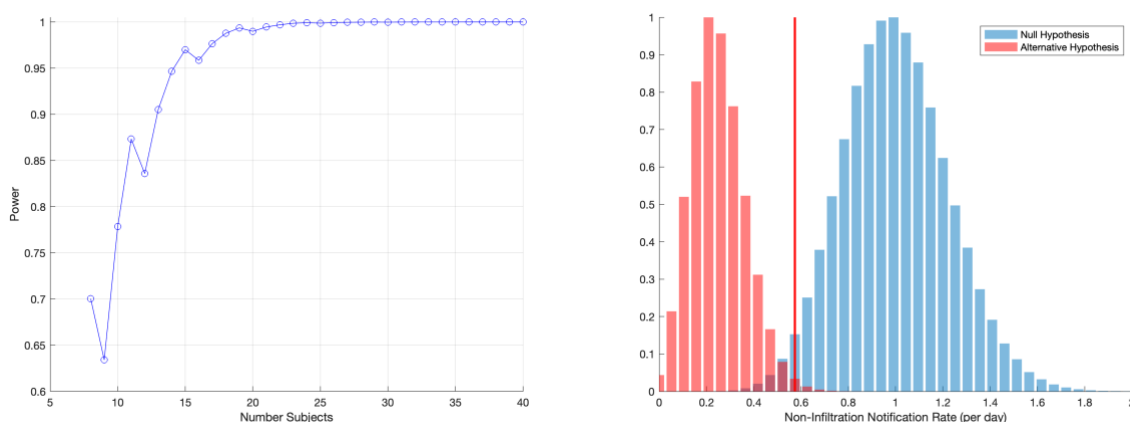


Figure 10. Statistical power analysis (left) and Monte Carlo simulation results from $n=20$ research subjects (right).

The first study objective is to quantify the non-infiltration notification rate of the Milky Way Sensor. A negative binomial maximum regression model will be used to quantify the mean and 95% confidence interval (CI) of the notification rate in units of notifications per day. Results of the negative binomial model can be compared to previous studies with the SmartTouch Sensor.

The second study objective is to identify conditions that may cause a non-infiltration notification, which does not include a specific statistical measure, but rather a list of possible events. To identify conditions associated with non-infiltration notifications, the monitoring video is examined for each non-infiltration notification to determine what conditions may have led to the notification. Previous studies have suggested that many of these false notifications occur when the tissue is deformed at the monitored site, such as when a patient is laying on the site.

There will be no interim analysis as this study takes place over approximately one month. Possible reasons a study may be rejected include, but are not limited to:

1. Equipment (Milky Way Sensor, Patient Monitor, Extension Module) not operating properly.
2. Significant deviations from research protocol.
3. Early termination by research participant leading to a significant loss of critical data.
4. Research participant protocol compliance.

Rejected cases will be documented using SF-1001041 and will not be used in the analysis. Enrollment will continue until there are 20 accepted cases, and these will be included in the analysis. If there is missing data, this will be documented using the form SF-1001021, Report of Protocol Deviation / Non-Compliance where significance of missing data will be discussed.

If there are any deviations from the statistical analysis plan, these may be detailed in the final report. All data analyses will be independently reviewed and verified by a second researcher.

Data Management

In this trial, an electronic data capture (EDC) system, known as the electronic clinical trial management system (eCTMS) will be used to ensure data is accurately recorded, processed, handled, and stored while maintaining the confidentiality and privacy of all participants, in compliance with applicable data protection laws.

Data Recording and Storage

Clinical observations and photographs will be entered directly into the eCTMS by authorized personnel at the study center using devices issued by the sponsor. Other data like ultrasound images and signal data will be uploaded to the eCTMS after the participant completes their case study, Appendix C – Electronic Case Report Form, shows the electronic Case Report Form (eCRF).

The electronic system is designed with built-in validation checks to reduce entry errors and ensure data integrity at the point of capture. Not all fields require validation checks, and this determined during the design of the study-specific eCTMS area. The system will track the completion status of each eCRF through workflows. Data will be securely stored in an encrypted format, and access will be restricted to authorized users only. Each user will have unique login credentials, with role-based access controls to ensure that only necessary information is available to different users.

Data Processing and Handling

Data is processed in real-time, with timestamps and audit trails maintained for every entry or modification. Routine data reviews to identify discrepancies or missing information will be performed on each case report form through the business process workflow (data entry / verification / validation stages). The eCTMS is designed to comply with 21 CFR Part 11 and EU MDR requirements, ensuring traceability and the integrity of the data. Direct personally identifiable information (PII), such as participant names and contact information, will be stored separately from clinical data to protect confidentiality in addition to other restrictions like limited access based on study role.

Post-Collection Data Accuracy and Completeness

After data is collected, accuracy and completeness are ensured through a series of validation procedures:

- Investigators perform routine quality checks on the database, cross-referencing entries with source documents.
- Data queries may be documented in the EDC system when discrepancies or incomplete entries are identified. These queries are resolved by investigators and all corrections are documented within the system.

Data Queries and Resolution

When a query is created, appropriate site staff must provide clarification, corrections, or justifications for the data in question. The responses are reviewed by Investigators, and any changes made in the eCTMS are logged with an audit trail to maintain data transparency.

Data Locking and Analysis

Before the start of data analysis, the database will undergo a formal database locking process:

1. A final review of all data, including audit trails, is conducted to confirm completeness and the resolution of all data queries.
2. Once all discrepancies are addressed, and no further changes are expected, a data lock meeting is held with key stakeholders, including the principal investigator and investigator.
3. Upon agreement, the database is locked, meaning no further changes can be made to the data without unlocking the system, which requires justification and documentation.

This rigorous process ensures that the data is ready for accurate reporting, interpretation, and verification, while safeguarding the confidentiality of participants' personal data throughout the trial. Records of clinical trial data shall be kept in accordance with regulatory requirements as listed in QP-1001001 Control of Records Procedure. If there is a data security breach, participants whose information was compromised will be notified directly so they may mitigate possible adverse effects.

Data Storage and Retention

For eTMS, data will be stored using Microsoft's Power Platform. Microsoft provides robust and reliable data protection for this platform through a comprehensive cloud infrastructure built on Microsoft Azure. All customer (ivWatch) data is automatically backed up and stored in geo-redundant datacenters, ensuring high availability, data durability, and disaster recovery. These backups are encrypted both in transit and at rest. Backups occur frequently—typically every few minutes—and are retained for a period that allows customers to recover data in the event of accidental deletion, corruption, or outage. Data is retained for at least 10 years after the last device has been placed on the market.

In case of data security breach

In the event of a data breach involving study participant information (e.g., names, contact information, or health history), the study team should immediately work with IT to secure the system, assess the scope of exposure, and preserve all relevant records. Then, the PI should report the incident to the IRB, and if applicable, to regulatory authorities in accordance with legal requirements (e.g., HIPAA, GDPR). According to HIPAA, affected participants must be notified within 60 days. This notification should be in clear language regarding the nature of the breach, the information involved and recommended protective actions. Reasonable support should also be offered to affected participants. Preventative steps should then be taken to strengthen data security and reduce the risk of recurrence.

Deviations from the Clinical Investigation Plan

Investigators are not allowed to deviate from the clinical investigation plan, except to protect the rights, safety and well-being of human subjects under emergency circumstances. Investigators will record the protocol deviation using the case report form, then report and analyze the deviation using SF-1001021, including whether a corrective and preventative action (CAPA) is necessary. Corrective and preventative action is documented using QF-1001058.

Investigators will notify the IRB of any deviation from the investigational plan to protect the life or physical well-being of a participant in an emergency as soon as possible, but not later than five (5) working days after the emergency occurred.

Investigators must also notify the IRB of any unapproved protocol deviations (an accidental or unintentional change to the IRB-approved protocol) that, in the investigator's judgment, potentially caused harm to participants or others, indicates that the participants or others are at an increased risk of harm, or has adversely impacted data integrity. This notification to the IRB must occur promptly and no later than 2 weeks (10 business days) from the time of identification of the unplanned or unintentional protocol deviation. Minor deviations that do not cause harm, place participants at increased risk of harm, or adversely affect data integrity do not need to be reported to the IRB.

Sponsors, investigators and/or research staff must notify the IRB in writing of any instance of potentially serious or continuing noncompliance with the regulations, the IRB Handbook, and/or determinations and requirements of the IRB. Serious noncompliance is defined as any action or omission in the conduct or oversight of research involving human subjects that affects the rights and welfare of subjects, increases risk to subjects, or compromises the scientific integrity or validity of the research. Continuing noncompliance is defined as a pattern of repeatedly failing to comply with applicable regulations, the IRB's Handbook, and/or the determinations and requirements of the IRB that may affect subjects' rights and welfare, increase risk to subjects, or may compromise the scientific integrity or validity of the research. Continuing noncompliance also includes frequent instances of minor noncompliance or failure to respond to a request to resolve an episode of noncompliance. Noncompliance and the need for a CAPA is evaluated with SF-1001021. This notification must be as soon as possible but no later than 2 weeks (10 business days) from the time of the event.

