Official Title: Measuring Thoracic Impedance in Hemodialysis Patients with the u-Cor Monitoring System

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Measuring Thoracic Impedance in Hemodialysis Patients with the µ-Cor System

A Pre-Market Validation Study (MaTcH)

Protocol #: 2016-KM-004

Version: 1.1

Date: October 3, 2016

Sponsor Information:

ZOLL Services LLC
121 Gamma Drive
Pittsburgh, PA 15238
Phone: +1-412-968-3333

CLINICAL INVESTIGATION PLAN SIGNATURE PAGE

I have read and understood the contents of the Clinical Investigational Plan (CIP) (also referred to as the protocol), 2016-KM-004 Version 1.1 (October 3, 2016).

I agree to follow and abide by the guidelines set forth in the protocol, and agree to carry out all of its terms in accordance with Good Clinical Practice (GCP), the Declaration of Helsinki, International Conference of Harmonization (ICH), and the applicable national and local regulations.

I accept the oversight of the study monitor and control procedures, including verification by access to source documents, as required by the study monitoring and audit functions of the Sponsor and audit functions of regulatory agencies in accordance with GCP.

I understand that any changes to this protocol (not associated with procedures necessary for the safety of subjects) instituted by the Principal Investigator (PI) without previous discussion with the Sponsor would constitute a violation of the protocol.

I agree the device and all other study-specific items supplied by the Sponsor will be used solely for the purpose of conducting this clinical research study.

Investigative Site Name

Principal Investigator name (printed)

Principal Investigator signature Date

Madhuri Bhat
Clinical and Regulatory Affairs Date

Protocol Summary

Title:	Measuring Thoracic Impedance in Hemodialysis Patients with the µ-Cor System– A Pre-Market Validation Study (MaTcH)
Protocol Number:	2016-KM-004 Version 1.1
Study Device:	µ-Cor V3.0 System (also referred to as µCor V3.0.0, µ-Cor V3.0.0, µ-Cor or µCor)
Proposed Indications For Use:	The µ-Cor System is intended to record, store, transmit, and display the following physiological data to medical professionals: • thoracic impedance, • ECG, • heart rate, • respiration rate, • activity, • posture. The µ-Cor System is indicated for patients who are 21 years of age or older who: • have fluid-management problems, • are taking diuretic medication, • are living with heart failure, • are living with end-stage renal disease, • are recovering from a coronary artery disease-related event, and/or • are suffering from recurrent dehydration.
Regulatory Status:	The µ-Cor System is an investigational device in the United States (US).Limited by Federal (US) law to investigational use only.
Number of Centers:	Three centers (with an option to add a fourth center)
Study Design:	Prospective, non-significant risk, randomized, 2-arm, pre-market validation study
Objectives:	• This clinical trial is intended to provide evidence of substantial equivalence between the µ-Cor System and the ZOE System in the ability to measure thoracic impedance, by comparing the correlation between µ-Cor measurement and ultrafiltration volume (UFV) as compared with the correlation between ZOE measurement and UFV. The actual UFV changes will be used to arbitrate any differences. • The ability of the µ-Cor System to measure thoracic impedance will be demonstrated at 2 body locations: side location (below left armpit, Study Arm 1), and front location (upper front chest, Study Arm 2).

Subject Population:	Forty patients undergoing hemodialysis (n = 40) in 2 study arms with at least 50% enrollment of patients diagnosed with congestive heart failure (CHF) in each arm: • Study Arm 1: 20 patients undergoing hemodialysis, with at least 10 of these patients having CHF, will have the μ-Cor device placed on the side location • Study Arm 2: 20 patients undergoing hemodialysis, with at least 10 of these patients having CHF, will have the μ-Cor device placed on the front location
Inclusion Criteria:	Candidates must meet **ALL** of the following criteria at the time of screening: 1. Men and women at least 21 years of age. 2. Is currently scheduled to undergo hemodialysis 3 times per week in a clinic setting and has been on this regimen for at least 3 months. 3. For those patients with CHF: were diagnosed with CHF by a qualified provider and show symptomatic signs of New York Heart Association (NYHA) Class II to IV at enrollment. 4. Is prescribed a net fluid removal of at least 2.5 L during the hemodialysis session. 5. Is willing and able to sign informed consent in English.
Exclusion Criteria:	Candidates must be excluded from this study if **ANY** of the following criteria are met at the time of screening: 1. Is a female patient with a known pregnancy or is unsure of pregnancy status. 2. Has known allergies or skin sensitivities to electrode hydrogel and/or acrylic based adhesive. 3. Has skin breakdown in areas where device and electrode placement is required. 4. Was hospitalized within the 2 weeks prior to enrollment. 5. Had intradialytic hypotension requiring administration of intravenous (IV) fluids of ≥250 mL or that resulted in a referral to urgent care, within 2 weeks prior to enrollment. 6. Had myocardial infarction, acute coronary syndrome, or stroke within 4 weeks prior to enrollment. 7. Has active nephrotic syndrome 8. Has severe malnutrition, as diagnosed per a qualified provider. 9. Is participating in another clinical trial. 10. Has an implanted device that might interfere with the μ-Cor.
Procedure Summary:	1. A patient will be considered enrolled when she/he satisfies all inclusion and exclusion criteria, signs the informed consent, **and** wears the μ-Cor device and is connected to the ZOE monitor. The patient will go through 1 hemodialysis session (ie, Session A). The patient may be consented from 21 days before (ie, A -21 d to A -1 d) Session A, or they may be consented prior to the start of any study procedures on the day of

	Session A. The μ-Cor device and ZOE monitor will be applied during Session A. 2. Patients will be randomly allocated to Study Arm 1 or Study Arm 2, with randomization stratified by CHF status (CHF or non-CHF). A randomization schedule will be provided to the clinical sites. 3. Weight, blood pressure, and heart rate will be recorded before the dialysis session. 4. During the hemodialysis session, the patient will wear 1 μ-Cor device and will be connected simultaneously to 1 ZOE monitor (via 2 ZOE electrodes) for comparative measurements and UFV correlation, from at least 15 minutes before the start of dialysis to at least 15 minutes after the end of the dialysis session. 5. The thoracic area of the patient will be cleaned and treated per the protocol procedures. The μ-Cor will be placed in accordance with instructions provided in the Investigator's Brochure (IB). 6. The ZOE electrodes will be placed according to the manufacturer's instructions for use (IFU). 7. The μ-Cor will record measurements during the dialysis session, including at least the 15 minutes before and 15 minutes after the session. 8. ZOE (Z_0) values will be measured every 6 minutes (± 1 minute) during the dialysis session. ZOE (Z_0) values also will be measured every 3 minutes (± 1 minute) before and after the session, for a minimum of 5 measurements. 9. The UFV during the course of hemodialysis will be measured by automated readings provided by the dialysis machine every 6 minutes (± 1 minute). 10. Any IV infusions administered during the course of hemodialysis will be recorded. 11. Any oral fluid or solid intake during the hemodialysis session will be recorded. 12. Any urine output during the hemodialysis session will be recorded. 13. At the end of the hemodialysis session, both the ZOE electrodes and μ-Cor device will be removed from the patient's body. 14. At the end of the hemodialysis session, weight, blood pressure, and heart rate will be recorded. 15. Adverse events will be collected from the time of enrollment through the end of the Session A. 16. The patient's involvement in the study ends after the completion of all procedures planned for Session A. Study duration for each patient is expected to last 1 day: a patient will undergo 1 session of hemodialysis in the clinic.
Estimated Enrollment Period:	Up to 4 months
Study Duration for Each Subject:	One (1) day

