Cover page for:

NCT02188147

ZOLL document number:

90D0119 rev C

January 15, 2016

Document title:

Ambulatory post-Syncope Arrhythmia Protection Feasibility Study Protocol

Short Title: ASAP

DOCUMENT APPROVAL PAGE

Document Number:	Rev:	Page:
90D0119	C	1 of 21

Title:
Ambulatory post-Syncope Arrhythmia Protection Feasibility Study Protocol

Author: Ramu Perumal, PhD **Date:** 15 January 2016

Approvals

("☒" indicates approval signature required)

☒ Medical Affairs:	Date: 01-15-2016	☒ Marketing: Michelle Simon	Date: 2/1/2016
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☐ Service Operations:	Date:	☐ Technology Applications:	Date:
☒ OEM Regulatory: G. Parten	Date: 01-15-16	☐ OEM Engineering:	Date:

Documentation Control:	Date Archived:
Kimberly Allester	2/11/16

Electronic File info: (if applicable) *If multiple files (such as multiple sheets of a drawing) list file info separately

File name:	Size (in bytes)	Time & Date (or Date & Time)
90D0119_rev C.docx	90KB	1/15/2016 10:21AM

Transferred File info: (To be completed by Documentation Control)

File name:	Size (in bytes)	Time & Date (or Date & Time)
90d0119_revc.doc	89 KB	2/11/16 2:05pm
90d0119_revc.pdf		

ZOLL Form Number: 90A0001-A01
Form REV Level: A

DOCUMENT REVISION HISTORY PAGE

Document Number:	Rev:	Page:
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Title:
Ambulatory post-Syncope Arrhythmia Protection Feasibility Study Protocol

Revision History Of Document

Rev	CO Number	Description of Change	Author	Effective Date
FI	NA	First version	RP	8/13/13
A	3545	Clarified the inclusion and exclusion criteria by removing examples and providing specifics	RP	3/14/14
B	3645	Added a protocol signature page for sponsor and investigator. Minor formatting that includes, adding protocol revision number in the header, numbering the inclusion/exclusion criteria, and bullet formatting throughout the document. Clarified that the Investigator will now record on the CRF only the adverse device effect determined to be caused by or associated with the use of SWD 1000 device or a protocol specific procedure. Clarified that the subject will sign an informed consent form that is IRB approved. Clarified the administrative responsibilities section wherein, sponsor providing a notebook to the investigator; document number referencing ZOLL's monitoring SOP; and investigator maintaining protocol amendment were removed. In addition, clarified that the investigator is responsible for ethics approval for their site only and reporting all IRB and other significant correspondence related to the study. Removed Appendix A which contained the bibliography of wearable cardioverter defibrillator publications.	RP	11/14/14
C	0170	Per Agency's recommendation, the investigator will now record all adverse device effects regardless of causality.	RP	2/11/16

ZOLL Form Number: 90A0001-A03
Form REV Level: FI

Ambulatory Post-Syncope Arrhythmia Protection Feasibility Study Protocol

IDE Sponsor	**ZOLL**
Protocol Number	**90D0119**
Version	**Rev C**

Sponsor Representative:

I have reviewed and approve this protocol. My signature assures that this study will be conducted according to all stipulations of the protocol, including all statements regarding confidentiality.

Sponsor's Signature _____

Name _____

Date of Signature (DD MMM YYYY) _____

Principal Investigator:

I have read this protocol and agree that it contains all necessary details for carrying out the study as described. I will conduct this protocol as outlined herein, including all statements regarding confidentiality. I will make a reasonable effort to complete the study within the time designated. I will provide copies of the protocol and access to all information furnished by the Sponsor to study personnel under my supervision. I will discuss this material with them to ensure that they are fully informed about the device and the study. I understand that the study may be terminated or enrollment suspended at any time by the Sponsor, with or without cause, or by me if it becomes necessary to protect the interests of the study subjects.

I agree to conduct this study in full accordance with all applicable regulations and Good Clinical Practices (GCP).

Investigator Signature _____

Name _____

Date of Signature (DD MMM YYYY) _____

PROTOCOL SUMMARY

OBJECTIVES

To conduct a prospective observational study assessing a unique outpatient care model in which syncope patients are provided with, and trained to use, a wearable defibrillator prior to discharge from the emergency department (ED). Observational data will be collected to assess the logistics of equipping patients with the device and providing training in the ED, and the ability of patients to receive follow-up care on an outpatient basis. In addition, data will be collected to confirm that the device meets expected safety. The experience gained from this stage of the study will be used to guide future studies of device's functionality enhancements and definitive device safety and efficacy.

STUDY POPULATION

Participants will be patients presenting to the ED following a syncopal event which has been defined as cardiac, or potentially cardiac, i.e. undiagnosed in nature.

INTERVENTION

A wearable defibrillator optimized for short-term ambulatory use with adhesive electrodes will be prescribed for up to 14 days of use following emergency department discharge or until the physician responsible for the subject's care defines an alternative treatment plan.

STUDY DESIGN

This is a single-arm feasibility study.