PI disqualification criteria include, but are not limited to non-compliance with regulations, falsification or fabrication of data, repeated informed consent violations, repeated protocol deviations without proper justification or approvals, adverse event reporting failures, patient safety concerns, and inadequate essential record-keeping.

Device Accountability

Investigational devices will be accounted for prior to, during, and after the study using REC-0000220, Investigational Device Accountability Log. This log will document information such as the name(s) of person(s) who received, used, returned, or disposed of the device, identification and quantity of each investigational device, date of use, and participant ID. The study will be taking place at the same location as the sponsor; therefore, there are no procedures for shipping or returning investigational devices.

Statements of Compliance and Regulations

The clinical investigation shall be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. ivWatch, LLC will follow this document while conducting the investigation as well as ISO 14155 Clinical Investigation of Medical Devices, ICH E6 (Good Clinical Practice), and FDA 21CFR50, 54, 56 and 812. The investigators will not proceed with the study until the required approval is obtained from the EC. Any additional requirements imposed by the EC shall be followed. Clinical trial insurance is provided to study subjects by the sponsor for medical expenses incurred from bodily injury during clinical testing. ivWatch, LLC will finance the entire clinical investigation. There is no separate financial agreement between the sponsor, the investigation site, or the ivWatch investigators (Jason Naramore and Marisa Brown) because they are all part of the same

organization. Additionally, no agreement is needed between the manufacturer and the sponsor since they are the same entity.

Informed Consent Process

The informed consent process will take place on the day of the participant's site visit, prior to any study procedures. The investigators will not proceed with a case study until the consent form has been completely read, understood, and signed by that participant. Prior to obtaining informed consent signatures, the study procedures will be verbally described to each participant, and the investigators or their designees will address any outstanding questions or concerns. Participants will be given a copy of their signed informed consent form prior to any study procedures. If new information becomes available during the study, current participants will be notified while they are at the study center. The investigators and staff members who are designated informed consent duties will receive the proper informed consent training prior to the study.

No minors will be included in the study, nor is there expected to be a scenario where the participant is unable to give their consent (i.e., no emergency treatment). See QF-1002159 for the informed consent form and information on compensation.

Adverse Events, Adverse Device Effects, and Device Deficiencies

The definitions for adverse events, adverse device effects, device deficiencies, and serious adverse events are listed in Procedure-0000244, Conducting Human Clinical Trials. Non-reportable adverse events for this study include: allergic reaction, a mild skin reaction (pain, inflammation, irritation, redness, razor bumps/burn/cut/nick), slip/trip/fall injury, foodborne illness, or illness from infectious disease (e.g., common cold). These are not reportable because they are common background events in daily life, unrelated to the investigational device/trial procedures, or they are mild, self-limiting, and not clinically significant. Since the investigation is self-funded and the site and sponsor are one in the same, it will not be necessary to report adverse events or device deficiencies to the sponsor. Adverse events and device deficiencies will both be recorded using the approved Case Report Form. Adverse events will be reported using Form-0000184 (Clinical Investigation Adverse Event Report) and device deficiencies will be reported using QF-1002063 (Clinical Investigation Device Deficiency Report). Both report forms will also be used to evaluate the need for follow-up on the event. Foreseeable adverse events and anticipated adverse device effects can be seen in Table 4.

Reportable adverse events will be reported as soon as possible, but no later than ten (10) business days from the time the Investigator learns of the event to the IRB. If that cannot be completed, emergency contact details for Advarra are listed in the General Information section. Reportable adverse events include any serious adverse events involving enrolled participants that are determined to be unexpected and possibly, probably, or definitely related to the test device or research procedures. A serious adverse event that is expected, as identified in the study documentation, but is occurring at greater frequency or severity will be reported to the IRB as an unanticipated problem.

Between Table 4 and Form-0000182, Medical Device and Clinical Trial Protocol Risk Determination Form, these two have foreseeable adverse events and anticipated adverse device effects with their likely incidence, mitigation,

and/or treatment for this study. Based on the risk assessment performed with Form-0000182, a data safety monitoring committee is not needed since the study has been classified as non-significant risk (NSR) and all risks are in the “acceptable” range pre- and post-mitigation.

Vulnerable Population

No vulnerable populations will be specifically targeted for enrollment. However, the elderly or those aged 65 years and older may participate in this study. This vulnerable population will be identified during recruitment and will be given ample time to review the informed consent form with family member(s) and/or significant other(s) prior to their study center visit.

The IRB is responsible for reviewing and approving information about the recruitment of potentially vulnerable participants and the procedures used to protect their rights and welfare. This review shall take place before these potentially vulnerable participants are recruited for the study.

Follow-up and medical care are not expected after the participant has completed the investigation. The investigation does not involve an expected direct benefit for the participant.

Suspension, Premature Termination, or End of Clinical Investigation

The clinical investigation will be complete when the last participant with acceptable data has finished their 24-hour study center visit, making 20 accepted case studies. Suspension or premature termination of the study may happen if the safety of participants or integrity of the trial are compromised. If suspension or premature termination of the investigation occurs, (1) the decision shall be justified in writing and communicated to all parties promptly (including the IRB), (2) ivWatch as sponsor shall provide resources to fulfil the obligations from this plan and any existing agreements for following up/continued care of participants enrolled in the clinical investigation, and the (3) PI shall promptly inform the enrolled participants.

There is no blinding or masking code in this study. There is also no expected need for follow-up or continued care following a termination or temporary halt of the investigation as this investigation is with healthy adults.

A termination report will be filed with the IRB within six months of the end of the study and a final report with an easily understandable summary will be created and stored with the sponsor, ivWatch, within six months.

Publication Policy

The clinical investigation plan will be registered in a publicly accessible database (clinicaltrials.gov) and results will be made publicly available after the conclusion of the trial. Results may also be published in various healthcare segments relating to vascular access, such as the Infusing Nurses Society and Association for Vascular Access within three years of completion. The sponsor, ivWatch, will approve any publication released because of this research study. Authorship, from the International Committee of Medical Journal Editors, will be based on the following criteria²:

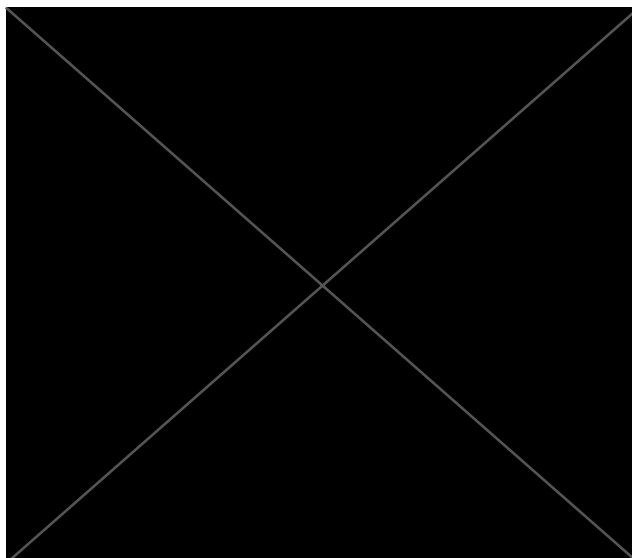
1. Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND
2. Drafting the work or reviewing it critically for important intellectual content; AND
3. Final approval of the version to be published; AND
4. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Investigator Signatures

I certify that I am knowledgeable about the regulations and policies governing research with human subjects. I have reviewed this document and agree to conduct the study in accordance with the approved protocol.

