Protocol Number: RHEA EL30-2017-001

Clinical Evaluation of the RHEA Vital Sign Vigilance System in Hospital Patients

Device:	RHEA Vital Sign Vigilance System
Model:	EL30
Sponsor:	Darma, Inc.
Contract Research Organization:	Technical Resources International, Inc.
Protocol Version:	Version 2.0 April 23, 2018

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LIST OF ABBREVIATIONS

Abbreviation	Term
AE	Adverse Event
CRF	Case Report Form
ECG	Electrocardiogram
EDC	Electronic Data Capture
$etCO_2$	End-tidal CO_2
FDA	U.S. Food & Drug Administration
GCP	Good Clinical Practice
HR	Heart Rate
ICU	Intensive Care Unit
ID	Identification
IEC	International Electrotechnical Commission
IRB	Institutional Review Board
LoS	Length of Stay
mm	Millimeter
RMSD	Root Mean Square Difference
RR	Respiratory Rate
sqrt	Square Root

1. Key Roles

1.1. Sponsor

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2. Introduction

2.1. Background and Rationale

The IntelliVue Patient Monitors MP/MX series (with the $etCO_2$ module) is an FDA-approved device made by PHILIPS MEDIZINSYSTEME BOEBLINGEN GMBH (FDA 510(k) clearance K161531). It is commonly used in U.S. hospital and serves as the gold standard for the measurement of heart rate (HR) derived from an ECG signal and for the respiratory rate (RR) derived from $etCO_2$ density. However, it requires attachment to the patient's body, and cable connection to a display unit.

The RHEA Vital Sign Vigilance System was developed by Shenzhen Fiber Medical Technology Co. Ltd. It is designed for automatic, continuous and contact-less measurement of heart rate and respiratory rate of patients in a hospital or clinic setting. The system uses a sensor placed under the patient's mattress, and does not require a sensor to be fixed to the body. This provides a more comfortable solution for long-term continuous patient monitoring. Continuous monitoring of people's vital signs, in particular heart rate (HR) and respiratory rate (RR), may provide a mechanism to alert doctors or nurses of disease deterioration or an imminent severe clinical event. Monitoring people's vital signs outside an ICU often relies on nursing staff conducting checks at set intervals. The device can reduce the workload for nursing staff in non-ICU wards. The FDA-cleared EarlySense System 2.0 (K131379) developed by EarlySense Ltd. is also a contact-less system designed for continuous monitoring heart rate and respiratory rate of patients. It has been sold in over 20 U.S. hospitals since 2013. No recalls and adverse events have been reported. According to publicly available clinical results, the EarlySense System has shown an 86% reduction in Code Blue events, and a 45% reduction in Length of Stay (LoS) in the ICU for patients coming from the medical/surgical unit (1, 2). The EarlySense device applies the piezoelectric sensor while in comparison, the RHEA investigational device applies the optical fiber sensor. This difference leads to the RHEA device having a higher accuracy, capacity for greater patient weight range, longer sensor life and a lower cost. A Pilot Study on 25 healthy volunteers (20 adults and 5 children) showed that the RHEA device can obtain accuracy of overall mean root mean square difference (RMSD) of both HR and RR of 1.9 with the same testing procedure described in this current protocol (3). When comparing with the reference device- the EarlySense device on 9 adults, the RHEA device obtained results with no significant difference (pair t test is used to evaluate the results according to this protocol.)

Heart beat or respiratory movement produces a slight vibration which cannot be observed visually. However, the fiber sensor contained in the RHEA sensor unit will be deformed by the vibration, resulting in a change in the optical signal being transmitted. This changed optical signal is received by the bedside unit and converted into an electrical signal. The HR and RR then can be calculated by the bedside and displayed in real-time. The change in the optical signal can also be used to determine if the patient has exited the bed with a notification displayed on the bedside unit.