Proposed Study Duration:	Approximately 6 months
Endpoints:	The primary endpoint is a comparison of correlations of thoracic impedance made with the μ-Cor System and UFV, with those of the ZOE and UFV. The non-inferiority assessment will be between each location (side and front) of the μ-Cor System/UFV correlation to the ZOE/UFV correlation. The secondary endpoints are: • Comparison of correlations of thoracic impedance made with the μ-Cor System and UFV, to those of the ZOE and UFV using all values from the μ-Cor System, regardless of location • Comparison of the precision of the ZOE and the μ-Cor System
Statistical Methods:	Since previous published studies have reported that bioimpedance measurements have been more reliably used before and after the dialysis treatment (5) (6) (7), data from these time points will be compared separately from data collected during dialysis. In general, summaries will be provided for all study patients and by study arm. Correlation between μ-Cor and UFV changes during the dialysis session will be summarized using average Pearson's correlation coefficient. Correlation between ZOE and UFV changes will be summarized in the same manner. The non-inferiority assessment will be between each location (side and front) of the μ-Cor System/UFV correlation to the ZOE/UFV correlation. The μ-Cor System will be considered as substantially equivalent with respect to clinical performance of the ZOE monitor if the correlation between the μ-Cor thoracic impedance measurements and UFV (r_ μ-Cor) is non-inferior to the correlation between ZOE bioimpedance measurements and UFV (r_ ZOE). Non-inferior is defined as r_ μ-Cor within the range [(r_ ZOE - 0.05), 0.9999]. The precision of each device will be compared using a Mann Whitney test.
Sponsor and Data Management:	ZOLL Services LLC 121 Gamma Drive Pittsburgh, PA 15238 Phone: +1-412- 968-3333

Table 1: Schedule of Assessments

Study Task	Dialysis Session A -21 d to A -1d[a]	Dialysis Session A[b]
Screening and informed consent	X[c]	X[c]
μ-Cor application (side location or front location)		X[d]
ZOE application and measurements		X[d]
Ultrafiltration volume (UFV)		X[e]
Measurements of vital signs and weight		X[f]
Adverse event assessment		X
Study exit		X

[a] Session A -21 d to A -1 d is defined visit immediately prior to Session A, which is the dialysis session under study.

[b] Session A is the dialysis session in which the device will be studied.

[c] The informed consent form can be signed by a patient from Session A -21d to A -1d or at Session A.

[d] Including measurements at least 15 minutes prior to and at least 15 minutes after the dialysis session.

[e] Volume of fluid extracted (UFV) every 6 minutes (± 1 minute) by dialysis machine, throughout the dialysis session.

[f] Blood pressure, heart rate, and weight before and after the dialysis session.

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1 BACKGROUND AND RATIONALE

A significant number of patients suffering from pathologies related to fluid management have frequent recurrence of acute episodes. Among these patients are those with congestive heart failure (CHF). Lung congestion is the leading cause of hospitalization and readmission among patients with CHF (1). To date, there is no effective method for direct measurement and monitoring of lung congestion, making physicians rely on non-specific, patient-dependent measurements such as a patient's weight and blood pressure. A tool that provides direct and accurate measurement of thoracic impedance has the potential to shorten the hospitalization period by enabling effective drug balance; it also may provide early edema detection in order to prevent hospital readmission.

Similarly, patients with chronic kidney disease (CKD) undergoing hemodialysis also require fluid management strategies. It has been documented that patients diagnosed with CKD undergoing maintenance hemodialysis have a high prevalence of heart failure (HF) and poor prognosis (2) (3). Congestive heart failure is a frequent clinical manifestation in patients undergoing dialysis (4).

For these reasons, body fluid assessment is important for managing CKD and HF. Bioimpedance technology has remained underutilized due to the lack of noninvasive, ambulatory measurement devices. In this study, we will evaluate the performance of the µ-Cor System, a noninvasive, wearable monitoring system for accurately assessing thoracic impedance by monitoring fluid changes during hemodialysis.

Fluid changes evaluated with the µ-Cor will be compared with those of an FDA-cleared fluid measurement device, the ZOE® Fluid Status Monitor (Noninvasive Medical Technologies) to establish significant equivalence. Qualified healthcare practitioners currently use the ZOE for monitoring patients who are living with fluid management problems, taking diuretic medication, living with heart failure, living with end stage renal disease, or suffering from recurrent dehydration.

During a typical hemodialysis session, approximately 2 to 4 L of fluid are removed. Using the common variable of fluid removed during a hemodialysis session will aid investigators in assessing the efficacy of the µ-Cor ability to detect fluid, as well as correlation to measurements taken with an FDA-cleared fluid measurement device.

2 DEVICE DESCRIPTION

The µ-Cor noninvasively monitors a patient's clinical parameters (thoracic impedance, ECG, heart rate, respiration rate, activity, and posture). Measurements are acquired via a patient-worn device and the raw data are transmitted wirelessly to a remote server with dedicated software to process the raw data. The µ-Cor is designed for use in outpatient clinics and home settings.

2.1 Device Components

The components of the µ-Cor can be found in Table 2.

Table 2: µ-Cor Components

Components and Description	Illustration
Patch – A single-use, disposable, adhesive piece adhered to the patient's body that allows for Cartridge attachment. The Patch is made of non-woven fabric with adhesive on one side, a polypropylene frame for housing the Cartridge (see below), 2 ECG electrodes covered with hydrogel on one end and a connection wire on the other end, and 2 polypropylene ECG covers.	
Cartridge – A patient-worn device for signal acquisition.	
Charger – The Charger charges the Cartridge (re-charging is needed typically after 5 days of wear) and houses the gateway that wirelessly transmits the data to the server.	
Server – The server refers to the hardware and the processing software and resides in a cyber-secure location. The software analyzes the raw data received from the Cartridge and processes the data into clinical values for eventual presentation to the end-users (such as physicians and caregivers).	

3 PROPOSED INDICATIONS FOR USE

The μ-Cor System is intended to record, store, transmit, and display the following physiological data to medical professionals:

- thoracic impedance,
- ECG,
- heart rate,
- respiration rate,
- activity,
- posture.

The μ-Cor System is indicated for patients who are 21 years of age or older who:

- have fluid-management problems,
- are taking diuretic medications,
- are living with heart failure,
- are living with end-stage renal disease,
- are recovering from a coronary artery disease-related event, and/or
- are suffering from recurrent dehydration.

4 INVESTIGATIONAL PLAN

4.1 Study Design

Prospective, non-significant risk, randomized, 2-arm, pre-market validation study.

4.2 Regulatory Status

The μ-Cor System is an investigational device in the US limited by Federal (US) law to investigational use only.

4.3 Objectives

This clinical trial is intended to provide evidence of substantial equivalence between the μ-Cor System and the ZOE System in the ability to measure thoracic impedance, by comparing the correlation between μ-Cor measurements and UFV as compared with the correlation between ZOE measurement and UFV. The actual UFV changes will be used to arbitrate any differences. The ability of the μ-Cor System to measure thoracic impedance will be demonstrated at 2 body locations: side location (below left armpit, Study Arm 1*)*, and front location (upper front chest, Study Arm 2*)*.