Principal Investigator

Investigator



Bibliography

1. Ho, B. K., & Robinson, J. K. (2015). Color bar tool for skin type self-identification: A cross-sectional study. *Journal of the American Academy of Dermatology*, 73(2), 312–3.e1.
<https://doi.org/10.1016/j.jaad.2015.05.024>
2. *Defining the role of authors and contributors*. ICMJE. (n.d.).
<https://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html>

Appendix A - Clinical studies performed with the Fiber Optic Sensor

Study	Purpose	Outcome	Key Performance Metrics
NIR Detection of PIV Infiltration <i>ivWatch Study ID: IVWRSCS-01</i> <i>Chesapeake IRB ID: 00008513</i> <i>Number of Subjects: 24</i> <i>Number of Sites: 48</i> <i>Dates: June-August 2013</i>	- Investigate <i>in vivo</i> model of subcutaneous injections near vascular bundles as substitute to through vein infiltrations. - Validate sensor and receptacle designs. - Investigate and validate effect of tissue blood volume changes on signal.	- Subcutaneous injections are more challenging to detect. - Validated the sensor and receptacle designs. - Insensitive to changes in the tissue blood volume.	Diagnostic Performance (all, subcutaneous, through-vein): - Sensitivity: 90%, 83%, 96% - Specificity: 100%, 100%, 100% Detected Volume: - Through-Vein: 2.0mL - Subcutaneous: 3.3mL
The Signal Variation of Normal Tissue <i>ivWatch Study ID: IVW400CS-01</i> <i>Chesapeake IRB ID: 00008218</i> <i>Number of Subjects: 30</i> <i>Number of Sites: 30</i> <i>Dates: August-November 2013</i>	- Identify sources of non-infiltration notifications. - Estimate rates of non-infiltration notifications for patients in an environment that mimics a hospital room. - Investigate potential interference between other near infrared devices.	- Negligible impact on clinical alarm fatigue. - Non-infiltration notifications generated by tissue deformation. - No infiltration notifications due to device interference.	Red Notification Rate: 0.11 red notifications / day 3 notifications in 661 hours Yellow Notification Rate: 0.40 yellow notifications / day 11 notifications in 661 hours
The Effect of Catheter Depth <i>ivWatch Study ID: IVW400CS-02</i> <i>Chesapeake IRB ID: 00008254</i> <i>Number of Subjects: 28</i> <i>Number of Sites: 56</i> <i>Dates: September-October 2013</i>	- Determine relationship between infiltration depth and ivWatch sensitivity. - Investigate tissue characteristics that affect ivWatch performance.	- Validation of optical modeling. - ivWatch sensitivity greatest for infiltration depths < 5mm. - Presence of a fascia interposed between catheter tip and sensor reduces sensitivity.	Depths Less than 5mm (On-Design) 1-3mm Deep: 100% sensitive (12/12) 3-5mm Deep: 100% sensitive (17/17) Depths Greater than 5mm (Off-Design): 5-7mm Deep: 38% sensitive (5/13) 7-9mm Deep: 50% sensitive (7/14)
The Effect of Infiltration Rate <i>ivWatch Study ID: IVW400CS-03</i> <i>Chesapeake IRB ID: 00008941</i> <i>Number of Subjects: 24</i> <i>Number of Sites: 48</i> <i>Dates: October-November 2013</i>	- Determine volumes of infiltration fluid required to generate notification as a function of infiltration flow rate. - Determine times required to generate a notification as a function of infiltration flow rate.	- Detected all infiltrations regardless of infiltration rate. - The response time of the system strongly determines the detected volume when the device notifies a clinician.	Sensitivity & Median Detected Volume 5mL/hr: 100% (12/12) and 0.9mL 50mL/hr: 100% (12/12) and 2.2mL 100mL/hr: 100% (12/12) and 3.7mL 150mL/hr: 100% (12/12) and 5.7mL

Study	Purpose	Outcome	Key Performance Metrics
Long Term Adhesion of the ivWatch Receptacle <i>ivWatch Study ID: IVW400CS-04</i> <i>Chesapeake IRB ID: 00008891</i> <i>Number of Subjects: 6</i> <i>Number of Sites: 18</i> <i>Dates: October 2013</i>	1. Evaluate ability of receptacle to remain adhered to skin over 96-hour period. 2. Evaluate skin integrity after receptacle was adhered for 96 hours. 3. Identify activities that may degrade adhesion of receptacle to the skin.	• ivWatch receptacles remained adhered to skin for 96 hours when combined with occlusive dressing. • The ivWatch receptacle did not cause significant disruption to skin integrity after 96 hours.	Average Adhesion Time: • <i>Receptacle Only:</i> 68 hrs (6 sites) • <i>Receptacle & Dressing:</i> 96 hrs (6 sites) • <i>Receptacle, Dressing, Sensor:</i> 96 hrs (6 sites)
Device Validation for Non-Infiltrated Tissues <i>ivWatch Study ID: IVW400CS-05</i> <i>Chesapeake IRB ID: 00009175</i> <i>Number of Subjects: 40</i> <i>Number of Sites: 40</i> <i>Dates: January 2014</i>	1. Validation trial measuring safety and efficacy of final Model 400 device when monitoring non-infiltrated tissues. 2. Estimate rates of non-infiltration notifications for active patients in a hospital room environment. 3. Demonstrate performance in the presence of interference sources.	• Device can monitor normal tissue with minimal impact on clinical alarm fatigue. • The device can be used without skin irritation or disruption to the skin integrity. • The device operates properly in cases of interference by other light sources.	Red Notification Rate: • 0.24 red notifications / day • 1 red notification every 4.2 days • 9 notifications in 900 hours Yellow-Only Notification Rate: • 0.51 yellow notifications / day • 1 yellow notification every 2.0 days • 19 notifications in 900 hours
Device Validation for Infiltrated Tissues <i>ivWatch Study ID: IVW400CS-06</i> <i>Chesapeake IRB ID: 00009285</i> <i>Number of Subjects: 70</i> <i>Number of Sites: 140</i> <i>Dates: February 2014</i>	2. Validation trial measuring safety and efficacy of final Model 400 device when monitoring infiltrated tissues. 3. Estimate sensitivities of device for detecting early-stage infiltrations (< 10mL infiltrated fluid). 4. Demonstrate significant improvement compared to routine observation by a perfect clinician.	• Detected vast majority of infiltrations regardless of infiltration rate, PIV location, skin pigmentation, or body type. • Significant improvement compared to the current standard – routine observation by a nurse. • No safety concerns were observed – no skin irritation or disruption to skin integrity	Red Notification Sensitivity: • 96.4% Sensitivity • Red notification on 135 out of 140 cases • 91.4 to 98.7% for 95% Conf. Interval Yellow Notification Sensitivity: • 99.3% Sensitivity • Yellow notification on 139 out of 140 cases • 95.5 to 99.96% for 95% Conf. Interval
The Effect of Sensor-to-Catheter Distance <i>ivWatch Study ID: IVW-CLR-CS12-400</i> <i>Chesapeake IRB ID: 00010217</i> <i>Number of Subjects: 23</i> <i>Number of Sites: 46</i> <i>Dates: November 2014</i>	1. Quantify the sensitivity of the ivWatch device for each catheter-to-sensor distance. 2. Estimate the detected volume for the yellow and red notifications of the ivWatch device as a function of catheter-to-sensor distance.	• The device detected most infiltrations although the detected volume increased for larger sensor-to-catheter separations • The device sensitivity decreases with larger separations consistent with the hypothesis that the infiltration does not always diffuse uniformly.	Sensitivity: • 100% for 10 & 20mm separations • 90% for 30mm separation • 89% for 40mm separation • 78% for 50mm separation Detected Volume (Median): • 2.8, 7.7, 12.3, 21.7, 32.8 mL for 10, 20, 30, 40, 50mm separations, respectively.

Study	Purpose	Outcome	Key Performance Metrics
Infiltration Detection when Placing Over the Dressing <i>ivWatch Study ID:</i> IVW-CLR-CS15-400 <i>Chesapeake IRB ID:</i> 00013715 <i>Number of Subjects:</i> 24 <i>Number of Sites:</i> 48 <i>Dates:</i> October 2015	1. Estimate the difference in detected volume when placing above and below dressing. 2. Demonstrate statistically significant improvement for detecting early stage infiltrations in comparison to hourly observations by a perfect clinician.	• The device detected most infiltrations with no statistically significant difference in sensitivities for over or under the dressing. • No statistically significant difference between detected volumes for over or under the dressing.	Sensitivity: • 100% (24/24) for under the dressing • 95.8% (23/24) for over the dressing Detected Volume (Mean): • 2.93 and 2.75 mL for under and over the dressing, respectively.
Performance for Non-Infiltrated Tissues when Placing Over Transparent Occlusive Dressing <i>ivWatch Study ID:</i> IVW-CLR-CS16-400 <i>Chesapeake IRB ID:</i> 00015068 <i>Number of Subjects:</i> 25 <i>Number of Sites:</i> 25 <i>Dates:</i> April-June 2016	1. Estimate the non-infiltration red and yellow notification rates for the ivWatch device. 2. Determine whether the over-the-dressing red notification rate is significantly less than 1 false red notification per day.	• Red and yellow notification rates occur less than once per day. • Device can monitor normal tissue while placed over a clear occlusive dressing with minimal impact on clinical alarm fatigue. • Slightly higher notification rates than previous motion studies.	Red Notification Rate: • 0.44 red notifications / day • 1 red notification every 2.28 days • 10 notifications in 548 hours Yellow-Only Notification Rate: • 0.57 yellow notifications / day • 1 yellow notification every 1.76 days • 13 notifications in 548 hours
Optical Detection of Intravenous Infiltration: A Pilot Study <i>ivWatch Study ID:</i> IVW400CS-09 <i>CCCHMC IRB ID:</i> 2015-0896 <i>Number of Subjects:</i> 243 <i>Dates:</i> August 2015 to July 2016	1. Clinical trial in a children's hospital to demonstrate safety and efficacy in pediatric subjects. 2. Time to detection – estimate difference in time when infiltration is detected by clinician and ivWatch. 3. Device sensitivity – estimate ivWatch sensitivity at identifying infiltrations before the clinician. 4. Notification Rate – estimate of the number of notifications per day without clinician-confirmed infiltrations.	• The device detected and alerted clinicians of infiltrations several hours before they are normally found by clinician assessment • The device performance did not depend on the age / size of the subject	Time to detection: • Median time difference: 15.2 hours • Range: 1.3 to 99.8 hours Sensitivity: • 78.3% (18/23) for Non-alarming group • 80.0% (12/15) for Alarming group Notification Rate: • 0.28 red notifications / day • 0.27 yellow notifications / day