The system is intended for use as a 'contact-free' under-mattress device monitoring heart rate

and respiratory rate during sleep or resting condition, and to notify users when the patient exits the bed. The data can be displayed, exported and reviewed.

This protocol aims at verifying the safety and effectiveness of the investigational device in a general-care clinical environment.

2.2. Study Objectives

This clinical trial aims to verify that the RHEA Vital Sign Vigilance System can fulfill its intended use and meet its declared performance and functional specifications. Statistical analysis comparing the performance of the RHEA Vital Sign Vigilance System and the reference device EarlySense System 2.0 to the MP/MX series separately aims to demonstrate that the investigational device is substantially equivalent to the cleared reference device-EarlySense System 2.0 in safety and effectiveness.

3. Study Design

This will be a cross-over, 'self-controlled' study comparing the investigational device RHEA Vital Sign Vigilance System to an approved under-mattress device, EarlySense System (Model 2.0) (K131379). Both will be compared to the 'gold standard' Philips MP/MX series model Patient Monitor. The same Monitor Device must be used across all hospital wards in this study.

The testing will be conducted in three periods. In the Accuracy Tests (periods 1 and 2), one of the contact-free devices will be used to monitor the HR and RR, while being compared with the MP/MX series Patient Monitor. The RHEA investigational device and reference device will be used to monitor the same subject at different times (cross-over design), as the sensors of the two devices are placed at a similar location of the bed. HR and RR will be recorded for all three devices. Comparison of the performance of the two contact-free devices will be performed on the recorded results via statistical analysis. The third test will assess the ability of the RHEA device to accurately detect motion on or exit from the bed, as compared to the manual observation.

Three clinical trial sites will be selected in the U.S. A total of 77 adult subjects will be enrolled to complete 73 subjects (5% drop-out rate anticipated). Please see Section 10 for Sample Size justification. A site may enroll no more than half the total number of subjects for the study; i.e., up to 39 total subjects per site. It is anticipated that 33 days are needed for 77 recruited patients in total.

The testing duration for each subject will be one to two hours, including device placement, measurements, and device removal.

This is a multi-center study to be conducted in three hospitals. Wards in each site should be representative of non-ICU wards in U.S. hospitals (e.g., medical/surgical, oncology, orthopedics, long term acute care).

4. Subject Selection

Subjects will be hospitalized patients in general care non-ICU settings, who fulfill the following inclusion and exclusion criteria.

4.1. Inclusion Criteria

Subjects will be included if they meet the following inclusion criteria:

1. Male or female, 18 years old and above.
2. Provide written informed consent.
3. Weight ranging from 20 to 150 kg inclusive.
4. Are located in a non-ICU hospital setting.
5. Agree to not eat during the testing period.
6. Agree to keep still.

4.2. Exclusion Criteria

Subjects will be excluded if they have any of the following inclusion criteria:

1. Are connected to a device which may interfere with the device monitoring in this study.
2. Are receiving any bedside care which may be incompatible with the study procedures.
3. Sleep apnea.
4. Pregnant or breast feeding.
5. A likely need to receive or undergo a procedure during the testing period.
6. Cannot accept a nasal cannula, or have a monitor lead placed on the chest.
7. A significant medical condition in the judgement of the investigator, which may compromise the study testing procedures.
8. Are wearing pacemaker or defibrillator.

5. Investigational Device and Reference Device

The RHEA Vital Sign Vigilance System EL30 developed by Shenzhen Fiber Medical Technology Co. Ltd are designed for continuous and contact-less measurement of heart rate and respiratory rate. The system will also notify users when the patient exits the bed. The following devices will be used in this study.