STUDY SIZE

The study will enroll a minimum of 50 and a maximum of 80 subjects. A maximum of 20 centers will be used for enrollment.

1. INTRODUCTION

Syncope, a transient loss of consciousness that spontaneously resolves without intervention, is one of the leading causes of hospitalization in the United States, making up 1.9% of hospital admissions from the emergency department (ED) and 1.3% of all hospital admissions.[1,2]

Patients presenting to the ED following a syncopal event receive a clinical work-up to help identify the etiology of the event, which in turn is used to establish the patient's risk of suffering subsequent adverse events. When medical staff are able to identify the underlying cause of syncope, events are diagnosed as being cardiac, neurally mediated, or due to orthostatic hypotension.[3] Once etiology is defined and the level of risk has been established, the patient can be triaged appropriately. However, the ED staff is frequently unable to diagnose the nature of the event. This is largely due to the episodic nature of syncope and the inability of patients to provide an accurate recounting of the event.[4,5] Following history taking and physical examination in the ED, 40% of syncope cases remain undiagnosed.[6]

When the ED staff is able to determine that the syncopal event is related to underlying cardiovascular dysfunction, the patient is considered to be at high risk of suffering a subsequent adverse event, including sudden cardiac death, and is routinely admitted to the hospital.[7,8] The American College of Emergency Physicians' most recent clinical policy on the management of syncope within the ED states that the primary reason patients should be admitted is to mitigate the risk of significant dysrhythmia or sudden death.[5] However, in the event that no clear diagnosis is established and cardiac syncope cannot be clearly dismissed, patients are still frequently admitted to mitigate the unknown level of risk. Retrospective chart review has shown that cardiac syncope is believed to account for only 9.5% to 12% of syncope cases.[9,10] Yet, 30% to 55% of ED presenting syncope patients are still admitted to the hospital.[2,11] When admitted to the hospital, patients rarely undergo diagnostic cardiac testing beyond basic monitoring, and as much as 42% of patients who are admitted are discharged without a clear cause for the event being established.[12] Further complicating the issue of inappropriate syncope admissions is the fact that roughly one third of ED-presenting syncope patients with indications of cardiovascular disease are still discharged from the ED despite being at high risk of suffering a subsequent adverse event.[2]

Consistent with this discrepancy between the occurrence of high-risk syncope cases and the syncope hospital admission rate is the body of work in emergency medicine literature aimed to more accurately identify at-risk syncope patients while safely reducing the number of syncope-related hospital admissions. Several syncope risk stratification models have been proposed to improve the rate of appropriate hospital admissions.[4,11,13–16] These models generally incorporate patient medical history to help risk stratify, which is intended to make them particularly useful when explicit evidence of cardiovascular dysfunction is not obtained during the ED workup. However, despite efforts to develop syncope management tools, it is has been stated that an adequately validated post-ED triage model has not been developed.[17] Current syncope admission practices, in which low risk patients are routinely admitted, place considerable financial burden on the healthcare systems while offering questionable diagnostic and therapeutic yields.[1] Furthermore, admitting low risk patients may unnecessarily expose them to hospital-specific hazards, including hospital-acquired infections, as well as economic loss and emotional disturbance.[18]

Advancements in ambulatory cardiac monitoring technology have promoted capturing evidence of transient cardiac events on an outpatient basis, and thus have proven useful in diagnosing the cause of syncope of unknown origins in certain groups of patients.[3] Enhanced recording and transmission capabilities and minimally obtrusive form factors help these devices to have minimal effect on quality of life during extended continuous monitoring sessions that may last up to weeks (K113187, K113862). While such devices potentially offer enhanced diagnostic utility and may even detect the onset of life-threatening events, they are incapable of providing time-critical life-saving treatment when adverse events occur. The lack of treatment functionality renders these devices inappropriate for outpatient use when patients are at known risk of suffering life-threatening arrhythmias, and they fail to fully mitigate the uncertain risk faced by patients for whom the cause of syncope has not yet been identified.

It is apparent that the ED staff has come to rely on hospital admission to mitigate the poorly defined risk of sudden cardiac death in syncope patients due to the complexities of diagnosing the underlying cause of syncope in the ED, the lack of adequately validated risk stratification tools, and the inability of currently-available outpatient devices to provide emergency intervention. It would therefore be desirable to utilize a wearable cardioverter defibrillator (WCD) as an integral component of syncope patient management; the WCD would offer patients protection from ventricular arrhythmias while care is managed on an outpatient basis, thus mitigating risk while reducing dependence on hospital admission.

WCDs have been prescribed to offer patients protection from lethal ventricular arrhythmias for both primary and secondary prevention. While worn, WCDs provide outpatient defibrillation faster than can be delivered by emergency medical services because event detection is automatic and the device is already positioned to deliver treatment. Since a WCD is non-invasive and can easily be removed, it makes an ideal device for protecting patients until long-term cardiovascular risk can be adequately defined.