4.4 Study Sample Size and Number of Participants

Forty patients undergoing hemodialysis (n = 40) in 2 study arms with at least 50% enrollment of patients diagnosed with congestive heart failure (CHF) in each arm:

- Study Arm 1: 20 patients undergoing hemodialysis, with at least 10 of these patients having CHF, will have the μ-Cor device placed on the side location
- Study Arm 2: 20 patients undergoing hemodialysis, with at least 10 of these patients having CHF, will have the μ-Cor device placed on the front location

Patients will be randomly allocated to Study Arm 1 or Study Arm 2, with randomization stratified by CHF status (CHF or non-CHF). A randomization schedule will be provided to the clinical sites. Appendix A shows the NYHA functional classification table.

4.5 Subject Recruitment, Eligibility, and Enrollment

Patients will be recruited directly from the research site. All patients will participate in the study voluntarily. If a patient does not want to participate, there will be no effect on their standard-of-care treatment. Enrollment is defined as the time when patients who have satisfied all of the inclusion and exclusion criteria, have signed the Institutional Review Board (IRB)-approved informed consent documents, and wears the μ-Cor device plus ZOE electrodes. The patient may be consented from 21 days before (ie, A -21d to A -1d) Session A, or they may be consented prior to the start of any study procedures on the day of Session A.

4.5.1 Inclusion Criteria

Prior to enrollment in this clinical investigation, candidates must meet **ALL** of the following criteria at the time of screening:

1. Men and women at least 21 years of age.
2. Is currently scheduled to undergo hemodialysis 3 times per week in a clinic setting and has been on this regimen for at least 3 months.
3. For those patents with CHF: were diagnosed with CHF by a qualified provider and show symptomatic signs of NYHA Class II to IV at enrollment.
4. Is prescribed a net fluid removal of at least 2.5 L during the hemodialysis session.
5. Is willing and able to sign informed consent in English.

4.5.2 Exclusion Criteria

Candidates must be excluded from this study if **ANY** of the following criteria are met at the time of screening:

1. Is a female patient with a known pregnancy or is unsure of pregnancy status.
2. Has allergies or skin sensitivities to electrode hydrogel and/or acrylic based adhesive.
3. Has skin breakdown in areas where device and electrode placement is required.
4. Was hospitalized within the 2 weeks prior to enrollment.

5. Had intradialytic hypotension requiring administration of IV fluids of ≥250 mL or that resulted in a referral to urgent care, within the 2 weeks prior to enrollment.
6. Had myocardial infarction, acute coronary syndrome, or stroke within the last 4 weeks prior to enrollment.
7. Has active nephrotic syndrome.
8. Has severe malnutrition, as diagnosed per a qualified provider.
9. Is participating in another clinical trial.
10. Has an implanted device that might interfere with the μ-Cor.

4.6 Duration of Study Participation

Patient enrollment is estimated to be up to 4 months. The expected study duration of each subject is 1 day. Each patient will go through 1 hemodialysis session in the clinic.

4.7 Investigator Selection

Investigators will be qualified professionals experienced with the management of the patient population fitting the subject eligibility criteria. The clinical study site will be selected upon interest and availability for participation of the study, ability to provide qualified patients, adequate support staff, and experience conducting clinical research. The Principal Investigator also will maintain compliance and oversight of the clinical study activities at the center and may delegate tasks appropriately to the Sub-Investigators or Study Coordinators.

5 STUDY PROCEDURE

The following sections outline the details of the clinical investigation procedures.

5.1 Informed Consent

To protect the rights and welfare of subjects, this clinical investigation will be conducted in conformance to ICH-GCP.

Prior to admission to the clinical investigation, an informed consent document will be given to each prospective patient, including an explanation of the clinical investigation, duration, expected benefits and risks, explanation of alternatives, medical record access, and patient anonymity, and if data are to be used for publications or submission for reimbursement support. The informed consent form (ICF) will contain language that is non-technical and is understandable to the patient. The Investigator must inform patients that they are in a clinical study, inform them of their rights as set forth in the informed consent document, and provide written documentation that such a discussion took place. A patient will be provided ample time and opportunity to inquire about the details of the study and decide whether to participate. A consent document will be provided that contains non-technical language that is understood by the patient. Informed consent shall be documented by a patient's dated signature on the consent form. The original, signed document will be kept with the patient's file, and a copy must be provided to the patient. Enrollment is defined as the patient agreement with and documentation

of written informed consent and the application of the μ-Cor device plus 2 ZOE electrodes on the patient's body.

If the Investigator fails to obtain a signed informed consent before enrollment, the Investigator must submit a report to the Sponsor indicating the circumstances of the occurrence. Post-dated informed consent documents are not permissible. Failure to obtain informed consent prior to enrolment is considered a major protocol deviation. The Sponsor must be notified and a Protocol Deviation Form must be completed.

A sample of the ICF is provided in Appendix B.

5.2 Screening and Enrollment

The Investigator at the site should screen all eligible patients for initial study eligibility. A Site Screening Log will be provided to the site to capture all patients screened for the study. All patients will be assigned a unique screening ID and documented on the Site Screening Log. Patients must sign an ICF prior to any study-related procedures. If, for any reason, a patient is excluded from the study (screen failure), the reason for exclusion should be captured on the Site Screening Log.

Patients will be considered enrolled in the study when they have signed the IRB-approved informed consent documents, met all inclusion and exclusion criteria, and the μ-Cor device and 2 ZOE electrodes are applied to their body. Once enrollment is confirmed, the patient will be assigned a unique patient identification number. The patient may be consented from21 days before (ie, A -21d to A -1d) Session A, or they may be consented prior to the start of any study procedures on the day of Session A.

5.3 Baseline Information

When the patient is enrolled into the study, the following baseline information will be collected:

- medical history
- physical examination
- current illness

All information will be recorded on the appropriate case report form (CRF).

5.4 Session A Procedures

The following clinical procedures will take place:

1. During the hemodialysis session (Session A) the patient will wear one μ-Cor device on the side location, below the left armpit (Study Arm 1) or one μ-Cor device on the front location, upper left chest (Study Arm 2) and 2 ZOE electrodes simultaneously for comparative measurements and UFV correlation, for at least 15 minutes before the start of dialysis and for at least 15 minutes after the end of the dialysis session.

2. Patients will be randomly assigned to Study Arm 1 or Study Arm 2, with randomization stratified by CHF status (CHF or non-CHF). A randomization schedule will be provided to the clinical sites.
3. Patients should be positioned in their dialysis chair per standard of care.
4. Preparation of the devices and patients will be as follows:

ZOE monitor (model Z2-100 and ZOE electrodes model Z2-711):

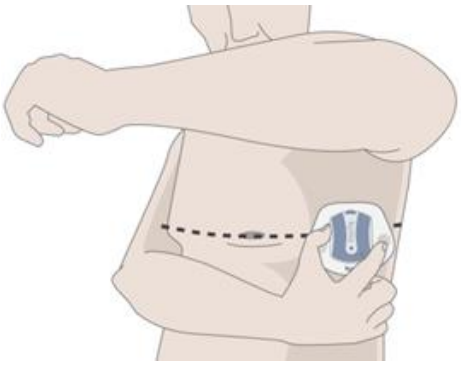
The patient's skin where the electrodes have to be placed should be clean and dry; all hair should be removed from the site where the electrodes will be placed to assure a good connection to the skin. The AC adapter is connected to the back of the ZOE, and the device plugged into an outlet (or insert batteries). Two new ZOE electrodes are to be snapped on the ZOE cable. Electrodes are to be placed on the skin: electrode 1 goes above the top of the breastbone with the arrow tip pointing down; electrode 2 goes below the bottom of the breastbone with the arrow tip pointing up.

After an information for user manual (IFU)-required 5-minute wait period to allow for the electrodes to seed, measurements can start by pressing the start button. During the time of the readings, the patient must remain still for about 30 seconds without moving or drinking until the Z_0 value displays on the screen. The Z_0 values turn off automatically within 30 seconds. The Z_0 values must be recorded manually on a Z_0 Tracking log.

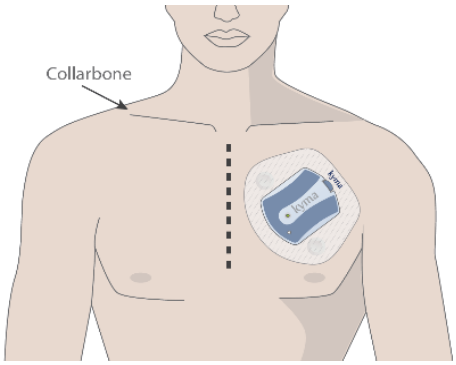
An illustrated user manual will be provided to the site as a part of the site training for additional guidance.

µ-Cor System:

The patient's skin where the patch will be placed should be clean and dry; all hair should be trimmed from the site where the patch will be placed to assure a good connection to the skin. The charger (and gateway placed inside the charger) is connected to an outlet using the power cord supplied by ZOLL. When a green LED light appears on the cartridge (not on charger), it is an indication that the unit is ready for use. The cartridge is to be placed on the charger for up to 60 minutes. The cartridge is then removed from the charger and placed on the adhesive patch: lower positioning tabs of the cartridge will go on the lower part of the adhesive patch; then the rest of the cartridge is pressed onto the patch. The cartridge should be firmly attached. The patch liner is to be peeled off and placed on the skin. The patch should be completely adhered to the skin. For Study Arm 1, the patch should be positioned below the left arm pit, with the word "Kyma" right side up, with the nipple aligned anywhere between the top and middle of the cartridge. For Study Arm 2, the patch should be placed on the upper left chest, just below the collarbone and the device should be angled as shown in the IB.



Study Arm 1 (Side Location)



Study Arm 2 (Front Location)

In order to remove the patch-cartridge from the skin, first, the cartridge must be removed from the adhesive patch by pressing the upper snap-in clip; then the cartridge should be tilted and removed from the patch. The cartridge should then be placed on the charger.

In order to detach the adhesive patch from the skin, it is necessary to hold the skin with one hand while peeling off gently with the other hand. A wet wipe can be used to assist with this process. Patches must be discarded and cannot be reused.

An illustrated IB will be provided to the site as part of the site training for additional guidance (Appendix C)

5. Weight, blood pressure, and heart rate will be recorded before the hemodialysis session.
6. The μ-Cor will be programmed to record measurements every 3 minutes during the hemodialysis session, including at least 15 minutes before and after the hemodialysis session. However, only every alternate μ-Cor recording taken during the dialysis session will be used for analysis (ie, the reading taken every 6th minute). This will be done in order to synchronize μ-Cor measurements with the ZOE (Z_0) measurements that also will be recorded every 6 minutes (±1 minute) during the hemodialysis session along with the UFV measurements.
7. ZOE (Z_0) values will be measured every 3 minutes (± 1 minute) before and after the hemodialysis session, for a minimum of 5 measurements (synchronized with the μ-Cor before and after dialysis measurements).
8. The UFV during the course of hemodialysis will be measured by automated readings provided by the dialysis machine every 6 minutes (± 1 minute) (synchronized with the μ-Cor and ZOE during dialysis measurements) as shown in Table 3.

Table 3: Schedule of Synchronized Measurements

Time Point	μ-Cor	ZOE	UFV
Before Dialysis	Every 3 minutes	Every 3 minutes	N/A
During Dialysis	Every 6th minute (measurement used for analysis)	Every 6 minutes	Every 6 minutes
After Dialysis	Every 3 minutes	Every 3 minutes	N/A

9. Any IV infusions administered during the course of hemodialysis session will be recorded.
10. Any oral fluid and/or solid intake during the hemodialysis session will be recorded.
11. Any urine output during the hemodialysis session will be recorded.
12. At the end of the hemodialysis session, the patients will be asked to remain in a position similar to the position they were in for the majority of the session (ie, if a patient was in a reclined position throughout the dialysis session, they should remain in this position while the dialysis needles are removed from the access site and for the subsequent 15 minutes).
13. Both the μ-Cor device and ZOE electrodes will be removed from the patient's body.
14. At the end of the hemodialysis session, weight, blood pressure, and heart rate will be recorded.
15. Adverse events will be collected from the time of enrollment through the end of the Session A.
16. The patient's involvement in the study ends after the completion of all procedures planned for Session A. Study duration for each patient is 1 day: a patient will undergo through 1 session of hemodialysis in the clinic.
17. Gateways, chargers, cartridges, and patches will remain at the clinic at all times.
18. Neither the investigator nor the patient will be informed of the μ-Cor readings and data. All patient medical care will be subjected to the medical teams/investigator's decision and standard of care.

5.5 Complete Schedule

The complete study schedule of assessments to take place during the clinical investigation is provided in Table 1.

5.6 Subject Withdrawal

Participation in this clinical investigation is voluntary and patients may withdraw at any time.

In the event the patient chooses to withdraw, he/she will be instructed to contact the Investigator immediately. The patient also may be terminated from the clinical investigation at any time if his/her primary physician and/or the Investigator consider it to be in his/her best medical interest. Withdrawal from the investigation will not affect patient's follow-up care. Patients will be informed of any significant information regarding new findings that may develop during the course of the research study that may relate to his/her willingness to continue participation as a clinical investigation patient.

Patients will either satisfactorily complete all requirements set forth in the clinical investigation plan or their participation in the clinical investigation will be prematurely terminated. The completion of a patient's participation in the clinical investigation or early departure from the clinical investigation must be fully documented in the patient's progress notes as well as on the appropriate CRF.

Should a patient choose to withdraw from the study, the reason(s) for withdrawal will be recorded on the appropriate CRF and in the patient's medical record.

An Investigator may remove a patient from the study for the following reasons:

- In the judgment of the Investigator, continuation in the study can adversely affect the safety of the patient
- Subject non-compliance with the clinical investigational plan

5.7 Return of Study Product

At the end of the patient enrollment period, patients will leave all devices at the clinic. The clinical site will return all systems to ZOLL.

5.8 Protocol Deviation

A protocol deviation is defined as not adhering to the clinical investigation plan. Protocol deviations can be major or minor. A major deviation is defined as an event that resulted in an increased risk to a patient or others; affected the rights, safety, or welfare of a patient; or affected the integrity of the clinical investigation. Major protocol deviations include (but are not limited to): failure to obtain informed consent prior to patient enrollment, an enrolled patient did not meet the inclusion/exclusion criteria, or unauthorized use of the devices.

Prior approval by the Sponsor is expected in situations where the Investigator anticipates, contemplates, or makes a conscious decision to deviate. Prior approval is not expected in situations where unforeseen circumstances are beyond the Investigator's control (eg, inadvertent errors, product failure, or inability to perform required procedures due to patient illness).

All major deviations will be documented on a Protocol Deviation CRF.

6 RISK ANALYSIS

ZOLL has conducted an analysis of the benefits and risks of the µ-Cor System. ZOLL has determined that this clinical investigation is justified as the overall potential benefit to the population outweighs its intended risks. This is a non-significant clinical study (the non-significant risk declaration is presented in Appendix D).

6.1 Benefits

Specific potential benefits with the use of the µ-Cor System may not be known at this time. However, participation in this clinical investigation may help further develop the technology such that it could be a potential benefit to others.

6.2 Risks

The µ-Cor System is a non-significant risk and noninvasive medical monitoring device.

The potential risks from wearing the patch are minimal and may include mild discomfort, skin irritation, redness, itching, rash, contact dermatitis, or breaching of the skin if the patch is removed too quickly. The μ-Cor System has not been tested for compatibility with magnetic resonance imaging (MRI) machines or external defibrillators. Re-use of the patch may result in patient cross-contamination and inaccurate measurements.

6.2.1 Minimization of Risks

Patients with known allergies to adhesives or hypersensitivity to the patch materials or hydrogel will be excluded from the study

Only qualified clinical Investigators who have training to conduct those procedures will participate in this study.

7 ADVERSE EVENTS AND DEVICE DEFICIENCIES

An adverse event (AE) is any undesirable experience (sign, symptom, illness, or other medical event) occurring to a patient, whether or not associated with the investigational product or related procedures that is considered a change from baseline, or pre-study status during the course of the study.

7.1 Adverse Event Reporting

Adverse events shall be assessed and documented and should include the following:

- The time of onset of any new AE or worsening of a previously observed AE
- A description of the event
- The duration of the event (start and stop dates, or ongoing)
- The severity of the event (mild/moderate/severe)
- Assessment of the relation of the AE to the study device and index procedure
- Description of action taken to treat the event
- Event outcome

Event severity will be categorized as follows:

- **Mild** - Easily tolerated by the patient, causing minimal discomfort and not interfering with everyday activities. These events generally do not require treatment.
- **Moderate** - Sufficiently discomforting to interfere with normal everyday activities. These events are usually relieved by simple therapeutic measures.
- **Severe** - Prevents normal, everyday activities. These events may require systemic drug therapy or other medical treatment.

The relationship between the AE, the study device, and the interventional procedure will be categorized as follows

- **None** - An AE for which sufficient information exists to indicate that the etiology is unrelated to the device; the AE is readily explained by the patient's clinical state or other therapies.

- **Possible** - The AE follows a known or expected response pattern to the device, but could readily have been produced by a number of other factors.
- **Probable** - The AE follows a known or expected response pattern to the device.
- **Definite** - The AE follows a known or expected response pattern to the device and the physician confirms the relationship through further testing or evidence.

Regardless of whether or not the AE is considered related to the device and/or interventional procedure, the AE must be reported on the appropriate AE CRF.

7.2 Serious Adverse Event (SAE)

A Serious Adverse Event (SAE) is defined as any adverse experience that results in any of the following outcomes: death, a life-threatening adverse experience, in-patient hospitalization or prolongation of an existing hospitalization, a persistent or significant disability/incapacity, permanent impairment of a body function or permanent damage to a body structure, or necessitated medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure.

In the event of an SAE, the Sponsor should be notified within 24 hours after identification of an SAE, followed by a written summary submitted within 2 days.

The Investigator will report all SAEs to the IRB according to local requirements.

7.3 Anticipated Adverse Events

Anticipated adverse events include the following:

- Skin irritation, redness, itching, or rash
- Contact dermatitis
- Tearing of skin
- Allergic reaction to hydrogel

The following are common symptoms or signs in patients undergoing hemodialysis. These events are not necessarily related to the study device:

- nausea
- vomiting
- heartburn
- constipation/diarrhea
- headaches
- back pain sitting in dialysis chair
- chest pain (heart)
- shortness of breath
- sensation of heart racing
- rash
- itching

- burning feet
- muscle cramps
- joint pain
- fatigue
- dizziness/lightheadness
- depression
- trouble sleeping at night
- decreased appetite
- dry mouth/hoarseness
- restless legs
- low blood pressures (hypotension)
- swelling (eg, legs, face)

7.4 Unanticipated Adverse Device Effect (UADE)

An Unanticipated Adverse Device Effect (UADE) is an AE related to the use of an investigational medical device, which by its nature, incidence, severity or outcome has not been previously identified in the risk management files.

In the event of an UADE, the Sponsor should be notified within 24 hours after identification.

7.5 Device Deficiencies

Device deficiencies are defined as inadequacies of a medical device with respect to its identity, quality, durability, reliability, safety, or performance. Device deficiencies (also referred to as device performance issues) also include malfunctions, use errors, and inadequate labeling.

All μ-Cor device deficiencies will be documented in the patient's medical record and on the appropriate CRF.

8 STATISTICAL CONSIDERATIONS

8.1 Outcome Measures

The primary endpoint is the comparison of correlations of thoracic impedance made with the μ-Cor System and UFV with those of the ZOE monitor and UFV. The non-inferiority assessment will be between each location (side and front) of the μ-Cor System/UFV correlation and ZOE/UFV correlation.

The secondary endpoints are:

- Comparison of correlations of thoracic impedance made with the μ-Cor System and UFV with those of the ZOE and UFV using all values from the μ-Cor System, regardless of location
- Comparison of the precision of the ZOE and the μ-Cor System

The primary endpoint assessment depicted in Figure 1.