Table 1: Study Devices

	Product name	Model	Manufacture	Clearance number
Investigational device	RHEA Vital Sign Vigilance System	EL30	Shenzhen Fiber Medical Technology Co. Ltd.	N/A

Reference device	EarlySense System	Model 2.0	EarlySense Ltd	K131379
Gold Standard device	IntelliVue Patient Monitors	MP/MX Series	PHILIPS MEDIZINSYSTEME BOEBLINGEN GMBH	K161531

5.1. Investigational Device Information

The RHEA Vital Sign Vigilance System is designed for continuous and contact-less measurement of heart rate and respiratory rate. The system will also notify users when the patient exits the bed. The system is intended for continuous measurement of respiration rate and heart rate for adults (≤150kg), in an automatic contact-less manner, in a hospital or clinic setting during sleep or resting condition.

The setup includes placing a sensor under the mattress, and a bedside unit on a nearby flat surface that can be viewed by the investigator.

5.2. Design Principle and Characteristics

Heart beat or respiratory movement produces a slight vibration which cannot be observed by the eyes. However, the fiber sensor contained in the sensor unit will be deformed by the vibration, resulting in a change in the optical signal being transmitted. This changed optical signal is received by the bedside unit and converted into an electrical signal. The heart rate and respiratory rate then can be calculated by the bedside and displayed in real-time. The change in the optical signal can also be used to determine if the patient has exited bed and a notification will be displayed on the bedside unit. The system does not require a sensor to be fixed to the patient body. This provides a more comfortable solution for long-term patient monitoring and solve the cable problems.

5.3. Device Components

The system incorporates the following three components:

- The bedside unit with battery [35 mm(Height) ×241mm (Width) × 600mm (Length]
- The sensor unit [30mm (Height) ×165mm (Width) × 261mm (Length)]
- Proprietary exporting data software

5.4. Operation Training

Investigators will be trained on the device prior to beginning the study. The training will include: basic information regarding the investigational device, device preparation, operational instructions, device considerations, possible faults and their solutions, test contents, basic requirements and procedures, and records related to the control of the test.

6. Study Procedures

6.1. Screening

Patients will be screened to assess eligibility per the inclusion and exclusion criteria. Patients must provide written informed consent before being enrolled in the study.

Review of the eligibility criteria checklist will be recorded on the Case Report Form (CRF).

6.2. Baseline

The following information will be recorded prior to beginning the testing procedures:

- Gender, age.
- Height and weight.
- Location (ward/unit) where the subject is located.
- Clinical diagnosis (primary, and secondary if applicable)

6.3. Testing Procedures

The test will be conducted in three parts:

- Reference Device accuracy test
- Investigational Device accuracy test
- Motion and bed exit test

The following terms are used in the testing procedures below:

- Investigational Device (RHEA device)
- Reference Device (EarlySense device)
- Monitor Device (Gold Standard MP/MX series device)

<u>Reference Device Accuracy Test</u>

1. Two testers (Reference Device tester and Monitor Device tester) will record the following subject information in the CRF: subject ID, gender, height, weight, primary clinical diagnosis, time, site location (hospital and ward).
2. Place the Reference Device sensor unit under the mattress and beneath the chest of the subject according to the instructions for use. Place the bedside unit on a flat surface.
3. Synchronize the date and time of the Reference Device and the Monitor Device (to be equivalent).
4. Place the main units of the Reference Device and the Monitor Device in different locations in the subject's room such that they can only be viewed by their respective testers.
5. After the subject lies down on the bed, place the Monitor Device lead on the subject's chest

in accordance with the operational instruction of the Monitor Device.

6. Connect the $etCO_2$ module to the Monitor Device and apply the nasal cannula to the subject.
7. Turn on the Monitor Device and the Reference Device. Set the Monitor Device to "real-time monitoring mode".
8. Instruct the subject to remain motionless. At one-minute intervals, the two testers will simultaneously record the heart rate (HR), respiratory rate (RR) and the current time using their respective device.
9. If the HR or RR value does not appear, or turns blurred on the screen (in this state only the last value is displayed rather than the current value), the Reference Device tester will mark it on the CRF.
10. Stop the test once 20 valid pairs of data are recorded for each subject. If certain values are marked (per Step 9 above), the data at that recorded point will not considered in the analysis. More than 20 pairs will be collected in order to ensure that there are at least 20 valid pairs.