The LifeVest WCD has been commercially approved for use by the FDA and CE marked for Europe since 2001, and over 100,000 patients have worn the device (P010030). Several published articles included in Appendix A demonstrate the impact the LifeVest WCD has had in successfully resuscitating patients from ventricular tachyarrhythmia, with a first shock success rate of 98% for sustained ventricular arrhythmias and a rate of 92% survival to conscious emergency room arrival. This survival rate is far superior to any other form of outpatient resuscitation, which has been reported at 16% in patients who suffer ventricular tachycardia / fibrillation relying on human-mediated resuscitation.[19]

The LifeVest WCD is ideal for continuous ambulatory wear that may last up to several months due to use of adhesive-free, dry electrodes. The electrodes are held in place by a reusable garment worn under the patient's clothing. The garment is fit for the patient based on their body-size. Patients are instructed to launder this garment regularly, and thus must be trained to disassemble the garment-electrode belt assembly and reassemble using the second garment which they are supplied.

In addition to the dry electrodes of the LifeVest most commonly used, another model using traditional adhesive electrodes has received approval for shorter term use (P010030/S0005). Using such an electrode configuration would be ideal for equipping patients with a wearable defibrillator prior to ED discharge for shorter term outpatient use. Because adhesive electrodes need to be removed or reapplied less frequently and have no associated garment, the patient's daily interaction with the electrodes is simplified as is their associated training. Furthermore, the requirements placed on the ED staff members who equip the patient with the WCD are simplified since the placement of adhesive defibrillation and electrocardiographic monitoring electrodes translates better to their existing skill set than does garment fitting.

Thus, the wearable defibrillator offers functionality that can significantly improve the management of patients that present to the ED with syncope. However, syncope is not an indication for the currently-approved wearable defibrillator, which is rarely prescribed from the ED. It would be appropriate to conduct a feasibility study to evaluate how a short-term use wearable defibrillator (SWD) may best be incorporated into syncope patient management protocols. Feasibility will be specifically assessed concerning the logistics of equipping patients with the device and providing training in the ED, and the ability of patients to receive follow-up care on an outpatient basis.

2. DEVICE DESCRIPTION

A complete description of the operation and management of the SWD 1000 is given in the Operator Manual.

2.1 Operative Summary

The SWD 1000 uses adhesive ECG monitoring electrodes to continuously collect the patient's electrocardiographic signal. The signal is analyzed for the presence of ventricular tachycardia or ventricular fibrillation (VT/VF) using the same algorithm as the commercially available LifeVest WCD. If VT/VF is detected, the patient undergoes a responsiveness test, which is an alarm sequence that lasts at least 25 seconds. The patient is trained and expected, if conscious, to react to these alarms by holding the response buttons of the SWD 1000, stopping the alarm sequence. If the patient responds but at some point loses consciousness and releases the response buttons, the SWD 1000 will restart the alarm sequence if still in VT/VF. The alarm sequence begins with audible tones that escalate in volume, and later in the sequence voice warnings are given to bystanders alerting them of an impending shock to be given. When the alarm sequence finishes, a defibrillation shock will be delivered to the patient. If at any time during the alarm sequence the response buttons are held or momentarily pressed and released, defibrillation will be delayed. If VT/VF stops before defibrillation, the alarms will be terminated and the defibrillation shock will not be delivered. The SWD 1000 will also detect the presence of bradycardia and asystole using the same algorithm as the commercially available LifeVest. In the event that bradycardia or asystole are detected the monitor will issue an alarm and provide messaging instructing bystanders to contact emergency medical service. As currently designed, the SWD 1000 will not provide electrical therapy in response to bradycardia or asystole.

2.2 Components

The SWD 1000 includes a wiring harness with connections for adhesive ECG and therapy (i.e. defibrillation) electrodes, a monitor/defibrillator ("monitor"), and a holster. The monitor is carried in the holster that can be worn on the patient's hip or supported by an over the shoulder strap. The entire SWD 1000 has a weight of approximately two pounds. The adhesive electrode configuration consists of three ECG electrodes and two therapy electrodes. The system is designed to use FDA-cleared ZOLL adhesive therapy electrodes.

The monitor enables patient interaction via a touch-sensitive LCD display and response buttons recessed on the sides of the unit. The display and speaker are used to communicate messages to the patient and caretakers. In the event of a detected arrhythmia and subsequent alarm sequence, the patient can depress the response buttons to indicate that they are conscious and the shock delivery is subsequently delayed.

The monitor contains the digital signal processing computer, a removable solid-state data storage device, and defibrillation electronic circuitry. The signal processor detects the presence of VT/VF, and asystole/near asystole (severe bradycardia). The defibrillation circuitry, including capacitors and batteries, will deliver up to five truncated exponential biphasic defibrillation pulses, as necessary, to convert a treatable VT/VF episode. The delivered energy of these pulses in this study will be programmed for 150 Joules.

2.3 Support Equipment

The support equipment for the SWD 1000 consists of two rechargeable batteries and a battery charger. Batteries are to be exchanged every 24 hours. Each battery, if fully charged when applied, can deliver five full energy shocks after monitoring the patient for 24 hours. The charger also establishes a wireless connection with the SWD 1000 monitor and transmits data collected by the monitor over a cellular network to a secure server.

2.4 Documents referenced

20B0058: Wearable Defibrillator Model SWD-1000 Clinician Manual
(Referred to as "Clinician Manual")

20B0059: Wearable Defibrillator Model SWD-1000 Patient Manual
(Referred to as "Patient Manual")

3. STUDY OBJECTIVES

The objectives of this feasibility study focus on demonstrating that patients presenting to the ED following a cardiac or potentially cardiac syncopal event, i.e., undiagnosed in nature, may be managed as outpatients and protected from sudden cardiac death by equipping them with, and training them to use, the SWD 1000 prior to ED discharge. Capturing accurate data on patient and caregiver behavior is critically dependent on utilizing the device in a real-world clinical setting.

3.1 To observe the level of care provided to SWD 1000-equipped syncope patients on an outpatient basis.

3.2 To confirm that the SWD 1000 meets expected safety. Monitoring quality will be used as a surrogate for safety in this feasibility study. Specifically, on average monitoring will be inhibited by noise no greater than 2% of the time worn and monitoring using single lead analysis will be no greater than 5% of the time worn.

It is not anticipated that any treatable events will be observed during this testing period. However, should any events occur, it is expected that the device will yield results at least comparable to those obtained through experience with the currently-approved LifeVest wearable defibrillator.

4. SUBJECT SELECTION CRITERIA

The study will enroll 50 to 80 patients presenting to the emergency department following suspected syncope. Patients eligible for enrollment must meet all of the inclusion criteria and none of the exclusion criteria prior to ED discharge:

Inclusion Criteria are as follows:

1) Age ≥ 18

2) Experienced a syncopal event within the past 48 hours

3) Either one of the following profiles apply:

   a) ED workup indicates that the patient may have experienced syncope that is cardiac in nature (any one or more of the following apply)

      - History or diagnosis of structural heart disease
      - History of cardiovascular disease
      - Age ≥ 40
      - Palpitations experienced pre-syncope
      - Major ECG abnormalities:
        - QRS duration greater than 140 ms
        - PR interval greater than 200 ms
        - Non-specific repolarization abnormality
      - Syncope experienced without any warning

- Syncope experienced while supine
- Syncope during exercise

b) ED workup does not indicate a clear cause of the syncopal event

Exclusion criteria are as follows:

1) Clear diagnosis of non-cardiac syncope (e.g. orthostatic hypotensive syncope, vasovagal syncope, carotid sinus syncope, situational fainting)

2) An active implantable cardioverter-defibrillator (ICD)

3) An active unipolar pacemaker

4) Significant risk or suffering a cardiovascular event such as:

   - Symptoms of NYHA class III or IV heart failure
   - ED diagnosis of acute coronary syndrome
   - Having required resuscitation in response to the index syncopal event

5) Advanced directive prohibiting resuscitation (DNR)

6) Physical or mental conditions preventing subjects from interacting with or wearing the device as determined by the investigating physician.

7) Bandages or other clinical condition preventing SWD 1000 use

8) Injuries or other conditions beyond simple syncope that require hospitalization

9) Travel out of town during the study participation period that prevents the field service representative from visiting the subject daily

10) Unable or unwilling to provide written informed consent

5. INVESTIGATIONAL PROCEDURE

At the beginning of the study, a ZOLL representative will train a site coordinator and designated ED staff in SWD 1000 use per the Clinician Manual. A training sheet will be used to document that device training was provided by ZOLL to the site coordinator and designated staff.

5.1 Pre-study Assessment

The subject's eligibility to enter the study will be determined during the pre-study assessment. This assessment is to be performed prior to ED discharge. The pre-study assessment will include:

- Reviewing the subject's medical history and symptoms to determine whether the inclusion and exclusion criteria are met using the enrollment questionnaire.
- Discussing the risks and benefits of the study with the subject.
- Obtaining informed consent.

5.2 SWD 1000 Device Setup

Each subject enrolled in the study will be assigned the following:

- one monitor
- one electrode cable
- Replacement electrodes
- two batteries (one battery will power the monitor while the other is being charged)
- one base station (battery charger)
- one patient manual

The monitor will be programmed in accordance with the instructions in the Clinician Manual, section 3, by the ED staff member. The following default settings will be used:

- The energy level for defibrillation will be set to 150 joules for all shocks.
- The rate at which VT is detected will be programmed to 150 BPM
- The rate at which VF is detected will be programmed to 200 BPM.

5.3 SWD 1000 Application

Application and training must occur prior to the subject leaving the hospital.

Once the SWD 1000 monitor is set up, the subject's skin will be prepared in the usual manner for the application of adhesive electrodes, and the electrodes will be applied in the locations described in the Clinician Manual, section 3 by the ED staff.

The ED staff member will then connect the electrode leads to the SWD 1000 electrode belt and allow the monitor to perform a baseline ECG as described in sections 3 and 1 of the Clinician Manual, respectively.