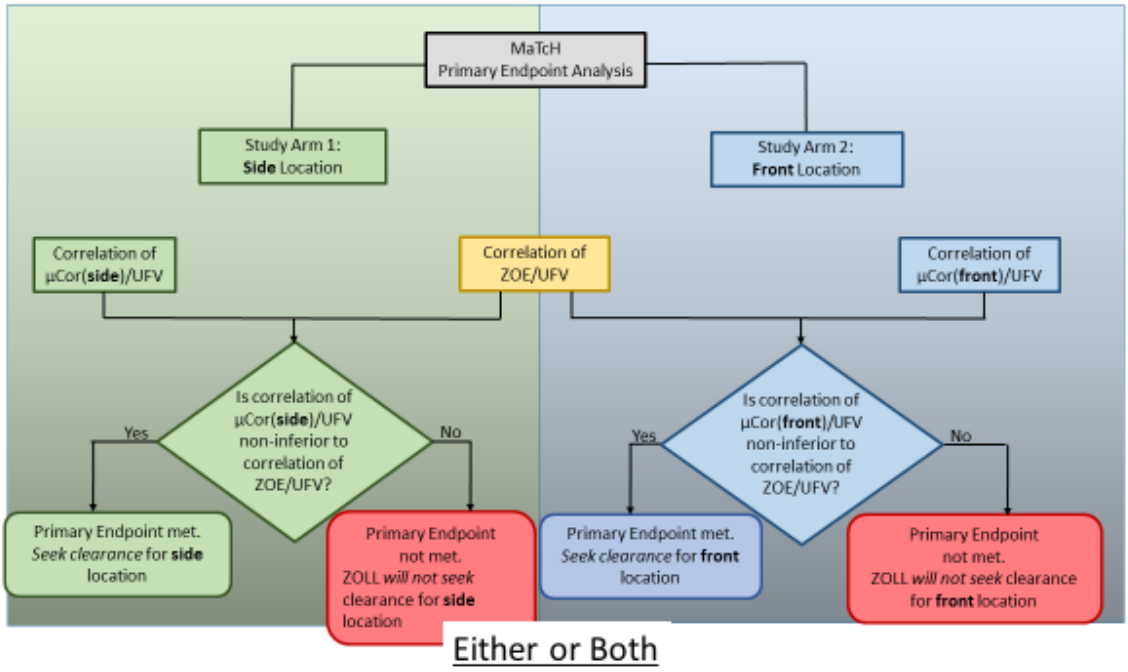


Figure 1: Primary Endpoint Assessment

8.2 General Statistical Considerations

A statistical analysis plan (SAP) will be created by ZOLL or a designee, and will be finalized prior to database lock.

For statistical analyses, data will be summarized by investigational site and by pooled sites.

All tests of differences will be conducted at a 2-sided alpha level of 0.05, unless otherwise stated. Any p-values produced for this study will be considered as exploratory due to the small sample size.

Data summaries will be provided for all patients combined and by each study arm, wherever appropriate. For continuous variables, summary statistics will include number of patients, mean, median, standard deviation, minimum, and maximum. Categorical endpoints will be summarized using number of patients, frequency, and percentages.

Additional exploratory analyses of the data will be conducted as deemed appropriate.

8.3 Patient Disposition

Patients who complete the study and those who prematurely discontinue from the study, will be summarized overall and by study arm. In addition, for patients who prematurely discontinue from the study, the reasons for discontinuation will be summarized.

8.4 Demographics and Baseline Characteristics

Descriptive summaries of demographics and baseline characteristics will be presented for all patients and by each study arm.

8.5 Analyses

The primary efficacy analysis will be conducted on all per-protocol enrolled patients that meet all selection criteria. Supportive analyses may be conducted on a subset of subjects, as defined in the statistical analysis plan.

8.5.1 Comparison of Correlations

The primary endpoint is the comparison of correlations of thoracic impedance made with the μ-Cor System and UFV with those of the ZOE monitor and UFV. Correlation between μ-Cor and UFV changes during the dialysis session will be summarized using average Pearson's correlation coefficient. Correlation between ZOE and UFV changes will be summarized in the same manner. The non-inferiority assessment will be between each location (side and front) of the μ-Cor System/UFV correlation and ZOE/UFV correlation. The μ-Cor System will be considered as substantially equivalent with respect to clinical performance of the ZOE monitor if the correlation between the μ-Cor thoracic impedance measurements and UFV (r_ μ-Cor) is non-inferior to the correlation between ZOE bioimpedance measurements and UFV (r_ZOE). Non-inferior is defined as r_ μ-Cor within the range [(r_ZOE – 0.05), 0.9999].

A similar, supporting comparison will be made using all values from the μ-Cor System, regardless of location. This comparison will be considered as a secondary comparison.

8.5.2 Precision Comparison of μ-Cor and ZOE

A Mann-Whitney test will be employed to compare the precision of the Zoe and the μ-Cor. The precision of each device will be calculated, using values obtained before dialysis, as:

$$\text{Precision} = \frac{\text{standard deviation of measurements before dialysis}}{\text{median measurement before dialysis}}$$

8.5.3 Safety Analyses

Safety summaries will be based on all enrolled patients.

All AEs will be summarized and listed. The incidence of AEs will be presented by severity and by relationship with the device and the interventional procedure, as perceived by the Investigator. Adverse events reported to occur prior to enrollment will be distinguished from those reported as new or increased in severity after enrollment.

In addition, vital sign measurements will be listed and summarized using standard descriptive statistics.

Additional analyses will be performed, if warranted, upon review of the data.

8.5.4 Interim Analyses

There is no planned interim analysis in this study.

9 DATA QUALITY ASSURANCE AND MONITORING

9.1 Site and Investigator Selection

The investigational site will be selected based on their resources and ability to complete the requirements specified in the clinical investigational plan (CIP). The following requirements must be met in order for a site to be eligible for participation:

- Operating physician must be trained in patient care
- Investigator must be willing to comply with the CIP, required procedures, federal and local regulations.
- Investigator must have experience with medical devices and/or regulated studies
- Investigator must have adequate staff, time, and resources to support the study

9.2 Data Collection and Processing

A CRF will be provided in order to collect data. The CRFs will be completed for each patient enrolled.

Completed CRFs will be verified against source data and/or medical records by the ZOLL designated study monitor for completeness and consistency. If corrections or modifications are needed during the monitoring visit, the Investigator or designee will correct the data directly on the CRF. All data corrections will comply with ICH.

The handling of data, including data quality assurance, will comply with all applicable regulatory requirements. Audits may be performed for quality assurance of data handling procedures.

ZOLL is the responsible coordinating center for data management. Data cleaning will be performed directly in their database. The study monitor, data management, and/or study team members also may check the data for completeness and consistency and raise data queries, which will be answered/resolved by the Investigator and or designee.

9.3 Study Management

ZOLL or its designee will assume overall study management. Specific personnel, as assigned by ZOLL, may serve as clinical monitors, study administrators, and/or be responsible for data review and data integrity. The address and telephone numbers are:

Contact:	ZOLL Services LLC
Attn:	Madhuri Bhat
Address:	121 Gamma Drive Pittsburgh, PA 15238
Office telephone:	+1-412-968-3333 x 31810

9.3.1 Monitoring

Monitoring of the clinical investigation will be a continuous process to ensure that high-quality data are obtained through compliance with the CIP and will be conducted in accordance with

GCP/ICH Guidelines and ZOLL approved procedures. Monitoring may be conducted remotely, via telephone, or an in-person visit. Case report forms will be reviewed for completeness, conformity with requirements, and safety monitoring of AEs. Accuracy of data reported on the CRFs will be verified by comparison to the patient's source documents and/or medical records, when applicable. If necessary, appropriate corrective action will be taken to ensure adherence to the CIP. Frequent communication will be maintained with the site to keep both the clinical site and ZOLL up-to-date and aware of the progress of the clinical investigation.

The Investigator guarantees direct access to source documents and medical and/or hospital records by ZOLL personnel or their designee and appropriate regulatory authorities. The clinical investigation may also be subject to a quality assurance audit by ZOLL or their designee, as well as inspection by appropriate regulatory authorities.

Scheduled monitoring will include, but is not limited to site qualification, site initiation, site interim monitoring, and site closeout.

9.3.2 Site Qualification

Prior to the site initiation, ZOLL will discuss CIP requirements with the Principal Investigator. ZOLL will also ensure the Principal Investigator understands and accepts the obligation to conduct the clinical investigation in accordance with the CIP, ZOLL's approved procedures for conducting clinical investigations, applicable national regulations, and GCP. ZOLL will ensure that the investigational site has the adequate resources and facilities to perform the study. This site qualification visit may be conducted at the Investigator's institution, remotely, or contact also may occur via telephone and will be documented by ZOLL.