Study	Purpose	Outcome	Key Performance Metrics
Long-Term Adhesion of 3-Year Real-Time Aged ivWatch Sensor Receptacle <i>ivWatch Study ID:</i> IVW-CLR-CS32-400 <i>Advarra IRB ID:</i> 00055473 <i>Number of Subjects:</i> 6 <i>Dates:</i> July 2021	1. Clinical investigation at ivWatch, LLC to determine if Sensor Receptacles that are real-time aged for 3 years maintain ability to remain well-adhered to the skin for at least 24 hours. 2. Determine if any updates are required for the instructions for use or labels to assure proper usage of the Sensor Receptacle. 3. Determine if there are issues with skin integrity after wearing the Sensor Receptacle for up to 96 hours, including potential allergic reactions.	• All Sensor Receptacles were adhered for more than 24 hours, five for 96 continuous hours. • Sensor Receptacle performance after a shelf life of 3 years is acceptable. • No allergic reactions or skin integrity issues resulting from adhesion.	• Five of six (5/6) receptacles remained adhered for 96-hours. • No updates to instructions for use were needed. • No issues with skin integrity after 96-hours of wear.

Appendix B - Clinical studies performed with SmartTouch Sensor

Study	Purpose	Outcome	Key Performance Metrics
Monitoring Infiltrated Tissues <i>ivWatch Study ID: IVW-CLR-CS19-400</i> <i>Chesapeake IRB ID: 00023277</i> <i>Number of Subjects: 64</i> <i>Number of Sites: 128</i> <i>Dates: November 2017</i>	1. Determine if infiltration signals measured with the SmartTouch Sensor are equivalent to those measured with the Model 400 sensor. 2. Contribute study data to a database of ivWatch signals of infiltrated tissue. 3. Evaluate processing algorithms to optimize performance of the ivWatch infiltration detection algorithm.	• No statistical difference in the performance of the SmartTouch Sensor versus the Model 400 fiber optic sensor, when accounting for catheter depth and distance using a linear regression model. • Catheter depth and distance were significantly different than IVW-CLR-CS06-400, impacting sensitivity but not detection volume.	Red Notification Sensitivity: • 91.4% Sensitivity • Red notification in 117 out of 128 cases Yellow Notification Sensitivity: • 93.0% Sensitivity • Yellow notification in 119 out of 128 cases Detected Volume (mean): • Red notification: 3.7mL • Yellow notification: 3.3mL
Signal Variation of Normal Tissue <i>ivWatch Study ID: IVW-CLR-CS20-400CS</i> <i>Chesapeake IRB ID: 00023891</i> <i>Number of Subjects: 30</i> <i>Number of Sites: 30</i> <i>Dates: December 2017- January 2018</i>	1. Quantify the signal variation of normal tissue in a setting that approximates the hospital room environment. This includes calculating distribution metrics such as mean and standard deviation for the collected signals. 2. Evaluate processing algorithms to optimize performance of the ivWatch device with SmartTouch Sensor. 3. Determine if non-infiltration red-notification and yellow-notification rates are equivalent to those recorded with the Model 400 sensor.	• The SmartTouch Sensor has a similar false-notification performance to the Model 400 fiber optic sensor. • Both red and yellow estimated notification rates are within the 95% confidence intervals reported in “ivWatch Model 400: Device Validation for Non-Infiltrated Tissues”.	Red Notification Rate: • 0.315 red notifications / day • 1 red notification every 3.2 days • 9 notifications in 686 hours • 95% confidence interval 0.133 to 0.733 red notifications / day Yellow Notification Rate: • 0.455 yellow notifications / day • 1 yellow notification every 2.2 days • 13 notifications in 686 hours • 95% confidence interval: 0.176 to 1.139 yellow notifications / day
Device Verification for Infiltrated Tissues <i>ivWatch Study ID: IVW-CLR-CS22-400</i> <i>Advarra IRB ID: 00030567</i> <i>Number of Subjects: 128</i> <i>Number of Sites: 256</i> <i>Dates: December 2018</i>	1. Determine if infiltration sensitivity measured with the SmartTouch Sensor is equivalent to the Model 400 fiber optic sensor. 2. Contribute study data to a database of ivWatch signals of infiltrated tissue. 3. Evaluate processing algorithms to optimize performance of the ivWatch device with SmartTouch Sensor.	• Sensitivity and detection volume performance of the SmartTouch and fiber optic sensors are equivalent. • SmartTouch Sensor is capable of issuing notifications at small volumes than the fiber optic sensor with the optimized detection algorithm.	SmartTouch Sensor: Red Notification Sensitivity • 96.9% sensitivity • Red notification in 124 out of 128 cases Yellow Notification Sensitivity • 98.4% sensitivity • Yellow notification in 126 out of 128 cases Detected Volume (mean) • Red notification: 2.36 mL • Yellow notification: 2.21 mL

Study	Purpose	Outcome	Key Performance Metrics
			Fiber Optic Sensor: Red Notification Sensitivity 85.9% sensitivity - Red notification in 110 out of 128 cases Yellow Notification Sensitivity 92.2% sensitivity - Yellow notification in 118 out of 128 cases Detected Volume (mean) - Red notification: 3.63 mL - Yellow notification: 3.41 mL
Device Verification for Non-Infiltrated Tissues <i>ivWatch Study ID: IVW-CLR-CS23-400</i> <i>Advarra IRB ID: 00030569</i> <i>Number of Subjects: 30</i> <i>Number of Sites: 60</i> <i>Dates: December 2018 – January 2019</i>	- Quantify the non-infiltration red-notification and yellow-notification rates for the SmartTouch Sensor. - Determine if non-infiltration red-notification and yellow-notification rates of the SmartTouch Sensor are equivalent to the Model 400 fiber optic sensor. - Evaluate signal processing algorithms to optimize performance of the ivWatch device with SmartTouch Sensor.	- Red and yellow notification rates occur less than once per day for both sensors. - SmartTouch Sensor has similar or better false-notification performance than the fiber optic sensor. - There were no cases of de-adhesion with the SmartTouch Sensor. - Both sensors can monitor normal tissue with minimal impact on clinical alarm fatigue. - Both sensors can be used without skin irritation or disruption to the skin integrity.	SmartTouch Sensor: Red Notification Rate 0.136 notifications / day 1 red notification every 7.3 days 4 notifications in 705 hours Yellow-Only Notification Rate 0.272 notifications / day 1 yellow notification every 3.7 days 8 notifications in 705 hours Fiber Optic Sensor: Red Notification Rate 0.374 notifications / day 1 yellow notification every 2.7 days 11 notifications in 707 hours Yellow-Only Notification Rate 0.272 notifications / day 1 yellow notification every 3.7 days 8 notifications in 707 hours