Investigational Device Accuracy Test:

1. Two testers (Investigational Device tester and the Monitor Device tester) will record the following subject information in the CRF: subject ID No., gender, height, weight, primary clinical diagnosis, time, site location (hospital and ward).
2. Place the Investigational Device sensor unit under the mattress and beneath the chest of the subject. Place the bedside unit on a flat surface or hang on the wall using the bracket.
3. Calibrate the device in accordance with the operator's manual.
4. Synchronize the date and time of the Investigational Device and Monitor Device (to be equivalent).
5. Place the main units of the Investigational Device and the Monitor in different locations in the subject's room such that they can only be viewed by their respective testers.
6. After the subject lies down on the bed, place the Monitor Device lead on the subject's chest in accordance with the operational instruction of the MP/MX series Patient Monitor.
7. Connect the $etCO_2$ module to the Monitor device and apply the nasal cannula to the subject.
8. Turn on the Monitor Device and the Investigational Device. Set the Monitor Device to "real-time monitoring mode".
9. Instruct the subject to remain motionless. At one-minute intervals, the two testers will simultaneously record the HR, RR and the current time using their respective device.
10. If HR or RR value does not appear or turns darker and with a mark "?" after the value on the screen (in this state only the last value is displayed rather than the current value), the Investigational Device tester will mark it on the CRF.

11. Stop the test once 20 valid pairs of data are recorded for each subject. If certain values are marked (per Step 10 above), the data at that recorded point will not considered in the analysis. More than 20 pairs will be collected in order to ensure that there are at least 20 valid pairs.

Motion and Bed Exit Test:

This test will be conducted only on subjects who can move and exit the bed easily.

The Monitor Device tester will ask the subject to turn or move ten times and exit the bed for three times randomly in five minutes. The Monitor Device tester will record the time of these events on the CRF. At the same time, the Investigational Device tester will observe if there is an "unexpected motion" or "bed exit" notification on the screen of the Investigational Device and will record the time of this event on the CRF.

Device Testing Considerations:

1. At the baseline for each subject, make sure the following information is recorded: subject ID, date of birth, gender, height, weight, location, time and clinical diagnosis. Adverse events should be recorded and kept during the tests. The record should be signed by the testers.
2. It is important that nothing be allowed to shake the bed during the test. Anything that will produce vibration (such as a phone or another person) is not allowed to be on the bed during the test.
3. Make sure there is sufficient stable time before the HR and RR results are recorded for the Investigational Device and Reference Device. Thirty seconds is considered to be reasonable for Investigational Device and 1 min for Reference Device. That is to say, if the subject has to turn, stand up or move during the test, record data 30 seconds after the subject lies down and keeps still again. One minute should be left between two record groups for the independence of the data. If the subject moves or is out of the bed, record data 30 seconds after the subject lies down and keeps still again.

7. Device Safety and Stability Evaluation

Safety and stability data should be recorded in the CRF for Investigational device only.

7.1. Safety Assessments

Included but shall not be limited to the following:

1) Electrical shock

2) Loose components leading to device failure

3) Failure of the device to resume normal operation after power is interrupted

7.2. Stability

Included but shall not be limited to the following:

1) Failure in starting the device
2) System shuts off unexpectedly during use
3) System pauses unexpectedly during use

8. Test Termination and Adverse Event Reporting

The Investigators will complete training before using the devices on any subjects. There is minimal risk of electric shock, overheating, or other mechanical harm from the devices.

8.1. Adverse Device Effects

If an Adverse Event (AE) occurs, the Investigator should terminate the test and take appropriate measures to treat the subject.

The Investigator will report unanticipated adverse device effects and adverse events to the IRB and the Sponsor no later than 10 working days after the Investigator first learns of the effects, and record it in the CRF. The date, time, treatment given, outcome, and relationship to the device in use should be recorded.