9.3.3 Site Initiation

Site initiation will be conducted by the ZOLL clinical team to train the Investigator and supporting clinical investigation staff on the CIP objectives, patient timelines, device operation, CRF completion, informed consent procedures, patient screening and enrollment, study documentation and administration, device accountability, record-keeping requirements, Investigator and ZOLL responsibilities, role of the IRB, AE and protocol deviation reporting, monitoring requirements, and any applicable regulatory documents prior to enrolling the first patient. The site initiation will occur after the clinical investigation site has received written IRB approval to conduct the CIP. The site may not enroll study patient into the clinical investigation until all applicable IRB approval has been received by ZOLL and the site initiation is completed. Site initiation training will be documented and the documentation will be filed at the investigational site and at ZOLL.

9.3.4 Site Monitoring

Monitoring will be performed by ZOLL (or ZOLL's designee) to assess the progress of the clinical investigation and to ensure the Investigator adheres to the CIP and all applicable regulations. The monitor also will identify any concerns that result from device performance or review of the Investigator's study records, study management documents, and patient Informed Consent documentation.

To assure the integrity of key data collected in the clinical investigation, the study monitor will compare individual patient medical records and/or source documentation and reports prepared by the Investigator or designee to the CRFs. The data captured on the CRFs will be compared to supporting site documents, and includes eligibility criteria, AEs, protocol deviations, device accountability, device performance, and all study objectives.

In some instances, site monitoring may be performed remotely as long as key data provided on CRFs are properly monitored against source documents.

If a clinical site is found to be out of compliance with the CIP and regulations, it will be terminated from the clinical investigation and shall be required to return all unused devices and/or associated clinical investigation materials and procedure manuals to ZOLL.

9.3.5 Site Close-out

Site closeout will be conducted at the completion of the clinical study. During the close-out visit, ZOLL or ZOLL's designee will ensure that all CRFs and data queries are signed, dated, and have been transmitted to ZOLL; the device accountability log has been reconciled; and any remaining study devices have been shipped back to ZOLL. Additionally, ZOLL will review the Investigator's ongoing study responsibilities, including reporting of any unexpected or device related AEs, submission of a final study report, notification of study close to the IRB, and the maintenance of study files per regulations. In some instances, the site closeouts may be conducted via telephone.

10 ETHICAL CONSIDERATIONS

10.1 Conformance with Regulatory Standards

The clinical investigation will be performed in accordance with ICH E6, the Declaration of Helsinki, and applicable local regulations. International Conference of Harmonization (ICH) and GCP will be used as guidance for the preparation and conduct of the clinical investigation.

Prior to enrollment of the first patient, ZOLL will notify the appropriate regulatory agencies and obtain approval as necessary to start the clinical investigation.

10.1.1 Institutional Review Board

Clinical investigations will not begin without documented approval of the clinical investigation by the IRB affiliated with the study site. Additional approvals (by investigational site hospital/organizations) may also be required. The Investigator will submit and obtain approval for the clinical investigation from their IRB and hospital management. Prior to submission to the IRB, ZOLL must review and approve the site-specific ICF. It is the responsibility of the Investigator to ensure that all aspects of the IRB and hospital management reviews and approvals are obtained, maintained and renewed as necessary. The Investigator will provide ZOLL with a copy of all communication from the IRB and hospital management including submission and/orapproval of the CIP, and approval of the ICF prior to initiation of the clinical investigation. Amendments to the CIP and revisions to the ICF will be subject to the same requirements. The

clinical investigation will be performed in accordance with ethical principles that have their origins in the Declaration of Helsinki.

Copies of the IRB submissions and/or approvals must be maintained in the site regulatory binder. It is the responsibility of the Investigator to report any withdrawals of approval by the reviewing IRB to ZOLL within 5 working days.

10.1.2 Patient Confidentiality

Patient confidentiality will be maintained throughout the study. For this purpose, a unique patient identification code (ID number and patient name code) will be used that allows identification of all data reported for each patient.

Data relating to the study might be made available to third parties (for example in case of an audit performed by regulatory authorities) provided data are treated as confidential and that the patient's privacy is guaranteed in accordance with HIPAA criteria and/or other applicable requirements.

10.1.3 Clinical Investigational Plan Compliance

The Investigator will carefully review the procedures defined in the CIP and in the CRFs with his/her research staff prior to the time of site initiation to ensure appropriate interpretation and implementation. The Investigator should not plan to deviate from the CIP without obtaining prior consent from ZOLL. ZOLL may approve minor protocol deviation on a case-by-case basis. All protocol deviations (from the CIP) will be reported to ZOLL.

Only ZOLL is allowed to modify this CIP. Any changes to the CIP will originate from ZOLL (in the form of an amendment) and must be re-submitted to each institution's IRB and must be approved. Any modification that potentially affects patients' rights or safety also must be approved by the IRB and other regulatory agencies. In an emergency where action is necessary to protect the life or physical well-being of the patient, a deviation from the CIP for an individual patient may be allowed on a per-patient basis. In such circumstances, the Investigator must notify their IRB and ZOLL and must describe the conditions necessitating the deviation from the CIP and the outcome of the emergency intervention in a written report. ZOLL will determine whether the patient is to continue in the clinical investigation.

10.1.4 Suspension or Termination of Clinical Study

ZOLL may suspend or prematurely terminate either a clinical investigation at an individual investigational site or the entire clinical investigation for significant and documented reasons. An Investigator, IRB, or appropriate regulatory authority may suspend or prematurely terminate participation in a clinical investigation at the Investigational Site for which they are responsible.

If suspension or premature termination occurs:

a) ZOLL shall remain responsible for providing resources to fulfill the obligations from the CIP and existing agreements for following up the patients enrolled in the clinical investigation, and
b) The Principal Investigator or authorized designee shall promptly inform the enrolled patients at his/her investigational site, if appropriate.

Although ZOLL may terminate the clinical investigation or the Investigator at any time, scheduled patient follow-up visits, if applicable, will continue on all patients treated prior to the termination of the clinical investigation.

10.1.5 Emergency Situations

ZOLL accepts the right of the Investigator to initiate emergency medical intervention that may not be defined in the CIP, when necessary, to safeguard the life or physical well-being of a clinical investigation patient. The Investigator must give notice of any emergency deviations and justification for the deviation to the study personnel responsible at ZOLL and the IRB as quickly as possible after the emergency, and in any event, no later than 24 hours after the emergency**.**

Investigator, Site, and Sponsor Responsibilities

10.2 Investigator Responsibilities

The Investigator is responsible for the preparation, review, signature, and retention of the records listed below, per ICH E6:

- Investigational device receipt, use, and disposition records,
- Patient case history records and exposure to use of the device, including CRFs, medical records, progress notes, nurses notes, etc.,
- All signed ICFs and evidence in the case history supporting that informed consent was obtained prior to study participation,
- All relevant observations relating to the device (including shipment and reconciliation)
- Signed Investigator's agreement and curriculum vitae.

Records are subject to Food and Drug Administration (FDA) inspection and must be retained for a period of at least 2 years after the latter of 2 dates: 1) the date on which the investigation is terminated or completed, or 2) the date that the records are no longer required for purposes of supporting an application to the FDA to market the device.

10.3 Site Responsibilities

The clinical investigation site coordinator is under the supervision of the Investigator. The site coordinator is typically a physician, nurse, or a similarly trained medical professional. The clinical investigation site coordinator is responsible for:

- Tracking all patients involved in the clinical investigation
- Maintaining all records defined in the CIP
- Collecting all clinical data from patients involved in the clinical investigation
- Ensuring that complete data obtained in accordance with the CIP are provided to ZOLL in a timely manner
- Maintaining control over any ZOLL devices received and maintained at the site
- Assisting in monitoring the integrity of the site records

10.4 Sponsor Responsibilities

ZOLL is responsible for maintaining the following:

- Obtaining IRB approvals prior to enrolling patients;
- Selecting qualified Investigators;
- Ensuring proper Investigator training;
- Ensuring proper clinical site support and monitoring;
- Ensuring that IRB are informed of any significant new information about the study;
- Maintaining accurate and complete study records and submitting required reports;
- Obtaining signed Investigator agreements;
- Providing CRFs and ensuring that completed forms match source documentation;
- Ensuring protocol compliance;
- Ensuring proper reporting of all AEs.

10.5 Completion of Case Report Forms

The Investigator or his/her designee (commonly the site coordinator) will be responsible for completing, in a timely manner, a CRF for each patient who is registered to participate in this clinical investigation. ZOLL will provide CRFs, instructions, and specific training for their completion. CRFs will be completed as information becomes available. If errors or omissions are found during a monitoring visit, the data will be corrected directly on the CRF.

The Investigator or designee will sign and date on the appropriate signature lines on the CRF. This signature will indicate that the data are accurate.

10.6 Training

ZOLL will provide in-depth training for the Investigators and study staff either at the investigational site or at a common location. ZOLL, clinical research personnel, or their designees, will conduct and document this training in accordance with appropriate procedures. All training will be documented and filed in ZOLL and site files.

The Investigator and relevant research staff will be trained on the following elements prior to enrolling the first patient:

- Review of the clinical investigation requirements set forth in the CIP
- CRFs
- Informed consent procedure
- Patient screening and enrolment
- Study documentation and administration
- Device accountability procedures
- Record-keeping requirements
- Investigator and Sponsor responsibilities
- Role of the IRB

- AE reporting procedures
- Protocol deviation reporting procedures
- Monitoring requirements and expectations
- Applicable regulatory requirements

ZOLL, or its medical consultants, on an individual basis will conduct training, generally during a site initiation visit. If necessary, additional training may be completed via telephone as well as prior to the treatment of the first patient. All training will be documented and filed in ZOLL and site files.

11 MAINTENANCE OF STUDY RECORDS

It is the responsibility of the Investigator and research staff to maintain a comprehensive and centralized filing system of all study-related documentation. This filing system must be suitable for inspection at any time by ZOLL, an auditor, and/or the IRB. The study records should include Patient Files and Regulatory Files:

11.1 Patient Files

Patient files contain the completed patient CRFs, supporting source documentation and/or medical records, a signed and dated ICF, and supporting documentation of the informed consent process.

11.2 Regulatory Files

Regulatory files (also referred to as a regulatory binder) contain the CIP; CIP amendments; IRB submissions, approvals, and communications; IRB-approved ICFs (current and previous); clinical study agreement; CRF, delegation of authority log; site screening and enrollment logs; investigational product accountability log; CVs, medical and/or professional licenses and financial disclosure forms; laboratory documents (eg, certification, normal reference ranges); and correspondence between the site and ZOLL.

11.3 Investigator Records and Reporting Requirements

Records may be audited by regulatory authorities and must be retained for the appropriate period (according to the local country regulations). The Investigator is responsible for the records cited below:

- All correspondence that pertains to the investigation
- Records of persons authorized to conduct the clinical investigation
- Records of receipt, use, or disposition of the device, if applicable
- Patient medical records, completed CRFs, and supporting documentation
- Informed consent documentation (including copy of an approved, blank ICF)
- AEs, SAEs, and UADE
- CIP (including certification of approval) and reasons for deviations from the CIP

- Signed Investigator agreement and CV of Investigators participating in the clinical investigation

Investigator records cannot be discarded without written consent from ZOLL. Data recorded on any imaging reports, CTAs, etc. are considered to be source data. The data collected on those forms must be as accurate, complete, and secure as possible to assure data integrity.

The Investigator is responsible for the preparation, review, signature, and submission of the reports listed in Table 4**,** in accordance with 21 CFR 812.2(b) (vi). These also are subject to FDA inspection and the retention requirements described above for the Investigator Records.

Table 4: Reporting Requirements

Report to	**Submit to**	**Description**
Unanticipated Adverse Device Effect (UADE)	Sponsor and IRB	The Investigator must submit to the Sponsor and reviewing IRB a report of any UADE as soon as possible but no more than 10 calendar days after the Investigator first learns of the UADE
Failure to obtain informed consent	Sponsor and IRB	If a study device is used without obtaining informed consent, the Investigator must notify the Sponsor and the IRB within 5 calendar days of the use of the device.
Other	IRB or FDA	Upon request of the IRB or FDA, the Investigator must provide accurate, complete, and current information about any aspect of the study.

11.4 Record Retention

ZOLL will maintain records for each investigational site for a period of at least 2 years following (a) the date the investigation is completed or terminated, or (b) the records are no longer required to support a regulatory submission, whichever is longer.

In order to constitute evidence with respect to product safety or regulatory or legal compliance, the Investigator agrees to retain study-related documents in a location that is secure and to which access can be gained if required. The following documents must be archived: the regulatory binder containing all regulatory agency and required GCP documents, as well as the patient files, which include the signed patient ICFs, CRFs, and data clarification forms, if necessary. Records must be retained for the appropriate period (according to the local country regulations).

11.5 Investigational Product Accountability and Labeling

The investigational site is responsible for maintaining control over any associated investigational devices that are received and used and for ensuring all investigational devices are segregated and provided only to Investigators who have been trained and are participating in the study.

Only institutions participating in the clinical study will be eligible to receive the investigational μ-Cor System and will send the investigational devices to the investigational site only when the following have been received:

- CV of the Investigator(s)
- A signed CSA
- Documented IRB approvals
- An IRB-approved patient ICF

ZOLL will supply the investigational devices as well as the study-related supplies to the investigational site, as described in the clinical investigation procedures for this study. The investigational site may be allowed to store controlled inventory, when qualified.

The Investigator or responsible designee will record the receipt and disposition of the μ-Cor System in the appropriate device log. ZOLL will monitor these logs on an ongoing basis. At the end of the clinical investigation, the original logs will be returned to ZOLL and a copy of the logs kept in the regulatory binder at the investigational site.

The μ-Cor System is an investigational device and will be packaged with a label with the name and place of business of the manufacturer and distributor. The device also will be labeled with the following:

"CAUTION: Investigational device. Limited by Federal (US) law to investigational use."

The Investigator should take adequate precautions, including storage of the investigational study device (also referred to as investigational product), to prevent theft or diversion of the products into unauthorized channels of distribution. Should a product not be used, the Investigator will return or dispose of the device per ZOLL's instructions. All μ-Cor Systems, used or unused, must be returned to ZOLL.

12 REFERENCES

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13 APPENDIX

Appendix A - New York Heart Association (NYHA) classification table

Appendix B - Informed Consent Form

Appendix C - Investigator's Brochure

Appendix D - Non-Significant Risk Declaration