5.4 Subject Training

The ED staff member will provide the subject instructions for the care and use of the SWD 1000, as described in section 4 of the Clinician Manual and section 3 of the Patient Manual. Specific training tasks are as follows:

- The subject will be trained on normal daily maintenance of the device, including the battery change and startup sequences.
- The subject will be trained to respond to alerts and alarms provided by the monitor, including the event detection alarm sequence.
- The subject will be trained to inspect the integrity of the adhesive electrodes and to self-remove and apply replacement electrodes in the event that they fail to adhere.
- The subject will be trained to monitor for and respond to alarms indicating that electrodes have failed to make adequate contact.

- The subject will be trained to initiate manually-flagged ECG recordings in response to certain symptoms, as described in further detail below.

5.5 SWD 1000 Use

The subject will wear the SWD 1000 continuously for the duration of the monitoring period, up to 14 days, unless one of the following conditions applies:

- The subject's index syncopal event has been determined to not be cardiac in nature.
- The subject's condition changes such that an exclusion criterion applies.
- The subject experiences an excessive amount of electrode noise that prevents effective monitoring by the SWD 1000.
- The subject decides to withdraw from the study.

The subject will wear the SWD 1000 continuously except:

- While showering (during which the patient may continue to wear the adhesive electrodes but not the monitor).
- While undergoing a medical procedure that requires SWD 1000 removal (e.g., MRI requires the removal of all metallic objects).

Subjects will not be limited in their daily activities except for being instructed to avoid fully submerging the electrodes in water, such as during bathing or swimming. Subjects are still permitted to shower with the electrodes attached as long as the electrodes are disconnected from the monitor. The subjects will be responsible for charging and exchanging the batteries every 24 hours.

Once the subject is discharged, a properly trained field service representative will be responsible for visiting the patient daily. This representative will be responsible for inspecting the integrity of the electrodes and exchanging them as needed.

Subjects may experience symptomatic events that will help their physician discern a specific cause of the original syncopal event. Symptoms may include dyspnea, lightheadedness or dizziness, or in more serious cases loss of consciousness or chest pain. In such scenarios, subjects will be trained how to initiate a manually-flagged ECG recording when possible so that physician may review the associated ECG and attempt to determine if the event was cardiac in nature. During such an event, subjects are instructed to perform the following steps as described in section 3 of the Patient Manual:

- Hold the SWD 1000 response buttons as described in the patient manual to create a data event flag. This enables the electrocardiographic activity associated with the event to be saved for review

5.6 Response to Cardiac Arrest

It is possible, but not expected, that one or more subjects may experience a spontaneous ventricular arrhythmia. In the event that this does occur, the SWD 1000 alarms that an event has been detected. If this occurs and the subject is conscious, they are instructed to press the device's response buttons to delay shock as described in section 4 of the Patient Manual. The subject's interaction with the device will be logged by the device and can be analyzed

retrospectively. As this is dependent upon the occurrence of a highly unpredictable event (sustained VT/VF, or asystole / near-asystole), studying the subject and device response to such an event is not an end point of the initial stage of this study.

5.7 Subject Monitoring Frequency

The subject and the SWD 1000 device will be evaluated by a trained field service representative within one day of enrollment in the study. Follow-up visits will continue to be performed on a daily basis until the patient monitoring period is complete. During each field service visit, the integrity of the adhesive electrodes will be evaluated for falloff as described in the report form.

6. EVALUATION OF RESULTS

6.1 Data Collection

6.1.1 Observational Data

Throughout the study, observational data will be collected to evaluate care provided to subjects on an outpatient basis. During the daily visits, the field service representative will be tasked with logging any follow up physician appointments ordered for and / or attended by the subject, as well as any return to the ED and / or hospital admission. In addition to the daily logging of said data, an exit evaluation will be conducted 30 days after study enrollment to capture information related to additional follow up care received by the subject after the active participation period. The evaluation will be conducted by study coordinators who will determine where the patient received follow-up care and obtain the appropriate release of records.

6.1.2 Device-Collected Data

While the SWD 1000 is in use by the subject, the monitor will collect and store ECG data, device performance data, and subject-device interaction data. These data can be used to evaluate the subject's ability to interact with the device and to evaluate device performance as needed within the context of this study. Specific data collected by the device are as follows.

- ECG Data
    - All automatically recorded arrhythmic events
    - All subject-initiated ECG recordings
- Device Performance Data
    - ECG signal quality, defined using electrode falloff and signal noise detected by the monitor
    - Therapy electrode preparedness, defined using subject-electrode impedance detected by the monitor
    - Arrhythmia detection and treatment sequence markers
    - Device measurements made during treatment sequences
        - Alarm timing in response to detected arrhythmia

- Transthoracic impedance
- Treatment energy delivered

- Subject-Device Interaction Data
  - Subject compliance (measured as the duration of time the SWD 1000 was powered and being worn).
  - Use of the response buttons during treatment sequences
  - Power cycling (indicative of battery replacement)

Data stored within the monitor will be downloaded to the data-enabled battery charger automatically when within Bluetooth radio range of the charger. Data stored in the charger can then be automatically upload to a secure server so that it may be remotely assessed as needed via a secure website. In addition to automatically transmitting data for analysis, all data from the SWD 1000 monitor's removable storage will be extracted upon return of the equipment to ZOLL.