If a Serious Adverse Event happens, investigator should terminate the test and take appropriate treatment measures to the subject. The Investigator should also report to the IRB and the Sponsor, and the Sponsor should report to the authority 5 working days after he knows, and will notify the other investigators taking part in this trial.

8.2. Contact Information

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Contact Person: Wu Zicui
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Regulatory Affairs and Quality Assurance Manager
Email: zicui@darma.co
Phone number：415-439-3645

9. Data Management

The Sponsor or designee will provide the sites with source document templates although sites may use their standard documentation processes if these collect all required data. Data will be reported to the sponsor through an Electronic Data Capture (EDC) system, which will include automated checks for completeness and accuracy. All users will attend a training webinar before

they are given access to the EDC system. Data should be entered in the EDC system not later than 48 hours after each subject testing. The Investigator is responsible for maintaining accurate, complete and up-to-date records for each subject.

9.1. Data Handling

The investigators should record the data clearly and correctly in the EDC based on observations on the subjects as collected in the source documents.

The sponsor should monitor whether the test is proceeding as per the protocol and make sure the CRF is reliable, complete and accurate. If omission and mistakes are found, the Investigator will make corrections in the EDC.

9.2. Data Entry and Validation

Data entered in the EDC system will be reviewed by the sponsor. If incomplete or inaccurate data are found a data clarification request will be forwarded to the site for a response. Manual and automated discrepancies will be presented to the site user for resolution or justification. A sponsor representative will review the justification for all unresolvable discrepancies and will close or re-query them. Once all discrepancies and queries have been resolved, the Investigator will review the data and confirm their accuracy with his/her electronic signature in the EDC.

10. Statistical Analysis

10.1. General Statistics Design

- Investigation site selection: three sites will be selected:
- Randomization: consecutive selection: selecting every subject in the order they present in the site if they meet the inclusion/exclusion criteria till it reach the pre-specified number.
- Blinding: Two investigators observe the results from the investigational device and reference device separately. Time-stamp method (see time synchronization as described in Section 6.3, Testing Procedures) will be used in the comparison.

10.2. Primary Variables

The primary variables for the analysis of heart rate (HR) and respiratory rate (RR) are each the overall mean root mean square difference (RMSD), defined as the mean of the individual subject RMSDs. For each subject, the RMSD is calculated as:

$$RMSD = sqrt\{ \Sigma(Y_R - Y_G)^2/n\}$$

where Y_R and Y_G are the paired values for the RHEA Vital Sign Vigilance System and the gold standard method (Patient Monitor), respectively, and n is the number of data pairs. If motion or a bed exit occurs within 20 seconds preceding the recording period for a given data pair, the data pair at that time point will not be used in the analysis. A total of 20 pairs of measurements are

planned for each subject. If more than 20 measurements are collected for a subject, then only the first 20 will be used. If fewer than 20 measurements are collected for a subject for any reason, that subject will still be included in the analyses.

The primary hypotheses for HR, are as follows:

Adults
H_O: $\mu = 3.25$
vs.
H_A: $\mu < 3.25$,

The primary hypotheses for RR, are as follows:

Adults
H_O: $\mu = 2.25$
vs.
H_A: $\mu < 2.25$,

where μ represents the population mean HR or RR.

10.3. Primary Analyses

For each subject, the RMSD will be calculated for both HR and RR. These individual values will be presented in both a listing and graphically as a cumulative distribution. The mean RMSD and its two-sided 95% confidence interval (mean RMSD ± $t_{0.975}$ * std err RMSD) will be presented. If the upper bound of the confidence interval is less than the hypothesized value, the corresponding null hypothesis will be rejected. For each rejected hypothesis, the study will have met its primary objective.