Study	Purpose	Outcome	Key Performance Metrics
The Effect of PIV Depth and Site <i>ivWatch Study ID: IVW-CLR-CS25-400</i> <i>Advarra IRB ID: 00032269</i> <i>Number of Subjects: 64</i> <i>Number of Sites: 128</i> <i>Dates: March 2019</i>	1. Determine whether the catheter depth has a significant effect on the measured infiltration signal. 2. Determine whether the catheter site has a significant effect on the measured infiltration signal. 3. Contribute study data to a database of ivWatch signals of infiltrated tissue. 4. Evaluate processing algorithms to optimize performance of future ivWatch devices.	• Detection volume decreases for infiltrated tissues closer to the skin surface due to a greater proportion of the detected photons propagating through the shallow layers of tissue relative to the deeper layers. • Depth coefficients from the linear regression models show a detection volume increase of ~0.65 mL / mm depth.	SmartTouch Sensor: Red Notification Sensitivity <i>Site Portion</i> • 100% (24/24) for hand • 96% (23/24) for forearm • 87% (21/24) for antecubital fossa (AC) <i>Depth Portion</i> • 100% (14/14) for 2 mm • 100% (14/14) for 4 mm • 93% (13/14) for 6 mm • 93% (13/14) for 8 mm Yellow Notification Sensitivity <i>Site Portion</i> • 100% (24/24) for hand • 100% (24/24) for forearm • 87% (21/24) for AC <i>Depth Portion</i> • 100% (14/14) for 2 mm • 100% (14/14) for 4 mm • 100% (14/14) for 6 mm • 93% (13/14) for 8 mm Detected Volume (mean) <i>Site Portion</i> • 2.06 mL for hand, 2.05 mL for forearm, and 5.37 mL for AC <i>Depth Portion</i> • 1.55 mL for 2 mm, 4.08 mL for 4 mm, 4.78 mL for 6 mm, 3.73 mL for 8 mm
Device Verification for Non-Infiltrated Tissues, Part II <i>ivWatch Study ID: IVW-CLR-CS26-400</i> <i>Advarra IRB ID: 00032326</i> <i>Number of Subjects: 15</i> <i>Number of Sites: 30</i> <i>Dates: February – March 2019</i>	1. Quantify the non-infiltration red-notification and yellow-notification rates for the SmartTouch Sensor. 2. Evaluate processing algorithms to optimize performance of the ivWatch device with the SmartTouch Sensor. 3. Determine if non-infiltration red-notification and yellow-notification rates are equivalent to those recorded with the Model 400 sensor.	• Red and yellow notification rates occur less than once per day for both sensors. • SmartTouch Sensor has similar or better false-notification performance than the fiber optic sensor. • Sensor placement on the AC site could cause a higher yellow notification rate than other sites	SmartTouch Sensor: Red Notification Rate • 0.137 notifications / day • 1 red notification every 7.3 days • 4 notifications in 700 hours Yellow-Only Notification Rate • 0.206 notifications / day • 1 yellow notification every 4.9 days • 6 notifications in 700 hours

Study	Purpose	Outcome	Key Performance Metrics
		due to the chance of the sensor being pressed into the tissue.	
Device Validation for Infiltrated Tissues <i>ivWatch Study ID: IVW-CLR-CS27-400</i> <i>Advarra IRB ID: 00032924</i> <i>Number of Subjects: 98</i> <i>Number of Sites: 196</i> <i>Dates: April 2019</i>	1. Demonstrate a statistically significant improvement for detecting early stage infiltrations in comparison to hourly observation by a perfect clinician. 2. Demonstrate statistical equivalence in infiltration detection volume of the SmartTouch and Fiber Optic sensors. 3. Demonstrate statistical equivalence in infiltration sensitivity of the SmartTouch and Fiber Optic sensors.	• Results indicate there is no difference in the sensitivity performance of the SmartTouch and fiber optic sensors when monitoring infiltrated tissues. • Both sensors are highly sensitive and can alert clinicians to early stages of an infiltrated PIV site. • Yellow and red notification sensitivity for infiltrated tissue was 99.0% for SmartTouch and fiber optic sensors. • No significant skin irritation or disruption to skin integrity was observed from the 198 sites in this study. Consequently, the results of the study suggest the SmartTouch Sensor is as effective and safe as the fiber optic sensor.	SmartTouch Sensor: Red Notification Sensitivity: • 99.0% Sensitivity • Red notification on 97 out of 98 cases • 94.5 to 100.0% for 95% Conf. Interval Red Notification Detection Volume • 2.13 ± 1.45 mL Yellow Notification Sensitivity: • 99.0% Sensitivity • Yellow Notification on 97 out of 98 cases • 94.5 to 100.0% for 95% Conf. Interval Yellow Notification Detection Volume • 2.02 ± 1.39 mL Fiber Optic Sensor: Red Notification Sensitivity: • 99.0% Sensitivity • Red notification on 97 out of 98 cases • 94.5 to 100.0% for 95% Conf. Interval Red Notification Detection Volume • 4.33 ± 2.11 mL Yellow Notification Sensitivity: • 99.0% Sensitivity • Yellow notification on 97 out of 98 cases • 94.5 to 100.0% for 95% Conf. Interval Yellow Notification Detection Volume • $3.87 \text{ mL} \pm 1.89 \text{ mL}$
Device Validation for Non-Infiltrated Tissues <i>ivWatch Study ID: IVW-CLR-CS24-400</i> <i>Advarra IRB ID: 00031926</i> <i>Number of Subjects: 40</i> <i>Number of Sites: 80</i> <i>Dates: April – June 2019</i>	1. Quantify the non-infiltration red-notification and yellow-notification rates for the SmartTouch Sensor and Model 400 fiber optic sensor side-by-side. 2. Determine if non-infiltration red-notification and yellow-notification rates of the SmartTouch Sensor are equivalent to the Model 400 fiber optic sensor. 3. Identify conditions that may cause a non-infiltration notification.	• Red and yellow notification rates occur less than once per day for both sensors. • Red and yellow non-infiltration notification rates of the SmartTouch Sensor are sufficiently small, suggesting the SmartTouch Sensor should have a minimal impact on clinical alarm fatigue.	SmartTouch Sensor: Red Notification Rate: • 0.159 red notifications / day • 1 red notification every 6.29 days • 6 notifications in 922 hours Yellow-Only Notification Rate: • 0.209 yellow notifications / day • 1 yellow notification every 4.78 days • 8 notifications in 922 hours

Study	Purpose	Outcome	Key Performance Metrics
		• More false notifications were observed with the fiber optic sensor, which appear to be related mostly to receptacle de-adhesion events that compromise sensor-to-skin optical coupling. • No cases of skin irritation, disruption to skin integrity, or adverse events, the study suggests the ivWatch SmartTouch Sensor is as safe as the fiber optic sensor and receptacle when used according to the instructions for use.	Fiber Optic Sensor: Red Notification Rate: • 0.419 red notifications / day • 1 red notification every 2.39 days • 16 notifications in 922 hours Yellow-Only Notification Rate: • 0.661 yellow notifications / day • 1 yellow notification every 1.51 days • 24 notifications in 922 hours
Long Term Adhesion of ivWatch SmartTouch Sensor <i>ivWatch Study ID: IVW-CLR-CS28-400</i> <i>Advarra IRB ID: 00036605</i> <i>Number of Subjects: 6</i> <i>Number of Sites: 12</i> <i>Dates: June 2019</i>	1. Evaluate the design of the SmartTouch Sensor and its ability to remain well-adhered to the skin for at least 24 hours. 2. Determine if SmartTouch Sensors aged for 1 year maintain ability to remain well-adhered to the skin for at least 24 hours. 3. Determine if any updates are required for the instructions for use or labels to assure proper usage of the SmartTouch Sensor. 4. Determine if there are issues with skin integrity after wearing the SmartTouch Sensor for 96 hours including potential allergic reactions.	• Unaged and aged SmartTouch Sensor remained well adhered to skin for the duration of the study (96 hours). • Both unaged and aged SmartTouch Sensors can be used without skin irritation or disruption to the skin integrity.	• All SmartTouch Sensors remained well-adhered for 96-hours. • No updates to instructions for use are needed. • No issues with skin integrity after 96-hours of wear.
Long Term Adhesion of 1-Year Real-Time Aged ivWatch SmartTouch Sensors and 2 Year Real-Time Aged Receptacles <i>ivWatch Study ID: IVW-CLR-CS30-400</i> <i>Advarra IRB ID: 00040968</i> <i>Number of Subjects: 6</i> <i>Number of Sites: 12</i> <i>Dates: January 2020</i>	SmartTouch Sensor 1. Determine if SmartTouch Sensors real-time aged for 1 year maintain ability to remain well-adhered to the skin for at least 24 hours. 2. Determine if any updates are required for the instructions for use or labels to assure proper usage of the SmartTouch Sensor. 3. Determine if there are issues with skin integrity after wearing the SmartTouch Sensor for 96 hours including potential allergic reactions. Fiber Optic Receptacle	• SmartTouch Sensor remained well adhered to skin for the duration of the study (96 hours). • SmartTouch Sensors real-time aged one year and receptacles real-time aged two years can be used without skin irritation or disruption to the skin integrity.	SmartTouch Sensor • All SmartTouch Sensors remained well-adhered for 96-hours. • No updates to instructions for use were needed. • No issues with skin integrity after 96-hours of wear. Fiber Optic Sensor • Five of six (5/6) receptacles remained adhered for 96-hours.

Study	Purpose	Outcome	Key Performance Metrics
	- Determine if the receptables real-time aged for 2 years maintain ability to remain well-adhered to the skin for at least 24 hours. - Determine if any updates are required for the instructions for use or labels to assure proper usage of the receptacle. - Determine if there are issues with skin integrity after wearing the receptacle for 96 hours including potential allergic reactions.		- No updates to instructions for use were needed. - No issues with skin integrity after 96-hours of wear.
Long-Term Adhesion of 2-Year Accelerated Aged ivWatch SmartTouch Sensor <i>ivWatch Study ID: IVW-CLR-CS31-400</i> <i>Advarra IRB ID: 00048146</i> <i>Number of Subjects: 6</i> <i>Dates: January 2021</i>	- Determine if SmartTouch Sensors aged for two years maintain ability to remain well-adhered to the skin for at least 24 hours. - Determine if any updates are required for the instructions for use or labels to assure proper usage of the SmartTouch Sensor. - Determine if there are issues with skin integrity after wearing the SmartTouch Sensor for 96 hours including potential allergic reactions.	- All SmartTouch Sensors were well-adhered for 96 hours. - No allergic reactions or skin integrity issues resulting from adhesion.	- All SmartTouch Sensors remained well-adhered for 96-hours. - No updates to instructions for use were needed. - No issues with skin integrity after 96-hours of wear.
Long-Term Adhesion of 2-Year Real-Time Aged ivWatch SmartTouch Sensor <i>ivWatch Study ID: IVW-CLR-CS33-400</i> <i>Advarra IRB ID: 00067760</i> <i>Number of Subjects: 6</i> <i>Dates: December 2022</i>	- Determine if SmartTouch Sensors real-time aged for two years maintain ability to remain well-adhered to the skin for at least 24 hours. - Determine if any updates are required for the instructions for use or labels to assure proper usage of the SmartTouch Sensor. - Determine if there are issues with skin integrity after wearing the SmartTouch Sensor for 96 hours including potential allergic reactions.	- All SmartTouch Sensors were well-adhered for 96 hours. - No allergic reactions or skin integrity issues resulting from adhesion.	- All SmartTouch Sensors remained well-adhered for 96-hours. - No updates to instructions for use were needed. - No issues with skin integrity after 96-hours of wear.
Long-Term Adhesion of 3-Year Real-Time Aged ivWatch SmartTouch Sensor <i>ivWatch Study ID: IVW-CLR-CS34-400</i> <i>Advarra IRB ID: 00074926</i> <i>Number of Subjects: 6</i> <i>Dates: Nov-Dec 2023</i>	- Determine if SmartTouch Sensors real-time aged for 3 years maintain ability to remain well-adhered to the skin for at least 24 hours. - Determine if any updates are required for the instructions for use or labels to assure proper usage of the SmartTouch Sensor. - Determine if there are issues with skin integrity after wearing the SmartTouch Sensor for 96 hours, including potential allergic reactions.	- All SmartTouch Sensors were adhered at 96 hours. - No allergic reactions or skin integrity issues resulting from adhesion.	- All SmartTouch Sensors remained adhered for 96-hours. - No updates to instructions for use were needed. - No issues with skin integrity after 96-hours of wear.

Appendix C – Electronic Case Report Form (eCRF)

 **New CS37 Case Report Form**

CRF Number

Camera ID

Normal
Status Reason

CS37 CRF
Active for less than one minute

Data Capture (< 1 Min)

Verification

Validation

Demographics

Pre-Study

Routine Checks

Post-Study

Investigator Questions

Form assist

General Study Information

CRF Number

*

Study Start Date

Checkpoint

Eligible via Health History Form

Participant received copy of complete ICF

Health History Note

Important health info. to relay to team?

Who presented information to the team?

Staff who were informed: N/A

Daytime staff

Investigator(s)

Overnight staff

Participant Information and Measurements

Sex

Age (years)

Weight (lbs)

Ⓢ Weight (lbs): Weight cannot be less than 50 lbs

Height (in)

Ⓢ Height (in): Height cannot be less than 12 in

Calculated BMI

1

2

3

4

5

6

Guided color bar survey number

Simulated IV Site Configuration

Side of site

Site

0

004 - Saved
CS37 Case Report Form

004
CRF Number

Camera ID

Normal
Status Reason

CS37 CRF
Active for less than one minute

Data Capture (< 1 Min)

Verification

Validation

DemographicsPre-StudyRoutine ChecksPost-StudyInvestigator QuestionsRelated

Form assist

Health History Note

Important health info. to relay to team?	---	Who presented information to the team?	---
Staff who were informed: N/A	☐	Daytime staff	☐
Investigator(s)	☐	Overnight staff	☐

Pre-Study Notes

Pre-study notes

Pre-Study Information

Camera ID	---	NIR Vein photo (pre-study)	Choose File No file chosen
Model 400 serial number	---	Bare site photo (pre-study)	Choose File No file chosen
Extension Module serial number	---	Dressed site photo (pre-study)	Choose File No file chosen
Patient Cable Lot Number	---	Ultrasound Image Time (Out-of-Plane, pre-study)	---
Milky Way sensor lot-serial number	---	Ultrasound Image Time (In-Plane, pre-study)	---
Has the participant applied lotion today at the monitoring site?	---		

Case Study Start Information

Data start date and time

Pre-Study Uploads

Ultrasound Image (Out-of-Plane, pre-study)	Choose File No file chosen	Ultrasound Image (In-Plane, pre-study)	Choose File No file chosen
--	---	--	---

004 - Saved
CS37 Case Report Form

004
CRF Number

Camera ID

Normal
Status Reason

CS37 CRF
Active for less than one minute

Data Capture (< 1 Min)

Verification

Validation

Demographics Pre-Study **Routine Checks** Post-Study Investigator Questions Related

Form assist

Health History Note

Important health info. to relay to team? ---
Staff who were informed: N/A ☐
Investigator(s) ☐
Who presented information to the team? ---
Daytime staff ☐
Overnight staff ☐

Routine Check Notes

Additional comments related to the case study ---

Routine Check 1

Date and time 1 ---
Site photo 1

Choose File

 No file chosen
N/A ☐

Routine Check 2

Date and time 2 ---
Site photo 2

Choose File

 No file chosen
N/A ☐

Routine Check 3

Date and time 3 ---
Site photo 3

Choose File

 No file chosen
N/A ☐

Routine Check 4

Date and time 4

Site photo 4

 No file chosen

N/A

☐**Routine Check 5**

Date and time 5

Site photo 5

 No file chosen

N/A

☐**Routine Check 6**

Date and time 6

Site photo 6

 No file chosen

N/A

☐**Routine Check 7**

Date and time 7

Site photo 7

 No file chosen

N/A

☐

0

004 - Saved
CS37 Case Report Form

004
CRF Number

Camera ID

Normal
Status Reason

CS37 CRF
Active for less than one minute

Data Capture (< 1 Min)

Verification

Validation

Demographics Pre-Study Routine Checks **Post-Study** Investigator Questions Related

Form assist

Health History Note

Important health info. to relay to team? ---

Who presented information to the team? ---

Staff who were informed: N/A ☐ Daytime staff ☐

Investigator(s) ☐ Overnight staff ☐

Closeout Notes

Closeout Notes ---

Case Study Stop Information

Data stop date and time ---

Post-Study Information

Dressed site photo (post-study)

Choose File

 No file chosen NIR Vein Photo (post-study)

Choose File

 No file chosen

Bare site photo (post-study)

Choose File

 No file chosen

Ultrasound Image Time (Out-of-Plane, post-study) --- Ultrasound Image Time (In-Plane, post-study) ---

Uploads

Miscellaneous file(s)

Choose File

 No file chosen Scanned participant activity log

Choose File

 No file chosen

Ultrasound Image (Out-of-Plane, post-study)

Choose File

 No file chosen Ultrasound Image (In-Plane, post-study)

Choose File

 No file chosen

0

004 - Saved
CS37 Case Report Form

004
CRF Number

Camera ID

Normal
Status Reason

CS37 CRF
Active for less than one minute

Data Capture (< 1 Min)

Verification

Validation

Demographics Pre-Study Routine Checks Post-Study Investigator Questions Related

Form assist

Protocol Deviations

Were there any protocol deviations?

Are any of these deviations reportable, as they affect a subject's rights, safety, and wellbeing, informed consent process, or the scientific integrity of the clinical investigation?

If yes to either deviation question, please explain and complete SF-1001021

Device Deficiencies/Malfunctions

Did the investigation device not perform as expected by the intended use when used per the instructions and the protocol? (device deficiency/malfunction)

Could this deficiency/malfunction have led to an adverse event?

If yes to either deficiency/malfunction question, please explain and complete QF-1002063

Adverse Events

Did the patient experience any unexpected harm associated with the device or the research protocol? (adverse event)

Is this adverse event reportable?

If yes to either adverse event question, please explain and complete Form-0000184

Risks

Were any new risks associated with the device, CIP, or clinical process identified? If yes, report to the PI, and complete Form-0000182.



Does the risk(s) pose a serious health threat? If yes, PI must suspend the clinical investigation immediately.

**Withdraw Status**

Please select the case closure status



Date of withdrawal

Reason for withdrawal, if identified

Describe the component(s) of the study from which the participant withdrew.

According to the protocol, is any follow up required?

Final Case Status

Final case status



Investigator signature



0

004 - Saved

CS37 Case Report Form

004

CRF Number

Camera ID

Normal

Status Reason

CS37 CRF

Active for less than one minute

Data Capture (< 1 Min)

Verification

Validation

Demographics

Pre-Study

Routine Checks

Post-Study

Documents

...

Form assist

Show Chart

New

Upload

Document Location

Open Location

Document Associated Grid

You don't have permissions to create folder in this location. Contact your Microsoft Teams owner or SharePoint administrator for access.

Appendix D – Pre-Screening Form

Interest in Upcoming ivWatch Study (CS37)

When you submit this form, it will not automatically collect your details like name and email address unless you provide it yourself.

* Required

By providing information in this form, you agree that ivWatch, LLC may contact you in relation to clinical trials at ivWatch and to contact you in the future to determine interest in related clinical trial activities. You also understand that the information you provide on this form will be added to an ivWatch, LLC database of persons who may qualify for study participation. ivWatch will not sell or disclose this information to third parties without my permission, except as required by law.

1. First name *

2. Last name *

3. Phone number *

4. Email address *

5. Age (years) *

6. Participant sex *

- ☐ Female
- ☐ Male
- ☐ Prefer not to say

7. Estimated height (ft & in) *

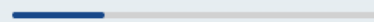
8. Estimated weight (lbs) *

9. Are you currently enrolled in any other research studies? *

- ☐ Yes
- ☐ No

[Next](#)

Page 1 of 4



Medical History

10. Do you have any allergies? *

Please consider medical adhesive allergies.

☒ Yes

☐ No

11. Please list your allergies and their severity.

Enter your answer

12. Do you have any medical conditions? *

Examples may include heart disease, chronic kidney disease, COPD, or cancer

☒ Yes

☐ No

13. Please list your medical conditions below.

Enter your answer

14. Do you take any medications on a regular basis? *

☒ Yes

☐ No

15. Please list the name(s) and a brief description(s) of the medications you take below.

Enter your answer

16. In the last 14 days, have you been sick, had an infection, or hospitalized? *

☒ Yes

☐ No

17. Please briefly describe your illness and/or hospitalization and the date it began.

Enter your answer

Back

Next

Page 2 of 4

Study-Specific Questions

18. Do you have any of the following on the back of either hand or either inner forearm? *

- ☐ Tattoos
- ☐ Extensive scarring
- ☐ Extensive bruising
- ☐ None of the above

19. Do you have any of the following? *

- ☐ Currently pregnant or trying to become pregnant
- ☐ Current alcohol or drug dependence
- ☐ Sleepwalking occurrence in the last year
- ☐ None of the above

[Back](#)[Next](#)

Page 3 of 4

20. Do you have a study partner that would also be interested in participating in the study with you?

☐ Yes

☐ No

21. Please list any overnight accommodations you may need (e.g. dietary restrictions or mobility concerns).

Enter your answer

22. Please list any other questions or comments below.

Enter your answer

23. I have been truthful about the information presented in this form. *

☐ I agree

Back

Submit

Page 4 of 4

Appendix E – Electronic Health History Form (eHHF)

New CS37 Health History Form - Unsaved

Active Status

Pending staff review
Status Reason

CS37 HHF
Active for less than one minute

Data Capture (< 1 Min)

Verification

Validation

General

Form assist

Participant Information

First name

Last name

Email

Phone

Age (years)

Participant sex

Estimated height (ft & in)

Estimated weight (lbs)

Medical History Questions

Other clinical studies?

No

Do you have any allergies?

No

Allergies list

N/A

Do you have any medical conditions?

No

Medical conditions list

N/A

Do you take any medications on a regular basis?

No

Medications list

N/A

Sick in the last 14 days

No

Describe illness/hospitalization

N/A

Study-Specific Questions

Do you have tattoos on the back of either hand or inner forearm?

No



Do you have extensive scar tissue on the back of either hand or inner forearm?

No



Do you have extensive bruising on the back of either hand or inner forearm?

No



(For females only) Are you currently pregnant or trying to become pregnant?

No



Do you have a current alcohol or drug dependence?

No



In the past year, have you had a sleepwalking occurrence?

No

**Additional Information**

Do you have a study partner that would also be interested in participating in this study with you?

No



Please list any overnight accommodations you may need (e.g. dietary restrictions or mobility concerns)

Please list any questions or comments below

Pre-study communication

Tattoo review - any tattoos that limit vein visualization on the dorsal aspect of the hand or the volar aspect of the forearm?

Appendix F – Participant Activity Log

Participant Activity Log ivWatch, LLC

CRF Number: _____

Whenever leaving the observation area, please provide the times and description of your activity. Examples may be “12:03-12:13 Went to kitchen for a snack”, “16:32-16:35 Bathroom”, “22:32-22:34 Brush teeth”, etc.

Start Time (HH:MM)	Stop Time (HH:MM)	Description of Activity

Appendix G – FDA Class Determination & Clearance Letters

The ivWatch technology is a non-significant risk device as determined by the FDA. In a face-to-face meeting with the FDA on March 28, 2014, the FDA classified the ivWatch Model 400 as a Class II, NSR device. The ivWatch Model 400 has received marketing clearance from the FDA for adults and pediatrics. Early prototypes of the Model 400 were evaluated in previous clinical studies with IRB approval. A list of these studies is included in Appendix A - Clinical studies performed with the Fiber Optic Sensor and Appendix B - Clinical studies performed with SmartTouch Sensor. **Error! Reference source not found..**



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

ivWatch, LLC
Javier Garriz
Vice President of Product Management
469 McLaws Circle
Williamsburg, VA 23185

Re: K142374
Trade/Device Name: ivWatch Model 400
Regulation Number: 21 CFR 880.5725
Regulation Name: Accessories, Pump, Infusion
Regulatory Class: Class II
Product Code: MRZ
Dated: January 16, 2015
Received: January 20, 2015

Dear Mr. Garriz:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA).

You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set

Page 2 – Javier Garriz

forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address

<http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to <http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm> for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address

<http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>.

Sincerely yours,

Erin Keith
Director
Division of Anesthesiology,
General Hospital, Respiratory, Infection
Control, and Dental Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center - WO66-G609
Silver Spring, MD 20993-0002

February 11, 2016

ivWatch, LLC
Ms. Jaclyn Lautz
Director of Regulatory Affairs and Quality Assurance
469 Mcclaws Circle
Williamsburg, Virginia 23185

Re: K153605

Trade/Device Name: ivWatch Model 400
Regulation Number: 21 CFR 880.5725
Regulation Name: Infusion Pump
Regulatory Class: II
Product Code: PMS
Dated: January 12, 2016
Received: January 14, 2016

Dear Ms. Lautz:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Page 2 - Ms. Jaclyn Lautz

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address

<http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to

<http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm> for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address

<http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>.

Sincerely yours,

for Erin I. Keith, M.S.
Director
Division of Anesthesiology,
General Hospital, Respiratory,
Infection Control, and Dental Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center - WO66-G609
Silver Spring, MD 20993-0002

December 22, 2016

ivWatch, LLC
Jaclyn Lautz
Director of Regulatory Affairs and Quality Assurance
1100 Exploration Way, Suite 209
Hampton, Virginia 23666

Re: K162478
Trade/Device Name: ivWatch Model 400
Regulation Number: 21 CFR 880.5725
Regulation Name: Infusion Pump
Regulatory Class: Class II
Product Code: PMS
Dated: November 22, 2016
Received: November 28, 2016

Dear Jaclyn Lautz:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the [Federal Register](#).

Page 2 - Jaclyn Lautz

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address

<http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to

<http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm> for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address

<http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>.

Sincerely,

Tina Kiang, Ph.D.
Acting Director
Division of Anesthesiology,
General Hospital, Respiratory,
Infection Control, and Dental Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure



July 2, 2020

ivWatch, LLC
Holly Novak
Director Regulatory Affairs and Quality Assurance
630 Hofstadter Road, Suite 300
Newport News, Virginia 23606

Re: K192385

Trade/Device Name: ivWatch Model 400, Device Accessories: Extension Module, SmartTouch Sensor,
Patient Cable
Regulation Number: 21 CFR 880.5725
Regulation Name: Infusion Pump
Regulatory Class: Class II
Product Code: PMS
Dated: May 29, 2020
Received: June 1, 2020

Dear Holly Novak:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm> identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's

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10903 New Hampshire Avenue
Silver Spring, MD 20993
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Doc ID# 04017.04.10

K192385 - Holly Novak

Page 2

requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see <https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products>); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to <https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems>.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (<https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance>) and CDRH Learn (<https://www.fda.gov/training-and-continuing-education/cdrh-learn>). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (<https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice>) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

for Tina Kiang, Ph.D.
Director
DHT3C: Division of Drug Delivery and
General Hospital Devices,
and Human Factors
OHT3: Office of Gastrorenal, ObGyn,
General Hospital and Urology Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure



August 24, 2022

ivWatch, LLC
Holly Novak
Vice President, Regulatory Affairs & Quality Assurance
700 Tech Center Parkway, Suite 300
Newport News, Virginia 23606

Re: K222212
Trade/Device Name: ivWatch Model 400
Regulation Number: 21 CFR 880.5725
Regulation Name: Infusion Pump
Regulatory Class: Class II
Product Code: PMS
Dated: July 22, 2022
Received: July 25, 2022

Dear Holly Novak:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm> identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the [Federal Register](#).

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Silver Spring, MD 20993
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Doc ID# 04017.03.00

K222212 - Holly Novak

Page 2

requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see <https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products>); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to <https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems>.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (<https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance>) and CDRH Learn (<https://www.fda.gov/training-and-continuing-education/cdrh-learn>). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (<https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice>) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Payal Patel
Assistant Director
DHT3C: Division of Drug Delivery and
General Hospital Devices,
and Human Factors
OHT3: Office of GastroRenal, ObGyn,
General Hospital and Urology Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure



March 15, 2024

ivWatch, LLC
Holly Novak
Vice President, Regulatory Affairs & Quality Assurance
700 Tech Center Parkway
Suite 300
Newport News, Virginia 23606

Re: K233881

Trade/Device Name: ivWatch® Model 400
Regulation Number: 21 CFR 880.5725
Regulation Name: Infusion pump
Regulatory Class: Class II
Product Code: PMS
Dated: February 16, 2024
Received: February 16, 2024

Dear Holly Novak:

We have reviewed your section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (the Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database available at <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm> identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the [Federal Register](#).

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (<https://www.fda.gov/media/99812/download>) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (<https://www.fda.gov/media/99785/download>).

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K233881 - Holly Novak

Page 2

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR Part 803) for devices or postmarketing safety reporting (21 CFR Part 4, Subpart B) for combination products (see <https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products>); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to <https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems>.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (<https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance>) and CDRH Learn (<https://www.fda.gov/training-and-continuing-education/cdrh-learn>). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (<https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice>) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

David Wolloscheck, Ph.D.
Assistant Director
DHT3C: Division of Drug Delivery and
General Hospital Devices,
and Human Factors
OHT3: Office of Gastrorenal, ObGyn,
General Hospital, and Urology Devices

Appendix H – Amendments

Any amendments needed throughout the clinical investigation shall be documented and a justification statement included with each amended section.

Proposed amendments shall be agreed upon between the sponsor, principal investigator, and other investigators.

Amendments to the approved Protocol and the Informed Consent Form shall be notified to, or approved by the IRB and regulatory authorities, if required. The version number and date of amendments shall be documented.

The investigator(s) shall need to wait for the time specified in article 75 of the MDR or for the approval of the substantial modification, whichever comes first, before implementing the changes.

Proposed Amended Section

[Insert]

Amendment Description

[Insert]

Justification

[Insert]

Impact changes have on performance, effectiveness, safety, endpoints, and identification of affected documents

Updates to CRFs due to Amendment

Amendment Version Number and Date

[Insert]

Amendment Approval

[Insert]

Appendix I – Statistical Monte Marlo Analysis

```
%-----
%Simulations at n=8 to n=40 for power analysis

clear all;

rate_h_red = 0.25/24;      %estimated red event rate
rate_h0     = 1/24;        %null hypothesis

n_subj_array = 8:1:40;

rng(100);

for s = 1:length(n_subj_array)
    display(['simulating ' num2str(n_subj_array(s)) ' subjects']);

    num_subjects = n_subj_array(s);

    hours_per_subject = 23;

    bins = 0:1:100;

    for i = 1:1000000
        %generate random samples between 0 and 1
        rand_prob_h = rand(num_subjects*hours_per_subject,1);

        %find number of samples less than the probability of a red event
        prob_mask_h = rand_prob_h < rate_h_red;
        num_notifications_h_red(i) = sum(prob_mask_h);

        %find number of samples less than the probability of the null
        %hypothesis
        rand_prob_h0 = rand(num_subjects*hours_per_subject,1);
        prob_mask_h0 = rand_prob_h0 < rate_h0;
        num_notifications_h0(i) = sum(prob_mask_h0);
    end

    %bin the number of notifications
    h_red_bins = hist(num_notifications_h_red,bins);
    h0_bins = hist(num_notifications_h0,bins);

    %identifiy the threshold for an alpha = .05
    h0_cumsum = cumsum(h0_bins)/sum(h0_bins);
    pos = find(h0_cumsum < 0.05);
    threshold = bins(pos(end));
    alpha = sum(h0_bins(bins<=threshold))/sum(h0_bins);

    %find beta and statistical power
    beta_h_red = sum(h_red_bins(bins>=threshold))/sum(h_red_bins);
    power_h_red(s) = 1-beta_h_red;

end
```

```

%power analysis figure
figure('Color','w'); hold on;
plot(n_subj_array,power_h_red,'bo-');
xlabel('Number Subjects')
ylabel('Power')
ylim([.6 1.005])
grid on
print(gcf,'CS37_power_analysis.png','-dpng','-r300');

%-----
%Simulation at n=20

clear all;

rate_h_red = 0.25/24;      %estimated red alarm rate
rate_h0     = 1/24;        %null hypothesis

rng(100);

num_subjects = 20;

hours_per_subject = 23;

bins = 0:1:100;

for i = 1:1000000
    %generate random samples between 0 and 1
    % rand_prob_h = rand(num_subjects*hours_per_subject,1);
    rand_prob_h = rand(num_subjects*hours_per_subject,1);

    %find number of samples less than the probability of a red event
    prob_mask_h = rand_prob_h < rate_h_red;
    num_notifications_h_red(i) = sum(prob_mask_h);

    %find number of samples less than the probability of the null
    %hypothesis
    rand_prob_h0 = rand(num_subjects*hours_per_subject,1);
    prob_mask_h0 = rand_prob_h0 < rate_h0;
    num_notifications_h0(i) = sum(prob_mask_h0);
end

%bin the number of notifications
h_red_bins = hist(num_notifications_h_red,bins);
h0_bins = hist(num_notifications_h0,bins);

%identifiy the threshold for an alpha = .05
h0_cumsum = cumsum(h0_bins)/sum(h0_bins);
pos = find(h0_cumsum < 0.05);
threshold = bins(pos(end));
alpha = sum(h0_bins(bins<=threshold))/sum(h0_bins);

%find beta and statistical power

```



```
beta_h_red = sum(h_red_bins(bins>=threshold))/sum(h_red_bins);
power_h_red = 1-beta_h_red;

%create figure
figure;hold on;
h1 =
bar(bins/(num_subjects*hours_per_subject/24),h0_bins/max(h0_bins),'FaceColor'
,[0.00,0.45,0.74],'FaceAlpha',.5,'LineStyle','none');
h2 =
bar(bins/(num_subjects*hours_per_subject/24),h_red_bins/max(h_red_bins),'Face
Color',[1 0 0],'FaceAlpha',.5,'LineStyle','none');
set(gcf,'Color',[1 1 1])
xlabel('Non-Infiltration Notification Rate (per day)');
xlim([0 2]);
h3 = plot([threshold/(num_subjects*hours_per_subject/24)
threshold/(num_subjects*hours_per_subject/24)], [0 1], 'r', 'LineWidth', 2);
legend([h1 h2], {'Null Hypothesis', 'Alternative Hypothesis'});
print(gcf, 'CS37_20samples.png', '-dpng', '-r300');
```