6.1.3 Subject Enrollment Data

General demographic and medical history information will be collected from subjects enrolled in the study (90D0119_CRF).

6.1.4 Therapy Contextual Information

In the unexpected event that a shock is delivered, anecdotal information may be collected from the patient and any witnesses. This information will be used to determine if the patient and other witnesses interacted with the device as instructed during the treatment sequence.

6.2 Data Evaluation

6.2.1 Safety Evaluation

The SWD 1000 safety endpoint will be evaluated based on signal quality. ECG quality relates to both safety (poor ECG quality may lead to inappropriate detections and/or shocks) and efficacy (poor ECG qualify may interfere with the detection of a ventricular arrhythmia). The criteria for success are that 1) at least one lead is available for ECG monitoring (signal quality acceptable for algorithm input on one or more leads) for ≥98% of the time the device is attached to the patient and 2) both leads are available for ≥95% of the time the device is attached to the patient. The evaluation will be an average derived from all patients using the internal device flags regarding algorithm performance.

6.2.2 Device Performance During Event

It is not expected that any subject will experience an arrhythmic event due to the low number of subjects that will be enrolled and the low frequency with which they occur in this patient population. However, if a subject does receive treatment from the device, the associated SWD 1000 treatment sequence performance variables will be investigated. Appropriate device response to an event will be evaluated based on:

- The device's ability to appropriately define the cardiac rhythm. Trained ECG reviewers will be used to manually asses the ECG signals and determine if the device accurately defined the rhythm.

- The subject's state of consciousness at the time the event was treated (if the SWD 1000 delivered treatment). Consciousness will be determined based on when the subject stopped using the device's response button and interviewing the patient and bystanders, if present at the time the event.

- The subject's transthoracic impedance detected during treatment (if the SWD 1000 delivered treatment)

- The energy delivered by the SWD 1000 during treatment (if the SWD 1000 delivered treatment)

- The subject's post-treatment cardiac rhythm (if the SWD 1000 delivered treatment)

All subject's receiving treatment from the device will be followed up promptly to establish the context of the event. Contextual information will be used to supplement the device-reported information. If the subject or caretaker is able to provide contextual information, it will be used to further assess subject activity at the time of treatment, subject consciousness at the time of treatment, subject perception of the treatment alarm sequence, and subject interactions with the device during the event.

There is no study endpoint associated with the review of these data.

7. RISKS AND BENEFITS

Excluding false shocks resulting from supraventricular tachycardia, there is risk of an inappropriate shock from ECG signal noise. Using non-adhesive electrodes with the commercial outpatient wearable cardioverter-defibrillator, this risk is less than one per 100 months of patient use. Other than being painful and startling, an inappropriate shock should not be life threatening or have serious effects. However, in a small percentage of cases, a false shock will induce VT or VF. If the SWD 1000 does not automatically convert an induced VT or VF, the result may be permanent disability or death.

The SWD 1000 may fail to detect an episode of VT/VF or, having detected the arrhythmia, fail to convert the VT/VF. In the event that a care taker is not capable of providing emergency resuscitation (i.e. CPR) or cannot summon emergency responders to arrive in a timely fashion, the result may be permanent disability or death.

If the subject experiences SCA due to bradycardia or asystole, the SWD 100 will alarm to notify bystanders to call for help and perform CPR, but will not provide any treatment. If the event were to occur with a hospitalized patient, medical personnel would be available to recognize the condition and respond. Bradycardia or asystole events are expected to be of very low incidence during this feasibility study.

If the monitor is not disconnected from the SWD 1000 cable prior to using a commercially available portable defibrillator (as may be attempted by emergency responders), there is a remote possibility that some of the portable defibrillator current may be shunted through the SWD 1000 electrodes. Although not directly harmful to the subject, such shunting may reduce the effectiveness of the rescue defibrillation.

It is likely that some subjects will experience a rash due to the adhesive electrodes occluding the skin or sensitivity to the materials used in the construction of the device. In addition, as with all defibrillators, burns are possible if therapy is delivered.

Because defibrillation transfers electricity between the device and the patient, it is theoretically possible for sparking to occur if a gap exists between the therapy pads and the patient. If the spark occurs in an oxygen-rich environment, a fire or explosion may occur. This event has not occurred with the commercially available LifeVest WCD but is a standard warning for all external defibrillators. As the pads

that transfer the electricity from the device to the body are generally under clothing, the risk may be less with the SWD 1000 than with other external defibrillators (no exposure to oxygen-rich surroundings).

There is a possibility that subjects may fail to properly dry the electrode cable as described in the patient manual. In this event, it is possible that the defibrillation circuit completed with the subjects will be shorted and the shock efficacy will be subsequently reduced.

A possible benefit of participating in this study is prompt defibrillation, should the subject have a VT/VF episode. The SWD 1000 is designed to deliver defibrillation treatment within one minute of VT/VF detection, and the median time from arrhythmia onset to shock in commercial use is approximately 45 seconds. Such prompt treatment may therefore be more effective than conventional defibrillation, even in an inpatient setting, because of the time typically required for VT/VF recognition, defibrillator transport to the bedside, application of electrodes, and delivery of a defibrillation pulse by hospital personnel.

This device also allows patients to be discharged from the hospital and to receive follow-up testing on an outpatient basis; doing so may reduce the patient's exposure to hospital-specific hazards.

In some hospital environments, unusually high levels of electromagnetic disturbance could be encountered. Examples of possible sources of such disturbance include: magnetic resonance imaging equipment, communication equipment such as microwave transmitters, arc welding equipment, high voltage transmission lines, electrocautery systems, and electronic muscle stimulators. These high levels of electromagnetic disturbances may cause arrhythmia detections or other device behavior.

8. SUBJECT CONSENT AND CONFIDENTIALITY

Each subject will be informed of the purpose of the investigation, the potential risks and benefits of the study, and the investigational nature of the SWD 1000 prior to their enrollment in the study. The subject must freely sign an IRB approved Informed Consent Form based on template,90D0119_ICD, prior to any study specific procedures.

Each subject will receive a unique subject identification number. The subject's name and identity will be known to the Investigator and ZOLL (the "Sponsor") but will be kept confidential. Authorized personnel from the ethics committee and regulatory authorities may have access to original subject records.

9. TRIAL DESIGN AND STUDY SIZE

The study is a single arm, open enrollment feasibility study. A maximum of twenty clinical sites will be used to enroll subjects. The multi-site approach is intended to increase variability in the observation of ED characteristics, such as differences in staffing, staff responsibilities, and patient demographic.

A minimum of 50 subjects and a maximum of 80 subjects will be enrolled. The sample size is based on the expected safety objective, which states:

> "Specifically, on average monitoring will be inhibited by noise no greater than 2% of the time worn and monitoring using single lead analysis will be no greater than 5% of the time worn."

This objective was taken directly from the LifeVest System Input Requirements (90A0118):

> "[R274] Monitoring shall be inhibited by noise no greater than 2% of the time worn on average within the intended patient populations. [R275] Monitoring using single lead analysis shall occur no greater than 5% of the time worn on average within the intended patient populations."

In 2012, the device records of approximately 14,000 patients who used the LifeVest 4000 system were analyzed to determine the system performance. The device records the time when the device is on, when

each of the two ECG channels is determined to be unsuitable for determining the presence of an arrhythmia, and when both leads are determined to be unsuitable. Using these, the time the device was unable to monitor (DUAL) and the time the device was using only a single lead for monitoring (SINGLE) was determined. Each patient's proportion of time spent in SINGLE or DUAL was calculated, then overall descriptive statistics were derived using Excel spreadsheet functions:

	SINGLE	DUAL
Mean	.040	.005
Standard Deviation	.051	.015
Median	.024	.002
Maximum	.762	.644
Minimum	.000	.000
Standard Error	.000431	.000127
95% lower bound	.039989	.004997
95% upper bound	.040011	.005003

The performance of the SWD 1000 is expected to be similar to the 4000 system. A confidence interval of 80% to 90% was used to define expectations of meeting the safety objective for the feasibility stage. A general formula for calculating sample size based on a confidence interval was used:

$$n = (2z_{\frac{\alpha}{2}}\sigma/L)^2$$

To calculate the sample size for SINGLE performance of the SWD 1000 against the 4000 system:

Confidence: 80%
$z_{\frac{\alpha}{2}} = 1.28$

Allowable difference = 0.01 (0.05 permitted, 0.04 is current 4000 performance)
L = 0.02

Standard deviation = 0.051 (assumed to be similar to the 4000)
$n = (2z_{\frac{\alpha}{2}}\sigma/L)^2 = 42$

Confidence: 90%
$z_{\frac{\alpha}{2}} = 1.645$

Allowable difference = 0.01 (0.05 permitted, 0.04 is current 4000 performance)
L = .02

Standard deviation = 0.051 (assumed to be similar to the 4000)
$n = (2z_{\frac{\alpha}{2}}\sigma/L)^2 = 71$

To calculate the sample size for DUAL performance of the SWD 1000 against the 4000 system:

Confidence: 90%
$z_{\frac{\alpha}{2}} = 1.645$

Allowable difference = 0.01 (0.02 permitted, 0.005 is current 4000 performance)
L = 0.02

Standard deviation = 0.015(assumed to be similar to the 4000)
$n = (2z_{\frac{\alpha}{2}}\sigma/L)^2$ =7

Thus, a sample size of 50 to 80 subjects is expected to demonstrate that both SINGLE and DUAL performance meet the safety objective of the feasibility study.

10. ANALYSIS OF PROTOCOL

This feasibility study will assess a unique outpatient care model in which syncope patients with cardiac or uncertain etiology, instead of being hospitalized, are provided with, and trained to use, the SWD 1000 prior to discharge from the ED. Only observational data will be collected to assess the logistics of equipping patients with the device and providing training in the ED, and the ability of patients to receive follow care on an outpatient basis. Therefore, the first primary objective where the level of care provided to syncope patients on an outpatient basis is observed is justified. The second primary objective using ECG signal quality as a surrogate for safety is justified because the signal quality relates to both safety (poor ECG quality may lead to inappropriate detections and/or shocks) and efficacy (poor ECG quality may interfere with the detection of a ventricular arrhythmia). In essence, because the detection and treatment sequence of the SWD 1000 is exactly the same as that of previously-approved LifeVest system, demonstrating similar ECG quality will provide reasonable assurance that the device will perform as expected.

The outcomes of this feasibility study will be used to guide the design of future studies in which device functionality enhancements and performance may be further investigated.

11. FORMS AND DATA HANDLING

As with any study, accurate and timely completion of documentation is essential for the successful completion of the trial. The Investigator will be responsible for obtaining and maintaining IRB approved Informed Consent Forms based on template, 90D0119_ICD, and Case Report Forms (90D0119_CRF). A signed copy of the Informed Consent Form will be given to every subject. A copy of each Case Report Form will be sent to the Sponsor, with the originals maintained by the Investigator.

12. ADVERSE EVENTS

The Investigator will be responsible for recording all adverse device effects regardless of causality on the Case Report Form. Serious adverse events include any event that is fatal or life threatening, requires or prolongs hospitalization, or is permanently disabling. The Investigator will assess whether the adverse event is anticipated or unexpected. An unexpected adverse event is any adverse event not identified by nature, severity or frequency prior to the investigation. Anticipated events include, but are not limited to:

- Skin rash or irritation is commonly associated with adhesive electrode use.
- Burns are common after a defibrillation shock.
- Inappropriate shocks from supraventricular tachycardia, t-wave misclassification or other forms of "double counting", or electrical interference (with the outpatient device, this occurs at a rate of about 1 per 100 months of use).
- Inappropriate shocks may induce a ventricular arrhythmia at a rate of about 1 per 100 inappropriate shocks.

- Alarms may awaken patients at night.
- Discomfort may arise from device placement.
- Some shunting of current may result if the SWD 1000 is not disconnected prior to a defibrillation. This may result in less effective defibrillation and possibly death.

The investigational device exemption (IDE) regulations define an unanticipated adverse device effect (UADE) as "any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects" (21 CFR 812.3(s)). UADEs must be reported by the clinical investigator to the sponsor and the reviewing IRB, as described below:

- For device studies, investigators are required to submit a report of a UADE to the sponsor and the reviewing IRB as soon as possible, but in no event later than 10 working days after the investigator first learns of the event (§ 812.150(a)(1)).
- Sponsors must immediately conduct an evaluation of a UADE and must report the results of the evaluation to FDA, all reviewing IRBs, and participating investigators within 10 working days after the sponsor first receives notice of the effect (§§ 812.46(b), 812.150(b)(1)).

The IDE regulations, therefore, require sponsors to submit reports to IRBs in a manner consistent with the recommendations made above for the reporting of unanticipated problems under the investigational new drug (IND) regulations.

13. STATISTICAL DATA ANALYSIS PLAN

Data from all subjects enrolled in the study will be considered and/or analyzed. All appropriate data stored in the monitor during the time the SWD 1000 is worn will be analyzed and may be correlated with arrhythmias. The data stored in the monitor includes:

- Automatically stored ECG recordings (including true arrhythmias and false arrhythmia declarations).
- Manually stored ECG recordings.
- Duration of time that the SWD 1000 was worn.
- Noise, arrhythmia, and other internal event flags.
- Device actions during a treatment sequence; i.e., transthoracic impedance measurement, energy delivered and outcome.
- Subject device interactions, including subject use of the response buttons.

If an event occurs, the stored data will be analyzed. The data will also be analyzed to determine frequency of noise events, frequency of false arrhythmia events, and percentage of subject wear time. The results obtained will be compared with the results of commercial LifeVest use.

14. ADMINISTRATIVE RESPONSIBILITIES

ZOLL, the Sponsor, is responsible for study administration and providing devices and related materials for the study. At the conclusion of the study, the Investigators will return all SWD 1000 units to the Sponsor.

The Sponsor will designate one or more appropriately trained and qualified individuals to monitor the investigation. These individuals will conduct at least one pre-investigation on-site visit and one on-site visit per site during the investigation to verify the adherence to procedures specified in the protocol, and verify maintenance of required subject and data records. Monitoring activities will be conducted according to ZOLL's Monitoring of Clinical Studies Standard Operating Procedures and will be documented.

The Investigator is responsible for obtaining and maintaining ethics approval of the study protocol for their site. The Investigator is responsible for obtaining patient consent, and maintaining Informed Consent Forms and Case Report Forms for each subject. The Investigator is responsible for reporting and maintaining records of study protocol deviations and all IRB correspondence and other significant correspondence relating to the study. At the conclusion of the study, the Investigator will provide a report to the ethics committee.

If the device malfunctions or fails to function as expected, the Investigator must report the incident to ZOLL immediately.

Patient identities will be kept confidential; however, ZOLL may provide study results to the USA's Food and Drug Administration (FDA) and other regulatory agencies.

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