10.4. Secondary Analyses

Accuracy of the RHEA will be compared with that of the Reference Device-EarlySense device. The RMSD for the Reference Device will be calculated for each subject in the same manner as described for the RHEA. Mean accuracy will then be compared between the RHEA and the Reference Device by comparing the individual subject RMSDs by a paired t test at the 5% level of significance.

Bland Altman plots will be presented separately for each subject's raw data, including the limits of agreement, for both the RHEA and the Reference Device methods. In addition, Bland Altman plots will be presented for the set of RMSD estimates across all subjects, along with two-sided

95% confidence intervals for their limits of agreement. Finally, Bland Altman plots of the raw data across all subjects will be presented, along with two-sided 95% confidence intervals for their limits of agreement. Methods discussed in Bland, JM and Altman, DG (4) and (5) will be used to calculate the confidence intervals of the limits of agreement due to the lack of independence of the repeated measurements on the same subject.

Motion and no motion accuracy will each be calculated along with their respective two-sided 95% confidence intervals. Motion accuracy will be calculated as the proportion of times that the device correctly detected motion among all actual occurrences of motion detected manually. Non-motion accuracy will be calculated as the proportion of times that the device correctly did not detect motion among all actual occurrences of no motion detected manually.

10.5. Subgroup Analyses

Between subject subgroup analyses will include the following subgroups:

- Primary disease
- Type of hospital ward
- Body weight in quartiles
- Study site

Each subgroup analysis will be based on a one-way analysis of variance on the individual RMSDs which includes the subgroup as the factor. Each analysis will be done at a significance level of 0.05.

Within subject subgroup analyses will be performed to compare results under awake and asleep conditions. The RMSD will be calculated for each subject while awake and while asleep. Mean RMSDs will be compared by paired t tests at a significance level of 0.05.

10.6. Sample Size

In a pilot study of 20 adult healthy volunteers with 20 paired observations each, the standard deviation of their RMSDs vs. the reference method were found to be approximately 0.75 for both HR and RR (2). Based on this standard deviation, 73 adult subjects will provide 80% power to reject each primary hypothesis if the population mean RMSD for HR is 3.0 and the population mean for RR is 2.0. To account for a dropout rate as high as 5%, a total of 77 adult subjects will be enrolled.

SAS Version 9.4 PROC POWER was used for all sample size calculations.

11. Regulatory and Reporting Requirements

11.1. IRB Approval

The investigator will ensure that IRB review and approval are obtained before beginning the study, or allowing any subject to participate. The Investigator will notify the Sponsor of any withdrawal of IRB approval of the study.

Any deviation from the investigational plan shall be reported to the Sponsor, and to the IRB per its requirements. Any revision to this protocol cannot be implemented without approval from the IRB and the Sponsor. The Investigator will submit a final report to the IRB after termination or completion of the study.

11.2. Informed Consent

The Investigator shall ensure that informed consent is obtained from subjects or their guardians.

11.3. Clinical Monitoring

The Sponsor or designee will be responsible for monitoring of compliance with the trial protocol, GCPs, and all applicable federal regulations concerning human subject research. The study monitors will perform on-site monitoring visits, including source document verification, device accountability, and assess compliance with safety reporting in accordance with Sponsor's procedures and all applicable regulatory requirements. The Investigator will agree to give full access of all study data, site procedures, and other relevant information to the study monitor (and auditor if needed) during each site visit.

At the site initiation visit the Sponsor or designee will review the study protocol and all associated study documentation and procedures with the Investigator and study personnel. All site personnel will receive training for device use and use of the data collection tool, as appropriate to their role. In addition, study-specific GCP training will be provided.

During the course of the study, the Sponsor or designee will maintain regular contact with the investigative sites and may conduct on-site monitoring visits and/or source data verification on a regular basis to ensure compliance with this study protocol.

The investigators shall conduct this study in accordance with this protocol. Failure to comply with and/or inability to meet these regulations may jeopardize further participation of the Investigator or investigative site in this and future clinical studies.

Investigators must report major protocol deviations that affect the safety and welfare of subjects or affect integrity of study (or if the investigator deviated from the protocol in order to save a life or prevent further harm to the subject) to the Sponsor within 5 working days of investigational site knowledge of the deviation.

a. Monitoring Method and Times

On-site visits will be made 3 times for each site when:

- the 1st patient completes testing
- the 5th patient completes testing
- the 15th patient completes testing

Remote monitoring will be done for the following items:

- Data on EDC system;
- Feedback from the investigators;
- Signature of the informed consent.

b. On-site monitoring procedures

1. Check if the device is used per the User's Manual.
2. Check if the investigator performs the procedures as per the clinical protocol and if there is any deviation from the protocol.
3. Check if subjects meet the inclusion criteria and excluded per the exclusion criteria.
4. Check if the informed consent is obtained before the testing.
5. Check the data, the date on the CRF. Check the consistency of CRF. Mark the questioned data and require the investigator to validate or correct it.
6. Check device preservation condition and device quantity to make sure to provide supplement in time.
7. Check if there is adverse event and if the adverse event is recorded.
8. Keep the monitoring record.

If there is any discrepancy or inconsistency found in remote monitoring, Sponsor can issue queries and require investigator to submit justification or corrections.

11.4. Confidentiality

Disclosure or making public the clinical research results to a third party is not allowed without written approval from the Sponsor. Documents provided by the Sponsor should be kept confidential.

Investigator shall maintain accurate, complete, and current records relating to the Investigator's participation 5 years after the completion or termination of the study, in a confidential and secure manner.

12. Risk-Benefit Analysis

This clinical trial aims at demonstrating the RHEA Vital Sign Vigilance System can fulfill its intended use and meet its accuracy and specification criteria. The contact-less manner of

monitoring can solve current cable management problem. It will decrease the possibility of accident arising from cables or leads. It also makes it possible to collect more vital sign information for analysis and diagnosis, in a more comfortable manner to the patient in long-term care monitoring.

The sensor of the RHEA Vital Sign Vigilance System will be placed under the mattress during the whole test. There is no patient contact part. The RHEA Vital Sign Vigilance System has been tested under the International Electrotechnical Commission (IEC) technical standards IEC 60601-1, IEC 60601-1-2, IEC 62304 and IEC 62366. Bench tests have been performed to help to ensure the safety of the system for this clinical trial.

The possibility of electricity shock, over heat, mechanical harm, over voltage and biocompatibility harm are small due to the above analysis. Training on the investigators before the clinical trial can also help in preventing the occurrence of the harm.

In conclusion, clinical trial on the Investigational Device may bring some risks, but the occurrence probability and severity of all risks have been minimized. Therefore, it is determined that the benefits of the product are more significant than the risks.

13. References

1. EarlySense Proactive Patient Care (http://www.earlysense.com/news-and-events/news/mar-20-2014/)
2. Harvey Brown, MD, Jamie Terrence, RN (2014), Continuous Monitoring in an Inpatient Medical-Surgical Unit: A Controlled Clinical Trial, The American Journal of Medicine 127: 226-232.
3. Pilot Study (January 17, 2017) and Pilot Study (March 25, 2017)
4. Bland JM, Altman DG (2007) Journal of Biopharmaceutical Statistics 17:571–82
5. Bland, JM and Altman, DG (1999) *Statistical Methods in Medical Research* 8:135-160

Investigator Statement

I agree to:

1. Conduct the clinical trial per Declaration of Helsinki, FDA regulations and this protocol.
2. Start the clinical trial only after IRB approval is obtained.
3. Start the clinical trial testing on each subject only after informed consent is obtained.
4. Fulfill the obligations in the signed agreement.

I have read all the contents of the protocol including the statement above. I agree to all of contents above.

Sponsor Name: Signature: Date:

Investigator Name: Signature: Date: