Validation Study: Extended Wear Performance of the Zio monitor – SHASTA II

Protocol Number	IRT-003-2024
Version Number	1.0
Date	October 31, 2024
Principal Investigator	Minang Turakhia, MD
Planned Number of Locations and Region(s)	Up to Five Study Centers in the US
Protocol Author	TJ Battisti, Ph.D.

Task	Name	Function	Signature	Date
Written by	TJ Battisti	Sr. Clinical Research Scientist	TJ Battisti	11/15/2024
Reviewed by	Chevy Brown	Sr. Manager, Clinical Research	Chevy Brown	11/15/2024
Reviewed by	Christine Dunn	Director, Regulatory Affairs	Christine Dunn	11/15/2024
Approved by	Charlotte Bame	Director, Clinical Research Operations	Charlotte M Bame	11/15/2024
Approved by	Chanda Owens	VP, Quality Assurance	Chanda Owens	11/15/2024
Approved by	Minang Turakhia	Chief Medical & Scientific Officer & EVP, Product Innovation	Minang Turakhia	11/15/2024
Approved by	Vladimir Fokin	Director, Data Management and Biostatistics	Vladimir Fokin	11/15/2024
Approved by	Kevin Clarkson	Sr. Director, Product Management	Kevin Clarkson	11/15/2024

Table of Contents

COMPLIANCE STATEMENT

This Study will be conducted in accordance with this Protocol, the Declaration of Helsinki, applicable Good Clinical Practices and applicable regulations and standards (e.g., US 21 CFR Parts 50, 56, 812, and 820.30, US 45 CFR Part 46, ISO 14155:2020, and ISO 13485) and the appropriate local legislation(s).

The most stringent requirements, guidelines or regulations must always be followed. The conduct of the study will be approved by the appropriate Review Board (IRB) of the respective sponsor locations and by the applicable regulatory authorities, when applicable.

INVESTIGATOR SIGNATURE PAGE

I have read this Clinical Investigation Plan and agree to adhere to the requirements described in this plan, including but not restricted to the latest version of the Declaration of Helsinki, Good Clinical Practice, ISO 14155, Code of Federal Regulations Title 21, and applicable local, regional and national regulatory requirements.

I will ensure that no study-specific tests or procedures will be undertaken prior to Institutional Review Board (IRB) approval and/or any other local, regional and national approvals have been obtained. Reporting requirements and conditions imposed by the relevant IRB will be observed and followed. Any participant enrolled in the study will be fully informed about the study objectives and scope and signed informed consent will be obtained before any study specific procedures are initiated.

I will also ensure that all site staff under my supervision will be trained adequately about the study scope and requirements, and I will supervise the study conduct in accordance with above stated regulations.

First Name: _____

Last Name: _____

Title: _____

Signature: **Date:**

DDMMMYYYY

One copy for the Principal Investigator, one copy for iRhythm Technologies, Inc.

PROTOCOL SUMMARY

Protocol Number	IRT-003-2024
Title	Design Validation Study: Extended Wear Performance of the Zio monitor[1]
Objective	To evaluate the wear performance of the Zio monitor device in a representative population over an extended wear period (of up to 30 continuous days) to demonstrate that the device can be worn with adequate patch adherence and signal quality through 21 days. Assessment of wear performance will include evaluation of the wear duration of the patch and percentage of analyzable electrocardiographic time. Product safety will be assessed by collection of all adverse events.
Study Device	Zio monitor
Targeted Number of Participants	A total of up to 75 participants will be enrolled at US locations. The study may enroll participants from the community surrounding San Francisco, CA and Deerfield, IL as referred by FieldWork® (or another recruitment vendor) at the iRhythm clinic in those locations. The study may also enroll participants from identified clinical locations at up to 3 additional health care institutions.
Study Design	A Prospective, multi-center, single-arm study to validate the design of the Zio monitor/Zio MCT device form factor in extended (21-day) wear.
Performance Objectives and Measures	**Performance Objectives** Mean wear duration and percent analyzable time of the Zio monitor will be assessed. Performance goals include mean wear duration of 21 days and percent analyzable time of 80%. Performance objectives will be met if the mean wear duration is greater than 21 days, and percent analyzable time is greater than 80% in 90% of subjects. **Safety Measures**

	The proportion of participants that experience clinically significant skin irritation through 30 days of wear will be assessed through capture and reporting of all adverse events. **Additional Device Measures** • Signal Artifact (%) – Defined as the proportion of ECG signal that is artifact over the wear duration, reported for each study device. • Device Functionality (%) – Defined as the proportion of Zio monitors recording a continuous ECG signal through 21 days, and through 30 days. **Other Measures** Observational assessment of participant skin types that will be reported include: • Participant Skin Type – Dry, Oily, Normal (Baseline only) • Known Hyperhidrosis Status – Primary, Secondary or None (Baseline only) • Fitzpatrick Skin Type (Baseline only) • Chest Hair Density – e.g., smooth/no hair, some hair, moderately hairy, or very hairy (baseline and follow-up) in the target patch placement area
Participant Visits	On-location visits are planned for Baseline (time of patch application), 21 days, and 30 days following patch application. Telephone calls to the participants are planned for 7-day and 14-day visits.
Inclusion Criteria	1. Participant must be 18 years or older at time of informed consent. 2. Participant is willing and able to provide informed consent and be able to complete all visits for the study.
Exclusion Criteria	1. Participant has a known allergy to adhesives. 2. Participant has a current skin infection or injury at location for study device placement. 3. Participant is a member of a vulnerable population. 4. Participant is a current or prior employee of iRhythm. 5. Participant is unable or unwilling to participate or comply with study protocol. 6. The local Investigator deems the participant has a condition that could limit the participant's ability or willingness to participate in the study, or ability to comply with study required procedures and/or follow-up visits. 7. Participant has experienced symptomatic episodes where instance variations in cardiac performance could result in immediate danger to the participant.

	8. Participant has an external cardiac defibrillator or may be exposed to high frequency surgical equipment near strong magnetic fields or devices such as MRI during the wear period. 9. Participant has a neuro-stimulator, as it may disrupt the quality of ECG data. 10. Participant does not have the competency to wear the device for the prescribed monitoring period. 11. Participant does not have the ability to consent for themselves (i.e., no LARs).
Analysis Populations	All analyses will be performed on the population of enrolled participants on whom the Zio monitor application was attempted. The age, sex at birth, and application type (HCP designee vs. self-application) of participants will be monitored throughout the enrollment period to ensure representation across key user groups. Performance within subgroups including (but not limited to) sex at birth, age, and application type will be assessed.

[1] The study device includes the wearable ECG adhesive assembly and symptom button common to both the Zio monitor and next generation Zio AT (Zio MCT) ambulatory cardiac monitoring devices. The gateway associated with Zio MCT necessary for transmission of ECG data during device wear will not be included as part of this study. For simplicity, the study device will be referred to Zio monitor within this protocol. Additional information regarding the study device is included in Section 2.3.

1.0 INTRODUCTION

1.1 Study Design

This study is a prospective, multi-center, single-arm study to validate the design of the Zio® monitor[2]/Zio MCT® device form factor in extended (21-day) wear.

1.2 Study Objectives

The objective of the study is to evaluate the wear performance of the Zio monitor device in a representative population over an extended wear period (of up to 30 continuous days) to demonstrate that the device can be worn with adequate patch adherence and signal quality through 21 days. Assessment of wear performance will include evaluation of the wear duration of the patch and percentage of analyzable electrocardiographic time. Product safety will be assessed by collection of all adverse events.

2.0 BACKGROUND AND RATIONALE

Patients who are suspected of suffering from an arrhythmia-related condition typically undergo electrocardiography (ECG) monitoring. Clinical symptoms associated with arrhythmia may include palpitations, shortness of breath, dizziness, lightheadedness, pre-syncope, syncope, or anxiety. Arrhythmias may also present asymptomatically. Arrhythmias often occur infrequently and may not be detected with in-clinic 12-lead ECG monitoring (which records 10 seconds of data), or traditional ambulatory monitoring (i.e., with a Holter device up to 48 hours). Long-term 14-day continuous ambulatory ECG monitoring is useful for the detection of infrequent arrhythmic events [1], though further extending the monitoring period may aid in detection of additional arrhythmias and provide additional clinical insights.

The Zio monitor (K202359) received FDA 510(k) clearance on May 21, 2021 and is a long-term continuous ambulatory patch ECG monitor which adheres to the patient's left pectoral region. Additional description of the device is provided in ***Table 1***. The Zio monitor is substantially equivalent to the predicate Zio XT device but is designed to be smaller and more than 50% lighter.

The Zio monitor is breathable with a waterproof housing[3], and a more flexible design for a secure attachment. These refinements allow for a more comfortable wear experience [2] with longer wear times and, therefore, provide more complete diagnostic data [3].

Like the predicate Zio XT device, Zio monitor is currently indicated for long-term continuous monitoring of up to 14 days. However, successful performance verification testing at iRhythm has demonstrated that the Zio monitor is capable of recording continuous ECG data for up to 21 days.

This extended wear clinical design validation study will assess the extended wear performance of the Zio monitor device, by having participants wear the device for as long as possible (up to 30 days) and recording their experience.

[2]The study device includes the wearable ECG adhesive assembly and symptom button common to both the Zio monitor and next generation Zio AT (Zio MCT) ambulatory cardiac monitoring devices. The gateway associated with Zio MCT necessary for transmission of ECG data during device wear will not be included as part of this study. For simplicity, the study device will be referred to Zio monitor within this protocol. Additional information regarding the study device is included in Section 2.3.

[3]The Zio monitor device should not be submerged in water. During a bath, keep the device above water. Please refer to the Zio monitor labeling instructions or Patient Guide for the full set of details.

Additionally, the percentage of analyzable ECG signal (i.e., percent analyzable time) will be assessed against a performance benchmark of 80%. The device tested in this extended wear study will be the design cleared in K202359, with minor improvements for manufacturability and with the programming configurations updated to allow for continuous ECG data recording for up to 30 days. Performance objectives include a mean wear time of at least 21 days, and percent analyzable time (i.e., artifact-free ECG signal) greater than 80% for at least 90% of study participants.

2.1 Name of the Device

The device to be tested is the modified Zio® monitor (iRhythm Technologies, Inc., San Francisco, CA), inventory part number DFG0001, or equivalent.

2.2 Intended Indication for Use

The Zio monitor is a prescription-only, single-patient-use ECG monitor that continuously records data for up to 14 days. It is indicated for use on patients who may be asymptomatic or who may suffer from transient symptoms such as palpitations, shortness of breath, dizziness, lightheadedness, pre-syncope, syncope, fatigue or anxiety.

In this extended wear clinical study, the Zio monitor is being evaluated in participants who will wear the device for up to 30 days, in order to achieve a mean wear time of greater than 21 days.

2.3 Description of the Device

The Zio monitor is a non-sterile, single-patient-use ECG monitor and recorder that provides a continuous, single-channel recording, and is substantially equivalent to the predicate commercial Zio XT Patch (K121319). The device is FDA cleared to be marketed commercially for recording of up to 14 days. See "**Table 1: Device Comparison**" for additional details. The predicate Zio XT device has been the subject of extensive clinical study. Findings have demonstrated improved diagnostic yield as compared to 24-48 Holter monitoring [4-7] and other ambulatory monitoring modalities [8].

The patch will be applied to the upper left pectoral region and activated by the study participants either in the clinic or at home, under the guidance of trained Study Staff. Once activated, the Zio monitor records ECG data without patient interaction, with the goal of improving patient compliance via simplicity of operation. There is a surface LED light that blinks to indicate proper activation and that the device is working or to indicate loss of connection with the skin or the presence of error conditions.

When applied, the device provides continuous, single-channel ECG recording into memory without patient interaction for the duration of the prescribed monitoring. The Zio monitor features an embedded real-time clock (RTC) for reporting purposes. The RTC is initialized at the manufacturing facility and requires no patient or user interaction. ECG data are acquired via electrodes mounted on the underside – the skin contact side – of the patch. Data are sampled with an analog/digital converter (ADC), and subsequently saved to the onboard memory. Stored ECG data are recorded into non-volatile memory, so data will not be lost in the event of power supply failure or battery expiry.

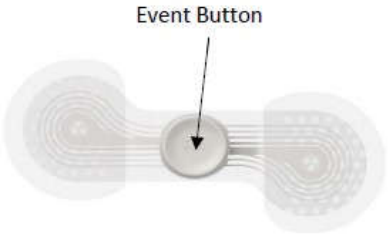
There is a button on the surface of the patch, which may be pressed by the patient to indicate when he or she is experiencing a symptom. This button press is logged by software into a secondary data stream, where event time is noted. Recording continues without interruption.

During normal operation, the device dynamically adjusts the input signal gain to a level that will maximize usage of ADC dynamic range and improve digital resolution of the recorded ECG signal, thereby improving the fidelity and contributing to improved interpretation results, particularly in situations of low-amplitude input signals.

At the conclusion of the wear period, the participant will remove the patch using the supplied materials and return it to the Sponsor. Once received, the recorded data will be downloaded for analysis by the Sponsor. The recorded ECG data are processed for detection of arrhythmias using an FDA-cleared (K222389) set of artificial intelligence algorithms [9] combined with trained cardiac technician review to generate a preliminary report describing rhythm findings.

Table 1: Device Comparison (Substantial Equivalence Summary)

Feature	**Predicate Commercial Device:** **Zio® XT Patch (K121319)**	**Study Device:** **Zio® monitor (K202359)**
Indications for Use		
Indications for Use Statements	The Zio® Patch is a prescription-only, single-patient-use, continuously recording ECG monitor that can be worn up to 14 days. It is indicated for use on patients who may be asymptomatic or who may suffer from transient symptoms such as palpitations, shortness of breath, dizziness, light-headedness, presyncope, syncope, fatigue, or anxiety.	The Zio® monitor is a prescription-only, single-patient-use ECG monitor that continuously records data for up to 14 days. It is indicated for use on patients who may be asymptomatic or who may suffer from transient symptoms such as palpitations, shortness of breath, dizziness, lightheadedness, pre-syncope, syncope, fatigue or anxiety.
General Characteristics		
Classification	Class II: 21CFR870.2800	Same
Product Code	DSH	Same
Patient Environment	Ambulatory	Same
Patient Population	Non-pediatric, non-critical care patients	Same
Programmed ECG Storage Duration	14 days	Up to 30 days
Technological Characteristics		
Event Trigger	Manually by patient	Same
Size	The Zio Monitor has a reduced form factor	
Performance Characteristics		
Weight	24.7 g	10.0 g
Dimensions	5.2 x 2.0 x 0.5 in	5.5 x 2.2 x 0.4 in
Photograph or Drawing		

Feature	Predicate Commercial Device: Zio® XT Patch (K121319)	Study Device: Zio® monitor (K202359)
	Zio XT (K121319) 	Zio® monitor (K202359) 

In addition to the Zio monitor and Zio XT long-term continuous ambulatory ECG monitors, a mobile cardiac telemetry device, Zio® MCT, is currently in development. Zio MCT will leverage the same patch ECG form factor and end-of-wear ECG review as Zio monitor, but also enables transmission and review of symptomatic or auto-triggered events during the wear period. Zio MCT-specific features, including auto-detection and event transmission during wear will not be enabled nor evaluated as part of this study. However, this assessment of extended wear performance is applicable to both Zio monitor and Zio MCT as the patch devices share the identical electrical, mechanical, and adhesive assembly. The main difference in the patch design is the firmware and the activation of the Bluetooth communication to the Gateway. This is not expected to impact wear duration on Zio MCT as it is not adding weight or changing adhesive area vs Zio Monitor.

The gateway which enables transmissions will not be included in this study.

2.4 Number of Participants

A total of up to 75 participants will be enrolled in this study.

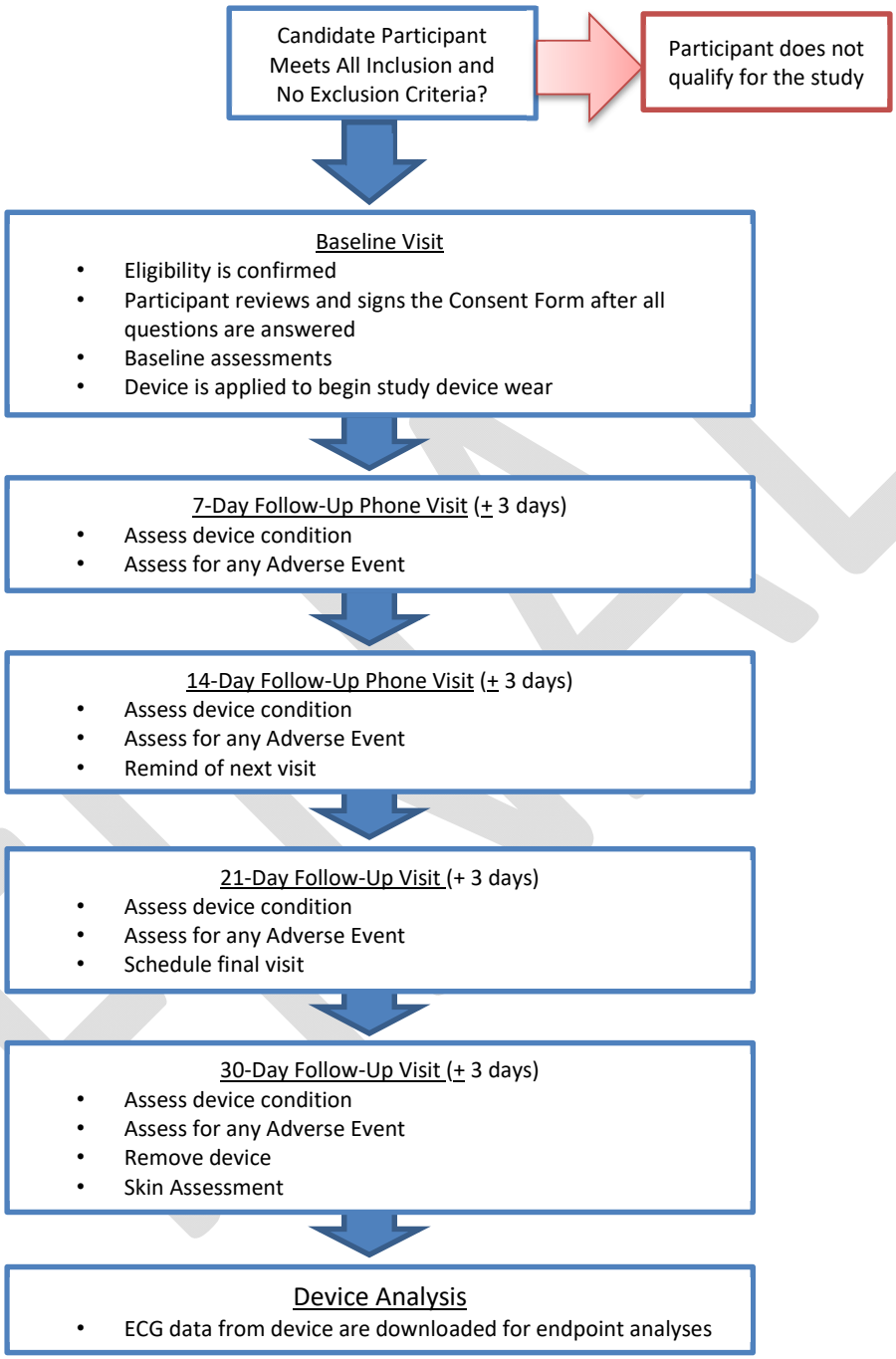
2.5 Overall Flow of the Study and Follow-up Schedule

Figure 1 shows the overall flow of the study. Participants who meet all inclusion and none of the exclusion criteria are eligible for enrollment into the study. Study visits will be performed in-clinic (Baseline, 21 day and 30 day) and by telephone (7 and 14 day).

Participants must read, understand, and sign (by hand or electronically) the study Informed Consent Form prior to the initiation of the baseline assessment visit and start of device wear. Once consented, participants will have a study device applied to their chest by a study staff member, or be provided a study device to self-apply at home or on-site. Study devices must be applied no later than the expiration date indicated on the kit. Participants will be considered enrolled after they have signed the Informed Consent Form and attempted patch application has occurred. Attempted patch application is defined as the opening of the patch kit and initiation of the shaving step necessary for skin preparation.

During the wear period, participants will be contacted by phone to determine adverse events and remind them of their next visit. Enrolled participants will undergo clinical evaluation at baseline and 21 days and 30 days after on-site or at-home patch application. They will also be provided a contact number to report any adverse events that occur between planned visits.

Figure 1: Overall Study Flow



Important Notes:

1. Participants will be considered enrolled after they have signed the Informed Consent Form and have attempted to apply the patch.
2. Follow-up visits are conducted at the indicated days following application of the patch, whether in clinic or by phone.
3. Early patch detachment and/or completion of the 30-day visit also includes a study completion form.

2.5.1 Study Safety Committee

A study safety committee will meet as needed to assess any safety events that may occur. The study safety committee meetings will be conducted according to a separate charter. The charter will include meeting scope, roles and activity specifics.

3.0 STUDY PERFORMANCE OBJECTIVES AND ADDITIONAL MEASURES

3.1 Wear Time Performance Objective

Wear duration is defined as the number of days the patch is attached to the participant. Wear duration measurement will start at the time of device application and will end at any of the following events:

- the device is removed at the 30-day follow-up visit, or
- the device fails to adequately adhere to the skin

All enrolled participants on whom patch application was attempted will be included as part of the mean wear duration analysis. However, participants who discontinue wear of the device for reasons outside of the study protocol, or occurrence of an adverse event not related to the study, will not be counted in the analysis. Full disclosure for reasons of discontinuation will be provided in the study report.

Mean wear duration will be compared to a performance goal of 21 days. The performance objectives will be met if the mean wear duration is greater than 21 days.

3.2 Analyzable Time Performance Objective

Analyzable time is the percentage of time during the wear of the Zio monitor device which yields analyzable ECG signal (i.e., free from signal artifact).

All enrolled participants in whom patch application was attempted will be included as part of the percent analyzable time analysis. However, participants who discontinue wear of the device for reasons outside of the study protocol, or occurrence of an adverse event not related to the study, will not be counted in the analysis. Full disclosure for reasons of discontinuation will be provided in the study report.

Percent analyzable time will be compared to a performance objective of 80%. The performance objective will be met if the percent analyzable time is greater than 80% in 90% of subjects.

3.3 Safety Measures

All enrolled participants on whom patch application was attempted will be included in the safety analysis. The proportion of participants that experience clinically significant skin irritation through 30 days of wear will be assessed.

- Reaction severity will be assessed and reported, as follows [10]:
  - Weak Positive Reaction: Presence of erythema infiltration, discrete papules
  - Strong Positive Reaction: Presence of erythema infiltration, papules, discrete vesicles
  - Extreme Positive Reaction: Presence of bullous or ulcerative reaction, coalescing vesicles

An ‘Extreme Positive Reaction’ will be considered a clinically significant skin irritation.

Any skin reaction should be reported as an adverse event.

3.4 Additional Device Measures

- Signal Artifact (%) – Defined as the proportion of ECG signal that is artifact over the wear duration, reported for each study device
- Device Functionality (%) – Defined as the proportion of Zio monitors recording a continuous ECG signal for (1) 21 days, and (2) for 30 days

3.5 Other Measures

Observational assessment[8] of participant skin types that will be reported include:

- Participant Skin Type – Dry, Oily, Normal (Baseline only)
- Known Hyperhidrosis Status – Primary, Secondary or None (Baseline only)
- Fitzpatrick Skin Type -Type I-VI (Baseline only)
- Chest Hair Density – e.g., smooth/no hair, some hair, moderately hairy, or very hairy (baseline and follow-up) in the target patch placement area

4.0 PARTICIPANT SELECTION AND WITHDRAWAL

4.1 Participant Recruitment Population and Retention

A study population representative of the intended population and who meet the study eligibility criteria will be approached for participation. iRhythm may utilize a recruitment firm such as FieldWorks® or community clinics who are qualified by experience and able to support this study.

The clinics and FieldWorks may utilize email solicitation, social media posting, review of their current research database of potential participants and/or flyer posting with prior approval by the IRB. Recruitment of at least 61 participants will be needed, and enrollment may continue up to a total of 75 participants.

To ensure recruitment of a population representative of patients undergoing long-term continuous monitoring, age, gender, and in-clinic (HCP designee) vs. self-application will be tracked by the study team. The following represent enrollment targets across these key groups:

- Approximately 1/3 of participants ≥51 and <70 years of age
- Approximately 1/3 of participants ≥70 years of age
- At least 40% of participants should be female
- Devices are self-applied for approximately 1/3 of the study population

4.2 Participant Screening and Informed Consent

Participant screening and informed consent may be performed in-person, by telephone, or by videotelephony (e.g., Zoom).

[8]See Appendix II for assessment definitions.

4.2.1 Participant Screening

A recruitment firm may be utilized for initial screening. Participants who have been identified by the recruitment firm will be seen at one of two Sponsor locations (San Francisco, CA or Deerfield, IL), the investigator or research staff, who have been trained to the Protocol, will verify all participants meet all inclusion and no exclusion criteria to determine if the potential participant is eligible for study enrollment.

Community clinics who have been identified, selected, trained and have provided all appropriate documentation for the study may also be utilized for screening and enrollment. The participants from this group may be clinically indicated for a Zio monitor prescription and willing to wear the Zio for an extended period of time.

In both cases, potential participants will be assigned a screening number (assigned sequentially/chronologically). An accurate and up-to-date screening log of all participants considered for the trial will be maintained at each study location. The result of the participant screening process shall be documented in the screening log to include presentation route, whether the participant met eligibility criteria (and if not, which eligibility criteria were not met), and whether the participant was subsequently enrolled.

4.2.2 Informed Consent

The Study and the Study Informed Consent Form (ICF) must receive approval by an independent IRB prior to beginning enrollment into the Study. The central IRB for this study is Advarra.

During the informed consent process, the investigator or designee, who has been trained on the Protocol, will explain the nature and scope of the trial, potential risks and benefits of participation, and answer questions from potential participants.

All participants must sign and date the IRB-approved informed consent form prior to any trial-specific procedures. Those who are not able to provide consent on their own will not be enrolled. Obtaining the consent, provision of copy to the participant, along with date and time must be documented in the participant's source documents.

The informed consent form must also be signed by the investigator or designee. The investigator or designee is responsible for advising the participant of any new information about the study or the study device(s) that may become known during the study. The consent may be administered by paper or through the use of an electronic consent form.

An authorization for use and disclosure of the participant's protected health information, in accordance with the Health Insurance Portability and Accountability Act (HIPAA), must be obtained from the participant. The requirements of HIPAA elements may be incorporated into the Informed Consent Form or it may exist as a standalone document

4.2.3 Disclosure of Participant Personal Contact Information

In order to conduct a phone visit with the participant, the study team at iRhythm may collect the participant's phone number and email. The participant's identity will be anonymized to the extent possible. Only those iRhythm study staff individuals who are directly involved with the study will have access to the participant's PHI for those individuals enrolled through the iRhythm clinics.

Participants enrolled in the community clinics will have their information pseudo anonymized and only the community clinic study staff will have access to their full information.

4.3 Eligibility Criteria

Participants shall be screened per the criteria listed below. Assessment for eligibility criteria will be completed through an interview with a potential participant. Participants must meet ALL of the inclusion criteria to be considered for the study. If ANY of the exclusion criteria are met, the participant is excluded from the study. Participants meeting these criteria will be approached to provide informed consent for participation in the Study and included on the screening log.

4.3.1 Inclusion Criteria

Participants must meet all of the following inclusion criteria in order to participate in the study:

1. Participant must be 18 years or older at time of informed consent.
2. Participant is willing and able to provide informed consent and able to complete all visits for this study.

4.3.2 Exclusion Criteria

Participants who meet any of the following exclusion criteria may not participate in the study:

1. Participant has a known allergy to adhesives.
2. Participant has a current skin infection or injury at location for study device placement.
3. Participant is a member of a vulnerable population.
4. Participant is a current or prior employee of iRhythm.
5. Participant is unable or unwilling to participate or comply with study protocol.
6. The local Investigator deems the participant has a condition that could limit their ability or willingness to participate in the study, or ability to comply with study required procedures and/or follow-up visits.
7. Participant has experienced symptomatic episodes where instance variations in cardiac performance could result in immediate danger to the participant.
8. Participant has an external cardiac defibrillator or may be exposed to high frequency surgical equipment near strong magnetic fields or devices such as MRI during the wear period.
9. Participant has a neuro-stimulator, as it may disrupt the quality of ECG data.
10. Participant does not have the competency to wear the device for the prescribed monitoring period.
11. Participant does not have the ability to consent for themselves (i.e., no LARs).

4.4 Participant Enrollment and Inclusion

Participants are considered enrolled after they have signed the Informed Consent Form and patch application has been attempted. Attempted patch application is defined as the opening of the Patch kit and initiation of the first step necessary for skin preparation.

Enrolled participants on whom patch application is attempted will be included in the analysis population. Consistent with recent FDA guidance on increasing diversity in clinical trial enrollment (Enhancing the Diversity of Clinical Trial Populations – Eligibility Criteria, Enrollment Practices, and Trial Designs: Guidance for Industry, Issued November 2020), iRhythm will attempt to implement measures to ensure that the study population reflects the characteristics of clinically relevant population. Section 4.1 above describes measures taken to ensure enrollment of a relevant population with respect to age, sex and device application (in clinic or self-application).

In addition, diversity across races and ethnic groups will be considered in selection of study sites and through recruitment activities. The study intends to enroll a diverse group of participants representative of the US population at large.

4.5 Participant Payment

Participants who meet eligibility and are enrolled in the study may be eligible to receive a stipend. In the event that the recruiting firm was utilized for the participant enrolled, the firm will manage all activities for payments including reporting of the payments to the Internal Revenue Service if required.

For those participants enrolled in the study through the clinical study site, stipends may also be included. However, the device is considered to be used in a clinical care setting and will be provided at no charge to the participant; the full study report will be provided to the ordering investigator at the conclusion of the wear time. No submission to the participant's insurance should be made for this portion of the visit.

For those participants enrolled through the recruitment firm to the iRhythm clinics payment for participation, parking, travel, etc. will be managed by the recruitment firm.

The amount of the participant stipend will be included in the Informed Consent form and approved by the IRB.

4.6 Participant Discontinuation

Participants shall remain in the study until completion of the required follow-up period, unless the device experiences early detachment. The participant's involvement in any clinical study is voluntary and the participant has the right to withdraw at any time without penalty or loss of benefit. Conceivable reasons for discontinuation may include, but are not limited to, the following:

- Participant death
- Participant voluntary withdrawal
- Participant withdrawal by physician as clinically-indicated
- Participant lost-to follow-up as described below

The Sponsor study staff must be notified of the reason(s) for participant discontinuation. Study staff are required to report this to the central IRB as defined by the IRB's requirements.

No additional follow-up will be required or data recorded from participants once withdrawn, except for the status (deceased/alive).

4.6.1 Lost-to-Follow-up:

If the participant misses the scheduled follow-up time point and the attempts at contacting the participant detailed below are unsuccessful, then the participant is considered lost to follow-up. Study personnel shall make all reasonable efforts to locate and communicate with the participant (and document these efforts in the source documents), including the following, at each contact time point:

- A minimum of 2 telephone calls or emails on different days over a 10-day period to contact the participant should be recorded in the source documentation, including date, time and initials of study personnel trying to make contact.
- If these attempts are unsuccessful, a certified letter should be sent to the participant. The letter will request the participant to contact the investigator. Study staff will also request return of the Zio to iRhythm as soon as possible.

4.7 Number of Participants Required to be Included in the Study

A total of up to 75 participants will be included in the study.

4.8 Estimated Time Needed to Enroll this Number

It is anticipated that it may take up to 8 weeks to enroll all required participants.

4.9 Expected Duration of Each Participant's Role

The expected duration of participation is approximately 30 days.

4.10 Total Expected Duration of the Study

The time to complete the Study is estimated to be approximately four months (two months to complete participant enrollment, one month follow-up and one month to complete analysis and generate the study report).

4.11 Study Completion

A participant is considered to have completed the study when any of the following has occurred:

- The participant is considered lost to follow-up per the above definition
- The participant withdraws consent
- The investigator withdraws the participant from the Study
- The participant has died
- The Study has been completed (e.g., the participant's 30-day or final follow-up time point has been reached)
- The patch has prematurely detached from the participant (in the case of early detachment the participant should notify study staff of the date and time of detachment, and a study completion visit will be scheduled).
- The Sponsor has terminated the Study

Sponsor must be notified of the reason for participant discontinuation. Investigators must also report this to their IRB, as required. Participants will not be replaced.

5.0 BASELINE VISIT AND FOLLOW-UP ASSESSMENTS

5.1 Baseline (Visit 1)

During the baseline visit (visit 1) the participant will be consented and the consent documented prior to patch application additional activities include:

Baseline health and demographic information:

The following information will be gathered from each participant in order to establish representation of the population and includes minimum:

- Medical Background/History, including:
  - Cardiac Disease History
    - Including indication for monitoring if enrolled at a clinical care site
  - Skin characteristics as reported by the participant
    - Skin Type (e.g., dry, oily, or normal)
    - Hyperhidrosis Status (e.g., primary, secondary, or none – see definitions in appendix)
    - Fitzpatrick Skin Type (e.g., Type I-VI) – using the Fitzpatrick Skin Type assessment questionnaire completed by the participant
    - Chest Hair Density by visual inspection (e.g., smooth/no hair, some hair, moderately hairy, or very hairy) in the target patch placement area
  - List of current medications
- Demographic Information
  - Age
  - Sex at birth
  - Race
  - Ethnicity
  - Weight
  - Height

Patch application:

The Zio monitor will be applied to the participant's left upper chest/pectoral region and may be completed by either the participant (self-application) or by a Health Care Provider (HCP) or designee (i.e. the study coordinator or cardiac technician). The application process for this study will be conducted as outlined in the Zio Monitor Instructions for Use – LB10117.01.

During the baseline visit, participants will either have a patch applied by a HCP designee or study staff member or participants will self-apply the patch. In the event of self-application, the study participant will open the Zio monitor kit and the Zio monitor Instructions for Use and will self-apply the device in the presence of a study staff member. The study staff member is allowed to provide some guidance, but every effort should be made to allow the participant to place the patch without intervention for the study staff.

If external community clinic sites are utilized the patch can be applied in the standard method for the site.

5.2 Patch Wear Period

All consented participants in whom the Zio monitor Patch application is attempted will be considered enrolled in the study. Patch application is considered to have been attempted when the Zio monitor Patch kit is opened and the first step necessary for skin preparation has been initiated. The participant will be instructed to wear the device for as long as possible, up to the 30-day visit.

Study participants will be instructed to press and hold along the edges of the patch if they notice the patch peeling or lifting at the edges during the wear period. If a patch completely detaches from the participant's chest, the patch will not be re-applied. In the case of early patch detachment, the participant should notify study staff of the date and time of detachment, and a study completion visit should be scheduled as soon as possible.

At any time after patch application, if the device is determined to no longer be functioning (for example, if a rapidly blinking orange light is observed), the device will not be replaced. The date and time the determination of function failure will be noted as close to accurate as possible. As a non-functioning device does not present a safety concern, the participant will be asked to continue wearing the non-functioning patch for as long as possible, in order to record wear duration and wear experience data.

5.3 Protocol Required Medications

There are no protocol required medications for this study, and no medications will be administered for the study. A complete list of current medications will be requested during the baseline visit. Updates to the list may be made if there is a change in the medication regime during the time of participation.

5.4 7-Day and 14-Day (± 3 days) Participant (Phone Call Visit 2 & 3)

A phone call at days 7 and 14 will be conducted in order to assess the status of the participant and the patch adherence.

5.5 21-Day (+3 days) Participant Follow-up (Visit 4)

At day 21 following patch application and up to day 24, participants will be asked to return to the clinic and the following activities will be conducted:

- Skin assessment by HCP or designee, including photograph of the area
- Adverse Event review
- Answering of any questions and verification of ongoing consent to study participation

5.6 30-Day (±3 days) Participant Follow-up (Visit 5)

At day 30 following patch application and up to day 33, participants will be asked to return to the clinic and the following activities will be conducted:

- Skin assessment by HCP or designee, including photograph of the area
- Adverse Event review
- Zio patch removal and visual inspection
- Patch return to iRhythm Technologies, Inc.

Participants who applied the Zio to themselves at the Baseline visit will be asked to remove the patch. They may ask a Study Staff member to provide guidance in the removal process.

Study clinical assessments and activities are summarized in **Table 2.**

This area intentionally left blank

Table 2: Clinical Assessment Schedule

Required Assessments to be Collected	Baseline (Visit 1)	7 & 14-Day (Visit 2 & 3)	21-Day[2] (Visit 4)	30-Day[2] (Visit 5)
		±3 days Phone Call only	+3 days	±3 days
Informed Consent[1]	X	X	-	-
Medical and Cardiac Background/History	X	-	-	-
Fitzpatrick Skin Assessment	X	-	-	-
Skin Condition Assessment[2]	X	-	X	X
Assessment of Device Adhesion Performance, Including photograph	-	-	X	X
Adverse Events[3]	X[4]	X	X	X

1. *Continued Informed Consent will be verified at each post-baseline contact.*
2. *Including chest hair density, as applicable.*
3. *Adverse Events include serious adverse events, all device-related complications, device deficiencies, device malfunctions, procedures and any hospitalizations.*
4. *AEs are only assessed following Informed Consent and participant enrollment into the study.*

The study device will be returned to iRhythm Technologies, Inc. for download and analysis of the ECG signal collected during the wear.

Upon completion of study follow-up, all devices will be retrieved from study participants and returned to the Sponsor for analysis. Those devices that were applied to participants in the community clinic setting will be processed through the algorithm and reviewed by the clinical research qualified cardiac technicians, the preliminary report will be provided to the Investigator at the clinic consistent with iRhythm Technologies, Inc. standard process. It will be up to the Investigator or HCP at that location for any needed clinical decision making.

For those devices that were applied to participants from the recruitment firm and enrolled at an iRhythm location will also be processed through the algorithm and reviewed by a clinical research qualified technician. The preliminary report will be provided to a Safety Committee and reviewed by a licensed cardiologist for finalization and determination of any diagnosis. A copy of the report will also be provided to the participant for their records and to share with their personal physicians.

6.0 ADVERSE EVENTS

Adverse events will be monitored and reviewed with the Study Investigator to determine any necessary action. To comply with standards and guidelines on clinical study adverse event reporting, the following standard definitions and reporting timelines will be adhered to for this study.

6.1 Definitions

6.1.1 Adverse Event

An adverse event (AE) is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in participants, users or other persons, whether or not related to the medical device. For those participants enrolled at the community clinic locations it is anticipated that arrhythmias will be noted on the scans. These are not considered adverse events and do not require reporting unless they have caused an adverse event (i.e., rapid atrial fibrillation is noted on scan, during this time the subject had a syncopal episode that resulted in bruising. The atrial fibrillation is not the AE but the syncopal episode is an AE and must be reported).

For this study AEs will be defined as follows:

- Mild: Transient or mild discomfort; no limitation in activity; no medical intervention/therapy required.
- Moderate: Mild-to-moderate limitation in activity, some assistance may be needed; no or minimal medical intervention/therapy required.
- Severe: Marked limitation in activity, some assistance usually required; medical intervention/therapy required, hospitalizations possible.
- Life-threatening: Extreme limitation in activity, significant assistance required; significant medical intervention/therapy required hospitalization or hospice care probable.

6.1.2 Serious Adverse Event

If the AE meets any of the criteria below, it is regarded as a serious adverse event (SAE) and is required to be reported according to the FDA guidelines for SAE reporting.

a) Led to a death,
b) Led to a serious deterioration in health that either:
    1) Resulted in a life-threatening illness or injury, or
    2) Resulted in a permanent impairment of a body structure or a body function, or
    3) Required in-patient hospitalization or prolongation of existing hospitalization, or
    4) Resulted in medical or surgical intervention to prevent life threatening illness or injury or permanent impairment to a body structure or a body function.
c) Led to fetal distress, fetal death or a congenital abnormality or birth defect.

An important medical event that may not result in death, be life-threatening, or require hospitalization but may be considered serious when, based upon appropriate medical judgment, may jeopardize the participant and/or may require intervention to prevent one of the outcomes listed in this definition may also be considered an SAE.

Note 1: This includes device deficiencies that might have led to a serious adverse event if a) suitable action had not been taken or b) intervention had not been made or c) if circumstances had been less fortunate. These are handled under the SAE reporting system.

Note 2: A planned hospitalization for pre-existing condition, or a procedure required by the Clinical Protocol, without a serious deterioration in health, is not considered to be a serious adverse event.

6.1.3 Device Malfunction

A device malfunction (DM) is the failure of a device to meet its performance specifications or otherwise perform as intended, when used in accordance with the IFU or protocol.

6.2 Device Relationship

Determination of whether there is a reasonable possibility that a product or device caused or contributed to an AE is to be determined by a study staff and recorded on the appropriate CRF. Determination should be based on assessment of temporal relationships, evidence of alternative etiology, medical/biologic plausibility, and patient condition (pre-existing condition).

6.2.1 Unanticipated (Serious Adverse) Device Effect [U(S)ADE]

Unanticipated serious adverse device effect (USADE) refers to any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the protocol or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of participants. See Anticipated Device Effects (**Section 12.2**).

6.3 Adverse Event/Device Deficiency/Product Experience Reporting

6.3.1 Adverse Event Reporting

Occurrences of adverse events will be monitored for each participant during the course of the study as required by this protocol, per AE and SAE definitions as noted in the sections above.

All information must be entered in the Electronic Data Capture (EDC) system as soon as feasible. AEs need to be collected for consented participants on the appropriate AE CRF. Additional information with regards to an adverse event should be updated within the appropriate CRF and source records.

Serious adverse events (SAEs) that occurred in the user or persons other than the study participant should not be entered in the CRF; they should be reported to researchstudies@irhythmtech.com. Study staff will regularly monitor this email address and will investigate all events reported.

The investigator will report all SAEs to the Sponsor as soon as possible but no later than 3 calendar days from the day the study personnel became aware of the event or as per the investigative location's local requirements, if the requirement is more stringent than those outlined. The date the study staff became aware that the event met the criteria of a serious adverse event must be recorded in the source document. The Investigator will further report the SAE to the local IRB according to reporting requirements.

6.3.2 Unanticipated Serious Adverse Device Effect Reporting

iRhythm (the Sponsor) is required to report and document any USADE as soon as possible, but at least within 24 hours of the Investigator's knowledge of the event.

6.3.3 Device Deficiency/Device Malfunction Reporting

All device deficiencies/malfunctions should be reported on the appropriate CRF no later than 3 calendar days from the day the study personnel became aware of the event or as per the investigative location's local requirements, if the requirement is more stringent than those outlined.

An email address (researchstudies@irhythmtech.com) will be made available to allow the investigator to report device deficiencies/malfunctions. This does not replace the CRF. All information must still be entered in the CRF as soon as feasible. Study staff will regularly monitor this email address and will investigate all events reported.

In case a device deficiency/malfunction occurred before *the patient ID has been assigned*, the device deficiency should also be reported to iRhythm via researchstudies@irhythmtech.com.

The device, if not applied or not remaining on the participant, should be returned to iRhythm Technologies, Inc.

Device deficiencies/malfunctions should be reported to the IRB per the investigative location's local requirements and IRB requirements.

6.3.4 Adverse Event Reporting to Country Regulatory Authorities by the Sponsor

Where required by local or regional requirements, the Sponsor will report the SAEs and DDs to the appropriate regulatory authority.

7.0 STATISTICAL ANALYSIS

7.1 Analysis Population

All analyses will be performed on the population of enrolled participants in whom patch application was attempted.

7.2 Sample Size Calculations and Assumptions

A prior study of 30 subjects instructed to wear the Zio monitor device up to 30 days resulted in a mean wear time of >24 days (24.9 ± 9.3 days).

Therefore, a power analysis was performed using the following assumptions:

- Performance goal: > 21 days
- Estimated wear duration with the Zio monitor patch: 24.0 days
- Estimated standard deviation of wear duration with the Zio monitor patch: 9.3 days
- Statistical test: One sample t-test
- Statistical Power: 80%
- Significance level: One-sided alpha = 0.05

Given these assumptions, enrollment of 61 participants is required to assess performance of wear duration performance.

SAS Enterprise Guide 8.3 was used for all calculations.

In order to assess the frequency of adverse events with reasonable precision, and to account for the possibility that up to 25% of enrolled participants may not provide ECG data at the 30-day visit due to device removal or loss to follow-up, enrollment of up to 75 participants is planned.

7.3 Planned Interim Analyses

There is no planned interim analysis for this study.

7.4 Statistical Analyses

For wear duration performance, mean wear duration, standard deviation and 95% confidence interval will be reported. For analyzable time performance, the mean percent analyzable time, standard deviation, 95% confidence interval, and percentage of patients with analyzable time >80% will be reported. Performance objectives will be met if the mean wear duration is greater than 21 days, and percent analyzable time is greater than 80% in 90% of subjects.

For other analyses, mean and standard deviation or median, interquartile range, minimum and maximum will be reported for continuous variables; counts and percentages will be reported for categorical variables.

7.4.1 Subgroup Analysis

Performance within subgroups including (but not limited to) sex, age, and application method (in-clinic HCP or designee vs. self-applied) will be assessed.

8.0 QUALITY CONTROL AND QUALITY ASSURANCE

8.1 Selection of Study Site Locations and Investigators

iRhythm Technologies, Inc. will utilize two iRhythm locations for the recruitment firm's referrals and participant enrollment. The locations will ensure study staff at their locations are trained appropriately. Contract Study Coordinators may be utilized at these locations to decrease any biases. The primary investigator of the study will also serve as the Principal Investigator at the iRhythm locations.

Community Clinic Study centers will be selected based on qualifications of the center. At a minimum, they will have an investigator who has experience in clinical research, has staffing to meet the needs of the study, has adequate population to recruit for the study and has passed the qualification process conducted by iRhythm's study management team.

Prior to receipt of study devices all locations must be trained to the protocol, the CRFs, and other appropriate study activities. For community clinic study centers they must also have a contract in place specific to this study. All centers and locations MUST have IRB approval to recruit and enroll participants.

Good Clinical Practice certification is required for all study staff who will have direct contact with the study participants or their data.

8.2 Protocol Amendments

The Sponsor will provide approved Protocol amendments to the Investigator(s) prior to implementing the amendment. The Principal Investigator is responsible for notifying the IRB or equivalent committee of the Protocol amendment (administrative changes) or obtaining IRB's approval of the Protocol amendment (changes in participant care or safety), according to the instructions provided by the Sponsor with the Protocol amendment.

Acknowledgement/approval by the IRB of the Protocol amendment must be documented in writing prior to implementation of the Protocol amendment. Copies of this documentation must also be provided to iRhythm Technologies, Inc.

8.3 Training

8.3.1 Study Training

All Investigators/study personnel, designee, etc. are required to attend the study training sessions, which may be conducted at a sponsor location initiation visit (SIV) or other appropriate training sessions. Over-the-phone, 'webinar', or self-training to the study and/or the device may take place as needed. Training of Investigators/study personnel will include, but is not limited to, the Protocol requirements, device usage, electronic CRF completion and study personnel responsibilities.

All Investigators/study personnel that are trained must sign a training log (or an equivalent) upon completion of the training. Prior to signing the training log, Investigator/study personnel must not perform any study-related activities that are not considered standard of care at the sponsor location.

All study personnel who has been trained to the study must also be listed on the Delegation of Authority log provided by iRhythm. The log must be kept updated throughout the study. A final copy of the DOA log will be collected from each study center and location for filing in the TMF for the study.

8.3.2 Training of Sponsor's Monitors

Sponsor and/or designated study monitors will be trained to the Protocol, case report forms and device usage (as appropriate). Documentation of this training will be according to written procedures.

8.4 Monitoring

Centralized monitoring will occur through routine internal data review. This monitoring is designed to identify missing and inconsistent data, data outliers, and potential Protocol deviations that may be indicative of non-compliance at the sponsor location. On-site monitoring may occur at the discretion of the Sponsor.

Prior to initiating any procedure, the Sponsor monitor (or delegate) will ensure that the following criteria are met:

- The investigator understands and accepts the obligation to conduct the research study according to the Protocol and applicable regulations and has signed the Investigator Agreement or the Clinical Study Agreement.
- The Investigator and his/her staff have sufficient time and facilities to conduct the study and that they have access to an adequate number of appropriate participants to conduct the study.
- Source documentation (including original medical records, if applicable) must be available to substantiate proper informed consent procedures, adherence to Protocol procedures, training records and appropriate delegation of roles, adequate reporting and follow-up of adverse events, accuracy of data collected on case report forms, and device information.
- If monitoring visits are scheduled, the Investigator/sponsor location will permit access to such records. A monitoring visit sign-in log will be maintained by study staff. The Investigator will agree to dedicate an adequate amount of time to the monitoring process. The Investigator and/or research coordinator will be available for monitoring visits. It is expected that the Investigator will provide the study monitor with a suitable working environment for review of study-related documents.

8.5 Deviations from Protocol

The Investigator will ensure that the study does not deviate from the IRB approved Protocol for any reason without prior written approval from Sponsor except in cases of medical emergencies, when the deviation is necessary to protect the rights, safety and well-being of the participant or eliminate an apparent immediate hazard to the participant. In that event, the Investigator will notify Sponsor immediately by phone or in writing. All deviations must be reported to the Sponsor. In participant-specific deviations from the Protocol, a Protocol deviation case report form will be completed. The occurrence of Protocol deviations will be monitored by the Sponsor for evaluation of investigator compliance to the Protocol and regulatory requirements and dealt with according to written procedures. Investigators will inform their IRB or equivalent committee of all Protocol deviations in accordance with their specific IRB or equivalent committee reporting policies and procedures.

In the event of repeated non-compliance, as determined by the Sponsor, a Sponsor's monitor or company representative will attempt to secure compliance by one or more of the following (and not limited to):

- Visiting the investigator and/or delegate
- Telephoning the investigator and/or delegate
- Corresponding with the investigator and/or delegate

Repeated non-compliance with the signed agreement, the Protocol or any other conditions of the study may result in further escalation in accordance with the Sponsor's written procedures including securing compliance or, at its sole discretion; Sponsor may terminate the investigator's participation in the study.

8.6 Quality Assurance Audit

A Sponsor representative or designee may request access to all clinical study records, including source documentation, for inspection and duplication during a Quality Assurance audit.

In the event that an investigator is contacted by a Regulatory Agency in relation to this clinical study, the Investigator will notify Sponsor immediately. The Investigator and Research Coordinator must be available to respond to reasonable requests and audit queries made during the audit process. The Investigator must provide Sponsor with copies of all correspondence that may affect the review of the current clinical study (e.g., Form FDA 483, Inspectional Observations, Warning Letters, Inspection Reports, etc.). Sponsor may provide any needed assistance in responding to regulatory audits.

9.0 DATA HANDLING AND RECORD KEEPING

All CRF data collection will be performed by authorized personnel to enter, review or correct data in a secure EDC System. Access will be strictly confidential.

For the clinical study duration, the Investigator will maintain complete and accurate documentation including, but not limited to, source documents, clinical study progress records, electronic case report forms, signed ICFs, device accountability records, correspondence with the IRB and clinical study monitor/Sponsor, adverse event reports, and information regarding participant discontinuation or completion of the clinical study. Protocol deviations are not anticipated, but if they occur, they will be recorded in the EDC System. All study related documents will be stored in a secured location.

The handling, storage, transfer and destruction of the data will comply with all applicable national and local laws.

The following persons will have access to identifiable data in order to review and ensure the Study is run appropriately: the Sponsor representatives (such as contract monitors or study managers) visiting the study sponsor location, the study staff participating and running the Study, regulatory (i.e. FDA) and health authorities. Participants consenting to participate will allow these persons to read the identifiable information.

The Sponsor (including persons working under the Sponsor) will have access to de-identified data only. The Sponsor will take reasonable measures to keep the data confidential and secure.

Data Management will include documentation of the systems and procedures used in data collection for the duration of the study.

All CRF data collection will be performed by personnel authorized to enter, review or correct data. Data will be strictly confidential.

All CRF data will be reformatted into a data structure acceptable to iRhythm. The data will be subjected to consistency and validation checks and will be subject to supplemental validation.

t the conclusion of the study, completed CRF images with the date-and-time stamped audit trail indicating the user, the data entered, and any reason for change (if applicable) will be archived for each sponsor location and a backup copy archived with iRhythm.

9.1 Source Documentation

Regulations and Good Clinical Practice (GCP) require that the Investigator maintain information in the participant's original source documents (including medical records) that corroborates data collected on the case report forms. In order to comply with these regulatory requirements/GCP, the following information should be included in the participant record as/if applicable to the study:

- Medical history/physical condition of the participant before involvement in the study sufficient to verify Protocol entry criteria
- Dated and signed notes on the day of entry into the study referencing the Sponsor, Protocol number, participant ID number and a statement that informed consent was obtained
- Dated and signed notes from each participant visit (for specific results of procedures and exams)
- Adverse events reported and their resolution including supporting documents such as discharge summaries, catheterization laboratory reports, ECGs, and lab results, etc. including documentation of awareness of SAEs and of investigator device relationship assessment of SAEs at the sponsor location
- Notes regarding prescription medications taken during the study. For those medications taken for the treatment of an Adverse Event the documentation should also include start and stop dates.
- Participant's condition upon completion of or withdrawal from the study
- Any other documents or records required to substantiate data entered into the CRF

9.2 Case Report Form Completion

Primary data collection based on source-document review will be performed clearly and accurately by study personnel trained on the Protocol and CRF completion. CRF data will be collected for all participants in the study. In the event the EDC System is unavailable, study personnel may complete paper CRFs and enter the data in the EDC System as soon as it is available.

9.3 Direct Access to Source Data/Documents

The investigator/institution will permit direct access to source data/documents in order for clinical study-related monitoring, audits, IRB review and regulatory inspections to be performed.

Participants providing informed consent are agreeing to allow Sponsor and/or its designee access and copying rights to pertinent information in their source document concerning their participation in this clinical study. The investigator will obtain, as part of the informed consent, permission for clinical study monitors or regulatory authorities to review, in confidence, any records identifying the participants in this clinical study. This information may be shared with regulatory agencies; however, Sponsor undertakes not to otherwise release the participant's personal and private information.

9.4 Record Retention

The Sponsor will archive and retain all documents pertaining to the study as per the applicable regulatory record retention requirements. The Investigator must obtain permission from Sponsor in writing before destroying or transferring control of any clinical study records.

10.0 ETHICAL CONSIDERATION

10.1 Institutional Review Board Review

Institutional Review Board approval for the Protocol, ICF and other written information provided to the patient will be obtained by the Principal Investigator at each sponsor location or community clinical study site prior to participation in this validation study. The approval letter must be received prior to the start of this validation study and a copy must be provided to the Sponsor. No changes will be made to the Protocol or ICF or other written information provided to the patient/participant without appropriate approvals, including IRB, the Sponsor, and/or the regulatory agencies.

Until the validation study is completed, the Investigator will advise the IRB of the progress of this study, per IRB requirements. Ongoing written approval will be obtained according to the IRB requirements. Additionally, any amendments to the Protocol as well as associated ICF changes will be submitted to the IRB and written approval obtained prior to implementation.

11.0 PUBLICATION POLICY

The data and results from the study are the sole property of the Sponsor. The Sponsor shall have the right to access and use all data and results generated during this wear validation study. The Sponsor may publish a manuscript regarding the study results. The recorded ECG information may be used for educational (including medical publications) or training purposes only, but only de-identified information will be used.

The preliminary and final reports from the patch for those participants who were enrolled through the community clinic study site belong to the participant as part of their medical record.

12.0 RISK ANALYSIS

12.1 Anticipated Clinical Benefits

This is a post-clearance study on the extended wear performance of the study device. Study participants will be asked to wear the device for as long as possible (up to 30 days) to validate performance of the device in up to 21 days of wear. There are no immediate potential benefits to study participants; the primary long-range potential benefit is improvement in clinical standard of care for others (altruistic benefit to study participants).

12.2 Foreseeable Adverse Events and Anticipated Adverse Device Effects

Table 3 provides a list of anticipated adverse events with wearing the study device. If a participant experiences severe reaction to the device, it is recommended that the participant remove the device.

Table 3: Foreseeable / Anticipated Adverse Device Effects

Anticipated Adverse Device Effects (ADE)	ADE Definition
Allergic reaction	Localized allergic reaction or allergic symptoms (i.e., acute urticaria) associated with serious injury.
Delayed healing	Atypical or otherwise prolonged recovery period post-wear resulting in non-permanent injury.
Discomfort	Transient physical or psychological distress.
Infection (local)	Localized evidence of tissue invasion by pathogenic microorganisms, resulting in non-permanent tissue injury.
Infection (systemic)	Evidence of pathogenic microorganism proliferation progressed to a systemic disease state associated with serious injury.
Non-functional defects	Defects that are imperceptible to participant but identified by study staff (i.e., compromised aesthetics).
Pain	Transient physical or psychological suffering or other unpleasant feelings.
Skin or soft tissue damage (permanent, major)	Serious injury presenting as permanent signs of tissue structural or functional damage (i.e., gross scarring, localized neuropathy).
Skin or soft tissue damage (permanent, minor)	Serious injury presenting as permanent changes in epidermis (i.e., abnormal pigmentation, blemishes).
Skin or soft tissue damage (temporary, major)	Signs of probable irritant contact dermatitis (edema, erythema, pruritus).
Skin or soft tissue damage (temporary, minor)	Minor irritation, not yet at probable irritant contact dermatitis.
Participant annoyance	Inconvenience perceptible to participant but unlikely to cause injury.
Participant inconvenience	Inconvenience imperceptible to participant but identified by study staff (i.e., burdensome packaging).

12.3 Risks Associated with Participation in Clinical Study

Participation in the study requires submission of data that may or may not be protected heath information. This information will be kept confidential, but there is a risk that some of the information could be unintentionally made non-confidential. The risk of this happening for this study is no greater than the risk of loss of confidentiality in any study.

12.4 Possible Interactions with Protocol-Required Concomitant Medications

There are no protocol-required medications being used as part of this study. Due to the nature of some medications having effect on the skin, a list of current medications will be requested at the Baseline visit. New medications that are added during the course of the patch wear will also be requested.

12.5 Steps That Will be Taken to Control or Mitigate Risks

Risks associated with the use of the device during this clinical study are minimized through device design, investigator selection and training, pre-specified patient eligibility requirements, and study monitoring to ensure adherence to the protocol.

Devices manufactured for this extended wear study will be the design cleared in K202359, with minor improvements in manufacturability and with the modifications necessary to allow for ECG recording up to 30 days. The Sponsor will have completed and documented internal Design Control requirements for all components of the study devices prior to first use in the extended wear study. All adverse events and device deficiencies will be reported to iRhythm and will be monitored internally for safety surveillance purposes.

The contraindications, warnings and precautions are listed in the IFU in the Zio monitor Clinical Reference Manual (Part Number DLB0035 or clinical study equivalent) that will be provided with all devices to be used during this study.

12.6 Risk to Benefit Rationale

Foreseeable risks are outlined in Table 3. There are no other types of foreseeable risk to participants by virtue of participation in this study. Apparently healthy study participants will equally be exposed to such physical risks, but will be fully informed in order to assess the wear performance of the investigational device on a human skin. The value of the information to be gained outweighs these procedural-related risks as it will support intended performance of the device.

Participants participating in this study will be receiving the latest technology of the currently cleared Zio monitor patch.

Participants participating in the study have a small risk of loss of confidentiality as part of the data collection process. This risk is mitigated to as low as possible with the use of data collection systems, methods and procedures that are used commonly in clinical research. This includes the use of only validated electronic systems, the training of study personnel and the use of pseudo anonymized data for all data entry. Based upon the established safety profile of the study device, the low risk of loss of confidentiality is adequately mitigated to justify use of the study device for participants in this study.

This area intentionally left blank

APPENDIX I: ABBREVIATIONS AND ACRONYMS

AE	Adverse Event
CRF	Case Report Form
DD	Device Deficiency
DM	Device Malfunction
ECG	Electrocardiogram
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
FDA	U.S. Food and Drug Administration
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
ICF	Informed Consent Form
IFU	Instructions for Use
IRB	Institutional Review Board
SAE	Serious Adverse Event
UADE	Unanticipated Adverse Device Event
USADE	Unanticipated Serious Adverse Device Event

APPENDIX II: DEFINITIONS

DEATH (All Cause)

All deaths regardless of cause. Death is further divided into 2 categories:

1. CARDIOVASCULAR DEATH

Per the Valve Academic Research Consortium (VARC) [11], as any one of the following:

- Any death due to proximate cardiac cause (e.g. MI, cardiac tamponade, worsening heart failure)
- Unwitnessed death and death of unknown cause
- All procedure-related deaths, including those related to a complication of the procedure or treatment for a complication of the procedure
- Death caused by non-coronary vascular conditions such as cerebrovascular disease, pulmonary embolism, ruptured aortic aneurysm, dissecting aneurysm, or other vascular disease

2. NON-CARDIOVASCULAR DEATH

Any death not covered by the VARC definitions of Cardiovascular Death, such as death caused by infection, malignancy, sepsis, pulmonary causes, accident, suicide, or trauma.

FITZPATRICK SKIN TYPE

The Fitzpatrick skin type is a 6-point scale [12].

Fitzpatrick Skin Type	Skin	Skin Reaction to Sun Exposure
I	Pale White	Always Burns, Never Tans
II	Fair	Usually Burns, Tans Minimally
III	Darker White	Sometimes Mild Burn, Tans Uniformly
IV	Light Brown	Burn Minimally, Always Tans Well
V	Brown	Very Rarely burns, Tans Very Easily
VI	Dark Brown or Black	Never Burns

HOSPITALIZATION (ALL CAUSE)

Defined as admission to inpatient unit or ward in the hospital for at least 24 hours, including emergency department stay. Excludes hospitalizations planned for pre-existing conditions, unless there is worsening of a pre-existing condition.

HYPERHYDROSIS STATE

Hyperhidrosis status will be determined by the following definition:

- Primary – Focal, visible, and excessive sweating for no apparent cause. Typically at axillae, palms, soles, inguinal areas, and face.

- Secondary – Caused by underlying medical condition. Can be either focal or general sweating.
- None – Only sweat during exercise, hot environment, physical, and/or psychological stress

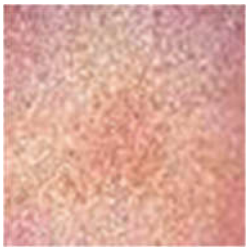
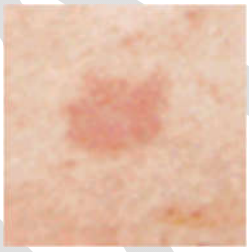
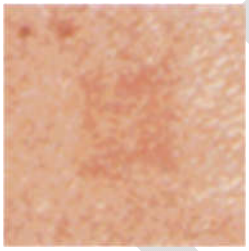
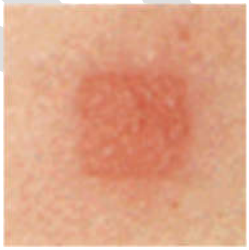
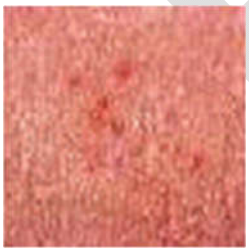
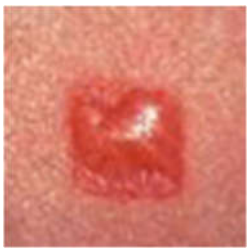
CHEST HAIR DENSITY

Chest hair density will be measured by visual inspection and classified as smooth/no hair, some hair, moderately hairy, or very hairy in the target patch placement area.

SKIN IRRITATION

Severity of skin irritation will be assessed per **Table 4** below. Interpretation of the reaction will be based on the method recommended by the International Contact Dermatitis Research Group (ICDRG) [10,13]. This scale has been modified to incorporate the U.S. Food & Drug Administration (FDA) *Guidance for Industry Skin Irritation and Sensitization Testing of Generic Transdermal Drug Products*.

Table 4: Skin Irritation Assessment

	Negative reaction (= -)		Weak positive reaction Erythema Infiltration Discrete papules (= +) FDA = 1 minimal erythema, barely perceptible
	Doubtful reaction Faint macular or homogeneous erythema, no infiltration (= ?) FDA = 0 no evidence of irritation		Strong positive reaction Erythema Infiltration Papules Discrete vesicles (= ++) FDA = 2-3 definite erythema, readily visible, papules
	Irritant reaction of different types* (= IR)		Extreme positive reaction Coalescing vesicles/bullous reaction (= +++) FDA = 4-7 definite edema, erythema, papules, vesicular eruption, spreading beyond site

SKIN TYPE

Skin type will be assessed at the planned patching location of the study device.

- Normal
- Dry – Scaling (visible peeling of outer skin layer) and skin cracking; also known as xeroderma
- Oily – Excess sebum (oil) production producing shiny appearance; also known as seborrhea

VULNERABLE POPULATION (ICH E6(R2) Definition)

Individuals whose willingness to volunteer in a clinical trial may be unduly influenced by the expectation, whether justified or not, of benefits associated with participation, or of a retaliatory response from senior members of a hierarchy in case of refusal to participate. Examples are members of a group with a hierarchical structure, such as medical, pharmacy, dental, and nursing students, subordinate hospital and laboratory personnel, employees of the pharmaceutical industry, members of the armed forces, and persons kept in detention. Other vulnerable participants include those with incurable diseases, persons in nursing homes, unemployed or impoverished persons, persons in emergency situations, ethnic minority groups, homeless persons, nomads, refugees, minors, and those incapable of giving consent.

BIBLIOGRAPHY

1. Turakhia MP, Hoang DD, Zimetbaum P, Miller JD, Froelicher VF, Kumar UN, Xu X, Yang F, Heidenreich PA. Diagnostic utility of a novel leadless arrhythmia monitoring device. Am J Cardiol. 2013;112:520–524.
2. Survey data on file.
3. Knight BP, et al. Performance of a Novel Next-Generation Ambulatory ECG Long-Term Patch Monitor: A Multicenter Post- Market Evaluation. Heart Rhythm 2024;21(9 Suppl):S796.
4. Barrett PM, Komatireddy R, Haaser S, Topol S, Sheard J, Encinas J, Fought AJ, Topol EJ. Comparison of 24-hour Holter Monitoring with 14-day Novel Adhesive Patch Electrocardiographic Monitoring. The American Journal of Medicine. 2014;127:95.e11-95.e17.
5. Rosenberg MA, Samuel M, Thosani A, Zimetbaum PJ. Use of a noninvasive continuous monitoring device in the management of atrial fibrillation: a pilot study. Pacing Clin Electrophysiol. 2013;36:328–333.
6. Kaura A, Sztriha L, Chan FK, Aeron-Thomas J, Gall N, Piechowski-Jozwiak B, Teo JT. Early prolonged ambulatory cardiac monitoring in stroke (EPACS): An open-label randomised controlled trial. Eur J Med Res. 2019;24:25.
7. Gupta N, Yang J, Reynolds K, Lenane J, Garcia E, Sung SH, Harrison TN, Solomon MD, Go AS. Diagnostic Yield, Outcomes, and Resource Utilization With Different Ambulatory Electrocardiographic Monitoring Strategies. Am J Cardiol. 2022;166:38-44.
8. Reynolds MR, Passman R, Swindle J, Mohammadi I, Wright B, Boyle K, Turakhia MP, Mittal S. Comparative effectiveness and healthcare utilization for ambulatory cardiac monitoring strategies in Medicare beneficiaries. Am Heart J. 2024;269:25-34.
9. Hannun AY, Rajpurkar P, Haghpanahi M, Tison GH, Bourn C, Turakhia MP, Ng AY. Cardiologist-level arrhythmia detection and classification in ambulatory electrocardiograms using a deep neural network. Nat Med. 2019;25:65–69.
10. Fonacier L, et. al.; American Academy of Allergy, Asthma & Immunology; American College of Allergy, Asthma & Immunology; Joint Council of Allergy, Asthma & Immunology. Contact dermatitis: a practice parameter-update 2015. *J Allergy Clin Immunol Pract*. 2015 May-Jun;3(3 Suppl):S1-39.
11. Updated standardized endpoint definitions for transcatheter aortic valve implantation: The Valve Academic Research Consortium-2 consensus document. Kappetein, A. Pieter et al. The Journal of Thoracic and Cardiovascular Surgery, Volume 145, Issue 1, 6 – 23
12. Fitzpatrick TB. The validity and practicality of sun-reactive skin types I through VI. Arch Dermatol. 1988 Jun;124(6):869-71.
13. Rietschel RL, Fowler JF Jr. Fisher's Contact Dermatitis. 5th ed. Baltimore, Md: Williams & Wilkins; 2001.

REVISION HISTORY

Version #	Released Date	Description of Change
01	15 November 2024	Initial Release

DocuSign

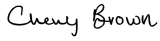
Certificate Of Completion

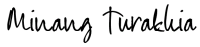
Envelope Id: D54974272AB84C9B9DCCE8C38FF42891
Status: Completed
Subject: Complete with Docusign: 2024-11-14_SHASTA II_Clean FINAL V1 PROT.pdf
Source Envelope:
Document Pages: 40
Signatures: 8
Certificate Pages: 6
Initials: 0
AutoNav: Enabled
EnvelopeId Stamping: Enabled
Time Zone: (UTC-08:00) Pacific Time (US & Canada)

Envelope Originator:
Char Bame
650 Townsend St Ste 380
San Francisco, CA 94103-6248
char.bame@irhythmtech.com
IP Address: 73.232.122.244

Record Tracking

Status: Original
11/15/2024 12:17:16 PM
Holder: Char Bame
char.bame@irhythmtech.com
Location: DocuSign

Signer Events	Signature	Timestamp
Chanda Owens chanda.owens@irhythmtech.com Security Level: Email, Account Authentication (None)	 Signature Adoption: Pre-selected Style Using IP Address: 68.5.133.129	Sent: 11/15/2024 12:23:56 PM Viewed: 11/15/2024 2:15:56 PM Signed: 11/15/2024 2:16:06 PM
Electronic Record and Signature Disclosure: Accepted: 11/15/2024 2:15:56 PM ID: 786934dc-5bbd-43f3-bc88-efbbfdb87c0f		
Charlotte M Bame char.bame@irhythmtech.com Director, Clin. Research Ops iRhythm Technologies, Inc. Security Level: Email, Account Authentication (None)	 Signature Adoption: Pre-selected Style Using IP Address: 73.232.122.244	Sent: 11/15/2024 12:23:57 PM Viewed: 11/15/2024 12:37:16 PM Signed: 11/15/2024 12:55:42 PM
Electronic Record and Signature Disclosure: Not Offered via DocuSign		
Chevy Brown chevy.brown@irhythmtech.com Security Level: Email, Account Authentication (None)	 Signature Adoption: Pre-selected Style Using IP Address: 99.147.221.54 Signed using mobile	Sent: 11/15/2024 12:23:58 PM Viewed: 11/15/2024 12:30:48 PM Signed: 11/15/2024 12:31:09 PM
Electronic Record and Signature Disclosure: Not Offered via DocuSign		
Christine Dunn christine.dunn@irhythmtech.com Sr. RA Mgr. International Security Level: Email, Account Authentication (None)	 Signature Adoption: Uploaded Signature Image Using IP Address: 67.160.87.74	Sent: 11/15/2024 12:24:01 PM Viewed: 11/15/2024 1:12:41 PM Signed: 11/15/2024 1:12:50 PM
Electronic Record and Signature Disclosure: Accepted: 11/15/2024 1:12:41 PM ID: 46ce8249-d0aa-4a1e-ae74-d340d400435a		

Signer Events	Signature	Timestamp
Kevin Clarkson kevin.clarkson@irhythmtech.com Director, Zio XT Security Level: Email, Account Authentication (None)	 Signature Adoption: Pre-selected Style Using IP Address: 71.255.89.116	Sent: 11/15/2024 12:23:58 PM Viewed: 11/15/2024 1:51:24 PM Signed: 11/15/2024 1:51:30 PM
Electronic Record and Signature Disclosure: Accepted: 11/15/2024 1:51:24 PM ID: 969daf84-c862-40fc-a06d-c777f5494b2a		
Minang Turakhia mintu.turakhia@irhythmtech.com CMO Security Level: Email, Account Authentication (None)	 Signature Adoption: Pre-selected Style Using IP Address: 205.220.129.25 Signed using mobile	Sent: 11/15/2024 12:23:59 PM Viewed: 11/15/2024 12:35:24 PM Signed: 11/15/2024 12:48:25 PM
Electronic Record and Signature Disclosure: Accepted: 11/15/2024 12:35:24 PM ID: 7ad8e83f-c5ce-4c04-8ef5-a58244cfdf39		
TJ Battisti tj.battisti@irhythmtech.com Security Level: Email, Account Authentication (None)	 Signature Adoption: Pre-selected Style Using IP Address: 99.196.129.117 Signed using mobile	Sent: 11/15/2024 12:24:00 PM Viewed: 11/15/2024 1:06:22 PM Signed: 11/15/2024 1:11:34 PM
Electronic Record and Signature Disclosure: Accepted: 11/15/2024 1:06:22 PM ID: a80456f6-2088-4415-8e92-d2a641081bc3		
Vladimir Fokin vladimir.fokin@irhythmtech.com Director, Data Management and Biostatistics Security Level: Email, Account Authentication (None)	 Signature Adoption: Pre-selected Style Using IP Address: 47.227.204.35	Sent: 11/15/2024 12:24:00 PM Viewed: 11/15/2024 12:27:07 PM Signed: 11/15/2024 12:32:06 PM
Electronic Record and Signature Disclosure: Accepted: 11/15/2024 12:27:07 PM ID: c650b1ee-f564-46d0-9932-31d110c5d9fc		

In Person Signer Events	Signature	Timestamp

Editor Delivery Events	Status	Timestamp

Agent Delivery Events	Status	Timestamp

Intermediary Delivery Events	Status	Timestamp

Certified Delivery Events	Status	Timestamp

Carbon Copy Events	Status	Timestamp

Witness Events	Signature	Timestamp

Notary Events	Signature	Timestamp

Envelope Summary Events	Status	Timestamps
Envelope Sent	Hashed/Encrypted	11/15/2024 12:24:01 PM
Certified Delivered	Security Checked	11/15/2024 12:27:07 PM
Signing Complete	Security Checked	11/15/2024 12:32:06 PM
Completed	Security Checked	11/15/2024 2:16:06 PM

Payment Events	Status	Timestamps

Electronic Record and Signature Disclosure

ELECTRONIC RECORD AND SIGNATURE DISCLOSURE

From time to time, iRhythm Technologies, Inc. (we, us or Company) may be required by law to provide to you certain written notices or disclosures. Described below are the terms and conditions for providing to you such notices and disclosures electronically through the DocuSign system. Please read the information below carefully and thoroughly, and if you can access this information electronically to your satisfaction and agree to this Electronic Record and Signature Disclosure (ERSD), please confirm your agreement by selecting the check-box next to 'I agree to use electronic records and signatures' before clicking 'CONTINUE' within the DocuSign system.

Getting paper copies

At any time, you may request from us a paper copy of any record provided or made available electronically to you by us. You will have the ability to download and print documents we send to you through the DocuSign system during and immediately after the signing session and, if you elect to create a DocuSign account, you may access the documents for a limited period of time (usually 30 days) after such documents are first sent to you. After such time, if you wish for us to send you paper copies of any such documents from our office to you, you will be charged a $0.00 per-page fee. You may request delivery of such paper copies from us by following the procedure described below.

Withdrawing your consent

If you decide to receive notices and disclosures from us electronically, you may at any time change your mind and tell us that thereafter you want to receive required notices and disclosures only in paper format. How you must inform us of your decision to receive future notices and disclosure in paper format and withdraw your consent to receive notices and disclosures electronically is described below.

Consequences of changing your mind

If you elect to receive required notices and disclosures only in paper format, it will slow the speed at which we can complete certain steps in transactions with you and delivering services to you because we will need first to send the required notices or disclosures to you in paper format, and then wait until we receive back from you your acknowledgment of your receipt of such paper notices or disclosures. Further, you will no longer be able to use the DocuSign system to receive required notices and consents electronically from us or to sign electronically documents from us.

All notices and disclosures will be sent to you electronically

Unless you tell us otherwise in accordance with the procedures described herein, we will provide electronically to you through the DocuSign system all required notices, disclosures, authorizations, acknowledgements, and other documents that are required to be provided or made available to you during the course of our relationship with you. To reduce the chance of you inadvertently not receiving any notice or disclosure, we prefer to provide all of the required notices and disclosures to you by the same method and to the same address that you have given us. Thus, you can receive all the disclosures and notices electronically or in paper format through the paper mail delivery system. If you do not agree with this process, please let us know as described below. Please also see the paragraph immediately above that describes the consequences of your electing not to receive delivery of the notices and disclosures electronically from us.

How to contact iRhythm Technologies, Inc.:

You may contact us to let us know of your changes as to how we may contact you electronically, to request paper copies of certain information from us, and to withdraw your prior consent to receive notices and disclosures electronically as follows:
To contact us by email send messages to: _hr@irhythmtech.com

To advise iRhythm Technologies, Inc. of your new email address

To let us know of a change in your email address where we should send notices and disclosures electronically to you, you must send an email message to us at _hr@irhythmtech.com and in the body of such request you must state: your previous email address, your new email address. We do not require any other information from you to change your email address.

If you created a DocuSign account, you may update it with your new email address through your account preferences.

To request paper copies from iRhythm Technologies, Inc.

To request delivery from us of paper copies of the notices and disclosures previously provided by us to you electronically, you must send us an email to _hr@irhythmtech.com and in the body of such request you must state your email address, full name, mailing address, and telephone number. We will bill you for any fees at that time, if any.

To withdraw your consent with iRhythm Technologies, Inc.

To inform us that you no longer wish to receive future notices and disclosures in electronic format you may:

i. decline to sign a document from within your signing session, and on the subsequent page, select the check-box indicating you wish to withdraw your consent, or you may;

ii. send us an email to _hr@irhythmtech.com and in the body of such request you must state your email, full name, mailing address, and telephone number. We do not need any other information from you to withdraw consent.. The consequences of your withdrawing consent for online documents will be that transactions may take a longer time to process..

Required hardware and software

The minimum system requirements for using the DocuSign system may change over time. The current system requirements are found here: https://support.docusign.com/guides/signer-guide-signing-system-requirements.

Acknowledging your access and consent to receive and sign documents electronically

To confirm to us that you can access this information electronically, which will be similar to other electronic notices and disclosures that we will provide to you, please confirm that you have read this ERSD, and (i) that you are able to print on paper or electronically save this ERSD for your future reference and access; or (ii) that you are able to email this ERSD to an email address where you will be able to print on paper or save it for your future reference and access. Further, if you consent to receiving notices and disclosures exclusively in electronic format as described herein, then select the check-box next to 'I agree to use electronic records and signatures' before clicking 'CONTINUE' within the DocuSign system.

By selecting the check-box next to 'I agree to use electronic records and signatures', you confirm that:

- You can access and read this Electronic Record and Signature Disclosure; and
- You can print on paper this Electronic Record and Signature Disclosure, or save or send this Electronic Record and Disclosure to a location where you can print it, for future reference and access; and
- Until or unless you notify iRhythm Technologies, Inc. as described above, you consent to receive exclusively through electronic means all notices, disclosures, authorizations, acknowledgements, and other documents that are required to be provided or made available to you by iRhythm Technologies, Inc. during the course of your relationship with iRhythm Technologies, Inc..

Validation Study: Extended Wear Performance of the Zio monitor – SHASTA II

Protocol Number	IRT-003-2024
Version Number	2.0
Date	April 15, 2025
Principal Investigator	Minang Turakhia, MD
Planned Number of Locations and Region(s)	Up to Five Study Centers in the US
Protocol Author	TJ Battisti, Ph.D.

Task	Name	Function	Signature	Date
Written by	TJ Battisti	Director, Scientific Affairs	TJ Battisti	04/23/2025
Reviewed by	Chevy Brown	Sr. Manager, Clinical Research	Chevy Brown	04/23/2025
Reviewed by	Christine Dunn	Director, Regulatory Affairs	Christine Dunn	04/24/2025
Approved by	Charlotte Bame	Sr. Director, Global Clinical Research Operations	Charlotte Bame	04/23/2025
Approved by	Chanda Owens	VP, Quality Assurance	Chanda Owens	04/29/2025
Approved by	Minang Turakhia	Chief Medical & Scientific Officer & EVP, Product Innovation	Minang Turakhia	04/30/2025
Approved by	Vladimir Fokin	Director, Data Management and Biostatistics	Vladimir Fokin	04/23/2025
Approved by	Kevin Clarkson	Sr. Director, Product Management	Kevin Clarkson	04/24/2025

Table of Contents

COMPLIANCE STATEMENT

This Study will be conducted in accordance with this Protocol, the Declaration of Helsinki, applicable Good Clinical Practices and applicable regulations and standards (e.g., US 21 CFR Parts 50, 56, 812, and 820.30, US 45 CFR Part 46, ISO 14155:2020, and ISO 13485) and the appropriate local legislation(s).

The most stringent requirements, guidelines or regulations must always be followed. The conduct of the study will be approved by the appropriate Institutional Review Board (IRB) of the respective sponsor locations and by the applicable regulatory authorities, when applicable.

INVESTIGATOR SIGNATURE PAGE

I have read this Clinical Investigation Plan and agree to adhere to the requirements described in this plan, including but not restricted to the latest version of the Declaration of Helsinki, Good Clinical Practice, ISO 14155, Code of Federal Regulations Title 21, and applicable local, regional and national regulatory requirements.

I will ensure that no study-specific tests or procedures will be undertaken prior to Institutional Review Board (IRB) approval and/or any other local, regional and national approvals have been obtained. Reporting requirements and conditions imposed by the relevant IRB will be observed and followed.
Any participant enrolled in the study will be fully informed about the study objectives and scope and signed informed consent will be obtained before any study specific procedures are initiated.

I will also ensure that all site staff under my supervision will be trained adequately about the study scope and requirements, and I will supervise the study conduct in accordance with above stated regulations.

First Name: _____

Last Name: _____

Title: _____

Signature: **Date:**

MM/DD/YYYY

One copy for the Principal Investigator, one copy for iRhythm Technologies, Inc.

PROTOCOL SUMMARY

Protocol Number	IRT-003-2024
Title	Validation Study: Extended Wear Performance of the Zio monitor[1] – SHASTA II
Objective	To evaluate the wear performance of the Zio monitor device in a representative population over an extended wear period (of up to 30 continuous days) to demonstrate that the device can be worn with adequate patch adherence and signal quality through 21 days. Assessment of wear performance will include evaluation of the wear duration of the patch and percentage of analyzable electrocardiographic time. Product safety will be assessed by collection of all adverse events.
Study Device	Zio monitor
Targeted Number of Participants	A total of up to 150 participants will be enrolled at US iRhythm locations. The study may enroll participants from the community surrounding San Francisco, CA and Deerfield, IL as referred by FieldWork® (or another recruitment vendor) at the iRhythm clinic in those locations.
Study Design	A prospective, multi-center, single-arm study to validate the design of the Zio monitor/Zio MCT device form factor in extended (21-day) wear when utilizing an updated skin prep process.
Performance Objectives and Measures	**Performance Objectives** Mean wear duration and percent analyzable time of the Zio monitor will be assessed. Performance goals include mean wear duration of 21 days and percent analyzable time of 80%. Performance objectives will be met if the mean wear duration is greater than 21 days, and percent analyzable time is greater than 80% in 90% of subjects. **Safety Measures** The proportion of participants that experience clinically significant skin irritation through 30 days of wear will be assessed through capture and reporting of all adverse events.

	Additional Device Measures • Signal Artifact (%) – Defined as the proportion of ECG signal that is artifact over the wear duration, reported for each study device. • Device Functionality (%) – Defined as the proportion of Zio monitors recording a continuous ECG signal through 21 days, and through 30 days. **Other Measures** Observational assessment of participant skin types that will be reported include: • Participant Skin Type – Dry, Oily, Normal (Baseline only) • Known Hyperhidrosis Status – Primary, Secondary or None (Baseline only) • Fitzpatrick Skin Type (Baseline only) • Chest Hair Density – e.g., smooth/no hair, some hair, moderately hairy, or very hairy (Baseline and follow-up) in the target patch placement area
Participant Visits	On-location visits are planned for Baseline (time of patch application), 21 days, and 30 days following patch application. Telephone/video calls to the participants are planned for 7-day and 14-day visits.
Inclusion Criteria	1. Participant must be 18 years or older at time of informed consent. 2. Participant is willing and able to provide informed consent and be able to complete all visits for the study.
Exclusion Criteria	1. Participant has a known allergy to adhesives. 2. Participant has a current skin infection or injury at location for study device placement. 3. Participant is a member of a vulnerable population. 4. Participant is a current or prior employee of iRhythm. 5. Participant is unable or unwilling to participate or comply with study protocol. 6. The local Investigator deems the participant has a condition that could limit the participant's ability or willingness to participate in the study, or ability to comply with study required procedures and/or follow-up visits. 7. Participant has experienced symptomatic episodes where instance variations in cardiac performance could result in immediate danger to the participant. 8. Participant has an external cardiac defibrillator or may be exposed to high frequency surgical equipment near strong magnetic fields or devices such as MRI during the wear period.

	9. Participant has a neuro-stimulator, as it may disrupt the quality of ECG data. 10. Participant does not have the competency to wear the device for the prescribed monitoring period. 11. Participant does not have the ability to consent for themselves (i.e., no LARs).
Analysis Populations	All analyses will be performed on the population of enrolled participants on whom the Zio monitor application was attempted. The age, sex at birth, and application type (HCP designee vs. self-application) of participants will be monitored throughout the enrollment period to ensure representation across key user groups. Performance within subgroups including (but not limited to) sex at birth, age, and application type will be assessed.

[1]The study device includes the wearable ECG adhesive assembly and symptom button common to both the Zio monitor and next generation Zio AT (Zio MCT) ambulatory cardiac monitoring devices. The gateway associated with Zio MCT necessary for transmission of ECG data during device wear will not be included as part of this study. For simplicity, the study device will be referred to Zio monitor within this protocol. Additional information regarding the study device is included in Section 2.3.

1.0 INTRODUCTION

1.1 Study Design

This study is a prospective, multi-center, single-arm study to validate the design of the Zio® monitor[2]/Zio MCT® device form factor in extended (21-day) wear.

1.2 Study Objectives

The objective of the study is to evaluate the wear performance of the Zio monitor device in a representative population over an extended wear period (of up to 30 continuous days) utilizing an updated skin preparation process to demonstrate that the device can be worn with adequate patch adherence and signal quality through 21 days. Assessment of wear performance will include evaluation of the wear duration of the patch and percentage of analyzable electrocardiographic time. Product safety will be assessed by collection of all adverse events.

2.0 BACKGROUND AND RATIONALE

Patients who are suspected of suffering from an arrhythmia-related condition typically undergo electrocardiography (ECG) monitoring. Clinical symptoms associated with arrhythmia may include palpitations, shortness of breath, dizziness, lightheadedness, pre-syncope, syncope, or anxiety. Arrhythmias may also present asymptomatically. Arrhythmias often occur infrequently and may not be detected with in-clinic 12-lead ECG monitoring (which records 10 seconds of data), or traditional ambulatory monitoring (i.e., with a Holter device up to 48 hours). Long-term 14-day continuous ambulatory ECG monitoring is useful for the detection of infrequent arrhythmic events [1], though further extending the monitoring period may aid in detection of additional arrhythmias and provide additional clinical insights.

The Zio monitor (K202359) received FDA 510(k) clearance on May 21, 2021 and is a long-term continuous ambulatory patch ECG monitor which adheres to the patient's left pectoral region. Additional description of the device is provided in **Table 1**. The Zio monitor is substantially equivalent to the predicate Zio XT device but is designed to be smaller and more than 50% lighter.

The Zio monitor is breathable with a waterproof housing[3], and a more flexible design for a secure attachment. These refinements allow for a more comfortable wear experience [2] with longer wear times and, therefore, provide more complete diagnostic data [3].

Like the predicate Zio XT device, Zio monitor is currently indicated for long-term continuous monitoring of up to 14 days. However, successful performance verification testing at iRhythm has demonstrated that the Zio monitor is capable of recording continuous ECG data for up to 21 days.

This extended wear clinical design validation study will assess the extended wear performance of the Zio monitor device, by having participants wear the device for as long as possible (up to 30 days) following an updated skin preparation process.

[2]The study device includes the wearable ECG adhesive assembly and symptom button common to both the Zio monitor and next generation Zio AT (Zio MCT) ambulatory cardiac monitoring devices. The gateway associated with Zio MCT necessary for transmission of ECG data during device wear will not be included as part of this study. For simplicity, the study device will be referred to Zio monitor within this protocol. Additional information regarding the study device is included in Section 2.3.

[3]The Zio monitor device should not be submerged in water. During a bath, keep the device above water. Please refer to the Zio monitor application instructions for the full set of details.

Additionally, the percentage of analyzable ECG signal (i.e., percent analyzable time) will be assessed against a performance benchmark of 80%. The device tested in this extended wear study will be the design cleared in K202359, with minor improvements for manufacturability and with the programming configurations updated to allow for continuous ECG data recording for up to 30 days. Performance objectives include a mean wear time of at least 21 days, and percent analyzable time (i.e., artifact-free ECG signal) greater than 80% for at least 90% of study participants.

2.1 Name of the Device

The device to be tested is the modified Zio® monitor (iRhythm Technologies, Inc., San Francisco, CA), inventory part number DFG0001, or equivalent.

2.2 Intended Indication for Use

The Zio monitor is a prescription-only, single-patient-use ECG monitor that continuously records data for up to 14 days. It is indicated for use on patients who may be asymptomatic or who may suffer from transient symptoms such as palpitations, shortness of breath, dizziness, lightheadedness, pre-syncope, syncope, fatigue or anxiety.

In this extended wear clinical study, the Zio monitor is being evaluated in participants who will wear the device for up to 30 days, in order to achieve a mean wear time of greater than 21 days.

2.3 Description of the Device

The Zio monitor is a non-sterile, single-patient-use ECG monitor and recorder that provides a continuous, single-channel recording, and is substantially equivalent to the predicate commercial Zio XT Patch (K121319). The device is FDA cleared to be marketed commercially for recording of up to 14 days. See "**Table 1: Device Comparison**" for additional details. The predicate Zio XT device has been the subject of extensive clinical study. Findings have demonstrated improved diagnostic yield as compared to 24-48 Holter monitoring [4-7] and other ambulatory monitoring modalities [8].

The patch will be applied to the upper left pectoral region and activated by either the patient at home or in the clinic by a trained health care provider. Once activated, the Zio monitor records ECG data without patient interaction, with the goal of improving patient compliance via simplicity of operation. There is a surface LED light that blinks to indicate proper activation and that the device is working or to indicate loss of connection with the skin or the presence of error conditions.

When applied, the device provides continuous, single-channel ECG recording into memory without patient interaction for the duration of the prescribed monitoring. The Zio monitor features an embedded real-time clock (RTC) for reporting purposes. The RTC is initialized at the manufacturing facility and requires no patient or user interaction. ECG data are acquired via electrodes mounted on the underside – the skin contact side – of the patch. Data are sampled with an analog/digital converter (ADC), and subsequently saved to the onboard memory. Stored ECG data are recorded into non-volatile memory, so data will not be lost in the event of power supply failure or battery expiry.

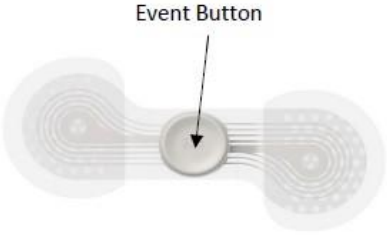
There is a button on the surface of the patch, which may be pressed by the patient to indicate when he or she is experiencing a symptom. This button press is logged by software into a secondary data stream, where event time is noted. Recording continues without interruption.

During normal operation, the device dynamically adjusts the input signal gain to a level that will maximize usage of ADC dynamic range and improve digital resolution of the recorded ECG signal, thereby improving the fidelity and contributing to improved interpretation results, particularly in situations of low-amplitude input signals.

At the conclusion of the wear period, the Study Staff or participant will remove the patch using the supplied materials and return it to the Sponsor. Once received, the recorded data will be downloaded for analysis by the Sponsor. The recorded ECG data are processed for detection of arrhythmias using an FDA-cleared (K222389) set of artificial intelligence algorithms [9] combined with trained cardiac technician review to generate a preliminary report describing rhythm findings.

Table 1: Device Comparison (Substantial Equivalence Summary)

Feature	**Predicate Commercial Device:** **Zio® XT Patch (K121319)**	**Study Device:** **Zio® monitor (K202359)**
Indications for Use		
Indications for Use Statements	The Zio® Patch is a prescription-only, single-patient-use, continuously recording ECG monitor that can be worn up to 14 days. It is indicated for use on patients who may be asymptomatic or who may suffer from transient symptoms such as palpitations, shortness of breath, dizziness, light-headedness, presyncope, syncope, fatigue, or anxiety.	The Zio® monitor is a prescription-only, single-patient-use ECG monitor that continuously records data for up to 14 days. It is indicated for use on patients who may be asymptomatic or who may suffer from transient symptoms such as palpitations, shortness of breath, dizziness, lightheadedness, pre-syncope, syncope, fatigue or anxiety.
General Characteristics		
Classification	Class II: 21CFR870.2800	Same
Product Code	DSH	Same
Patient Environment	Ambulatory	Same
Patient Population	Non-pediatric, non-critical care patients	Same
Programmed ECG Storage Duration	14 days	Up to 30 days
Technological Characteristics		
Event Trigger	Manually by patient	Same
Size	The Zio Monitor has a reduced form factor	
Performance Characteristics		
Weight	24.7 g	10.0 g
Dimensions	5.2 x 2.0 x 0.5 in	5.5 x 2.2 x 0.4 in
Photograph or Drawing		

Feature	Predicate Commercial Device: Zio® XT Patch (K121319)	Study Device: Zio® monitor (K202359)
	Zio XT (K121319) 	Zio® monitor (K202359) 

In addition to the Zio monitor and Zio XT long-term continuous ambulatory ECG monitors, a mobile cardiac telemetry device, Zio® MCT, is currently in development. Zio MCT will leverage the same patch ECG form factor and end-of-wear ECG review as Zio monitor, but also enables transmission and review of symptomatic or auto-triggered events during the wear period. Zio MCT-specific features, including auto-detection and event transmission during wear will not be enabled nor evaluated as part of this study. However, this assessment of extended wear performance is applicable to both Zio monitor and Zio MCT as the patch devices share the identical electrical, mechanical, and adhesive assembly. The main difference in the patch design is the firmware and the activation of the Bluetooth communication to the Gateway. This is not expected to impact wear duration on Zio MCT as it is not adding weight or changing adhesive area vs Zio Monitor.

The gateway which enables transmissions will not be included in this study.

2.4 Number of Participants

A total of up to 150 participants will be enrolled in this study. Seventy-five participants have already been enrolled in the first phase of this study which utilized the iRhythm legacy skin preparation process. An additional 75 participants will be enrolled utilizing an updated skin prep process detailed in Section 5.1.

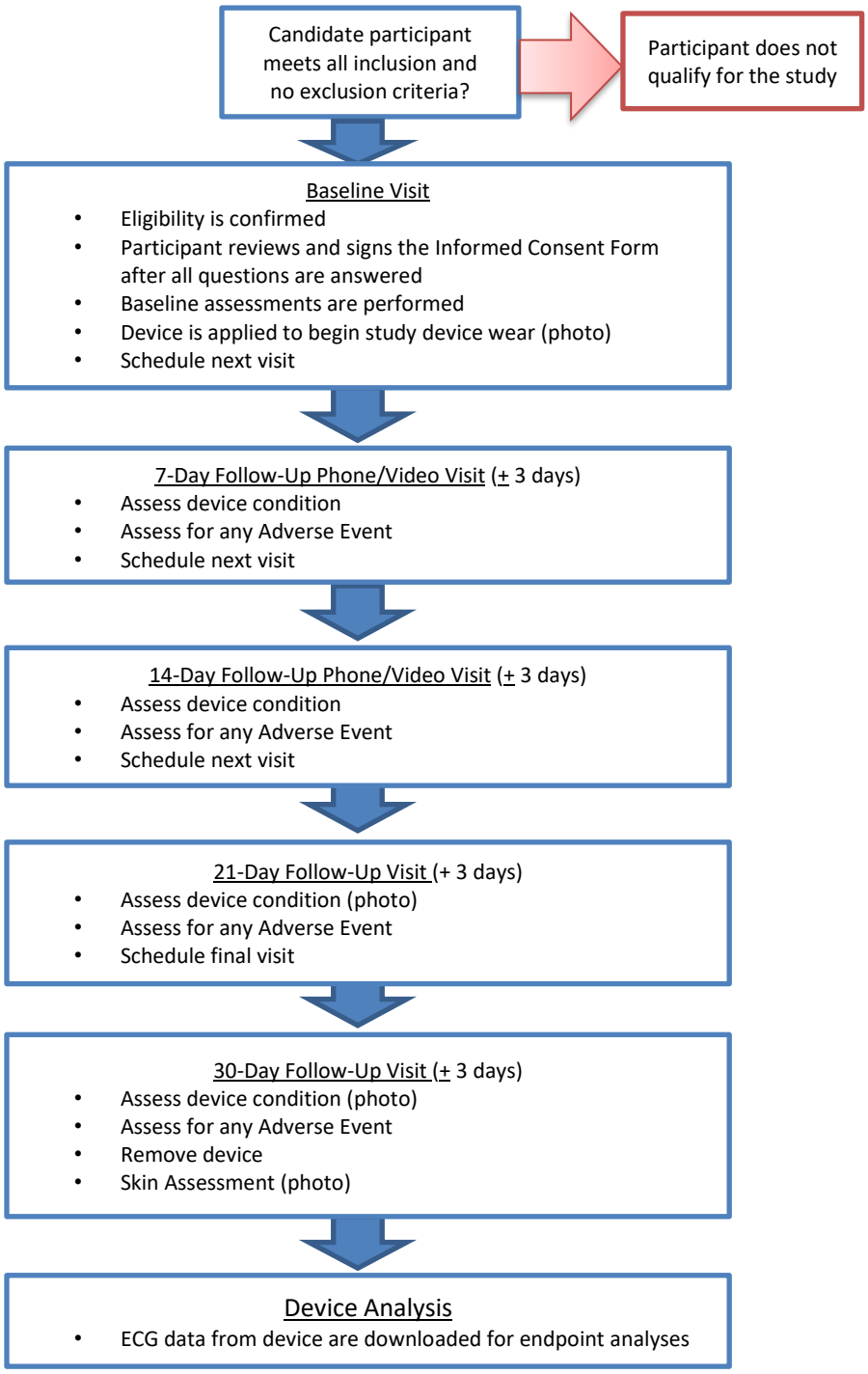
2.5 Overall Flow of the Study and Follow-up Schedule

Figure 1 shows the overall flow of the study. Participants who meet all inclusion and no exclusion criteria are eligible for enrollment into the study. Study visits will be performed in-clinic (Baseline, 21-day and 30-day) and by telephone or video (7- and 14-day).

Participants must read, understand, and sign (by hand) the study Informed Consent Form prior to the initiation of the Baseline assessment visit and start of device wear. Once consented, participants will have a study device applied to their chest by a Study Staff member or be provided a study device to self-apply (i.e., simulated at-home patch application) on-site. Study devices must be applied no later than the expiration date indicated on the kit. Participants will be considered enrolled after they have signed the Informed Consent Form and attempted patch application has occurred. Attempted patch application is defined as the opening of the patch kit and initiation of the shaving step necessary for skin preparation.

During the wear period, participants will be contacted by phone or video call to determine adverse events and remind them of their next visit. Enrolled participants will undergo clinical evaluation at Baseline and 21 days and 30 days after on-site or simulated at-home patch application. They will also be provided a contact number to report any adverse events that occur between planned visits.

Figure 1: Overall Study Flow



Important Notes:

1. Participants will be considered enrolled after they have signed the Informed Consent Form and have attempted to apply the patch.

2. Follow-up visits are conducted at the indicated days following application of the patch, whether in clinic or by phone/video call.
3. Early patch detachment and/or completion of the 30-day visit also includes a study completion form.
4. Photos are to be taken at Baseline before and after application, at the 21-day visit of the device, at the 30-day visit of the device both on and off the participant as well as a photo of the skin at the location the patch was worn. Optionally, photos may also be taken at the 7-day and/or 14-day visits if they occur via video call.

2.5.1 Study Safety Committee

A study safety committee will meet as needed to assess any safety events that may occur. The study safety committee meetings will be conducted according to a separate charter. The charter will include meeting scope, roles and activity specifics.

3.0 STUDY PERFORMANCE OBJECTIVES AND ADDITIONAL MEASURES

3.1 Wear Time Performance Objective

Wear duration is defined as the number of days the patch is attached to the participant. Wear duration measurement will start at the time of device application and will end at any of the following events:

- the device is removed at the 30-day follow-up visit, or
- the device fails to adequately adhere to the skin.

All enrolled participants on whom patch application was attempted will be included as part of the mean wear duration analysis. However, participants who discontinue wear of the device for reasons outside of the study protocol, or occurrence of an adverse event not related to the study, will not be counted in the analysis. Full disclosure for reasons of discontinuation will be provided in the study report.

Mean wear duration will be compared to a performance goal of 21 days. The performance objectives will be met if the mean wear duration is greater than 21 days.

3.2 Analyzable Time Performance Objective

Analyzable time is the percentage of time during the wear of the Zio monitor device which yields analyzable ECG signal (i.e., free from signal artifact).

All enrolled participants in whom patch application was attempted will be included as part of the percent analyzable time analysis. However, participants who discontinue wear of the device for reasons outside of the study protocol, or occurrence of an adverse event not related to the study, will not be counted in the analysis. Full disclosure for reasons of discontinuation will be provided in the study report.

Percent analyzable time will be compared to a performance objective of 80%. The performance objective will be met if the percent analyzable time is greater than 80% in 90% of subjects.

3.3 Safety Measures

All enrolled participants on whom patch application was attempted will be included in the safety analysis. The proportion of participants that experience clinically significant skin irritation through 30 days of wear will be assessed.

- Reaction severity will be assessed and reported, as follows [10]:
    - Weak Positive Reaction: Presence of erythema infiltration, discrete papules
    - Strong Positive Reaction: Presence of erythema infiltration, papules, discrete vesicles
    - Extreme Positive Reaction: Presence of bullous or ulcerative reaction, coalescing vesicles

An 'Extreme Positive Reaction' will be considered a clinically significant skin irritation.

Any skin reaction should be reported as an adverse event. Skin reactions are anticipated (see Section 12.2). All adverse events will be reviewed by a physician on the safety committee.

3.4 Additional Device Measures

- Signal Artifact (%) – Defined as the proportion of ECG signal that is artifact over the wear duration, reported for each study device.
- Device Functionality (%) – Defined as the proportion of Zio monitors recording a continuous ECG signal for (1) 21 days, and (2) for 30 days.

3.5 Other Measures

Observational assessment[8] of participant skin types that will be reported include:

- Participant Skin Type – Dry, Oily, Normal (Baseline only)
- Known Hyperhidrosis Status – Primary, Secondary or None (Baseline only)
- Fitzpatrick Skin Type -Type I-VI (Baseline only)
- Chest Hair Density – e.g., smooth/no hair, some hair, moderately hairy, or very hairy (baseline and follow-up) in the target patch placement area

4.0 PARTICIPANT SELECTION AND WITHDRAWAL

4.1 Participant Recruitment Population and Retention

A study population representative of the intended population and who meet the study eligibility criteria will be approached for participation. iRhythm may utilize a recruitment firm such as FieldWork® or community clinics who are qualified by experience and able to support this study.

The clinics and FieldWork may utilize email solicitation, social media posting, review of their current research database of potential participants and/or flyer posting with prior approval by the IRB. Recruitment of at least 61 participants will be needed, and enrollment may continue up to a total of 75 participants for each of the two (2) phases. Seventy-five participants have already been enrolled in the first phase of this study which utilized the iRhythm legacy skin preparation process. An additional 75 participants will be enrolled utilizing an updated skin prep process. Therefore, up to 150 participants will be enrolled.

To ensure recruitment of a population representative of patients undergoing long-term continuous monitoring, age, gender, and in-clinic HCP designee vs. self-application (i.e., simulated at-home patch application) will be tracked by the study team. The following represent enrollment targets across these key groups:

- Approximately 1/3 of participants <51 years of age
- Approximately 1/3 of participants ≥51 and <70 years of age
- Approximately 1/3 of participants ≥70 years of age
- At least 40% of participants should be female
- Devices are self-applied for approximately 1/3 of the study population.

4.2 Participant Screening and Informed Consent

Informed consent will be obtained in-person, in the clinic. Participant screening may be performed in-person, by telephone, or by videotelephony (e.g., Zoom).

[8]See Appendix II for assessment definitions.

4.2.1 Participant Screening

A recruitment firm (FieldWork or similar) will be utilized for initial screening. Participants who have been identified by the recruitment firm will be seen at one of two Sponsor locations (San Francisco, CA or

Deerfield, IL), the Investigator or research staff, who have been trained to the Protocol, will verify all participants meet all inclusion and no exclusion criteria to determine if the potential participant is eligible for study enrollment.

Potential participants will be assigned a screening number (assigned sequentially/chronologically). An accurate and up-to-date screening log of all participants considered for the trial will be maintained at each study location. The result of the participant screening process shall be documented in the screening log to include presentation route, whether the participant met eligibility criteria (and if not, which eligibility criteria were not met), and whether the participant was subsequently enrolled.

4.2.2 Informed Consent

The Study and the Study Informed Consent Form (ICF) must receive approval by an independent IRB prior to beginning enrollment into the Study. The central IRB for this study is Advarra.

During the informed consent process, the Investigator or designee, who has been trained on the Protocol, will explain the nature and scope of the trial, potential risks and benefits of participation, and answer questions from potential participants.

All participants must sign and date the IRB-approved Informed Consent Form prior to any trial-specific procedures. Those who are not able to provide consent on their own will not be enrolled. Obtaining the consent, provision of copy to the participant, along with date and time must be documented in the participant's source documents.

The Informed Consent Form must also be signed by the investigator or designee. The Investigator or designee is responsible for advising the participant of any new information about the study or the study device(s) that may become known during the study. The consent will be administered by paper.

An authorization for use and disclosure of the participant's protected health information, in accordance with the Health Insurance Portability and Accountability Act (HIPAA), must be obtained from the participant. The requirements of HIPAA elements may be incorporated into the Informed Consent Form or it may exist as a standalone document.

4.2.3 Disclosure of Participant Personal Contact Information

In order to conduct a phone or video visit, or to follow-up regarding study-related activities with the participant, the study team at iRhythm will collect the participant's phone number and email. The participant's identity will be anonymized to the extent possible. Only those iRhythm Study Staff individuals who are directly involved with the study will have access to the participant's protected health information (PHI) for those individuals enrolled through the iRhythm clinics.

4.3 Eligibility Criteria

Participants shall be screened per the criteria listed below. Assessment for eligibility criteria will be completed through an interview with a potential participant. Participants must meet ALL of the inclusion criteria to be considered for the study. If ANY of the exclusion criteria are met, the participant is excluded from the study. Participants meeting these criteria will be approached to provide informed consent for participation in the Study and included on the screening log.

4.3.1 Inclusion Criteria

Participants must meet all of the following inclusion criteria in order to participate in the study:

1. Participant must be 18 years or older at time of informed consent.
2. Participant is willing and able to provide informed consent and able to complete all visits for this study.

4.3.2 Exclusion Criteria

Participants who meet any of the following exclusion criteria may not participate in the study:

1. Participant has a known allergy to adhesives.
2. Participant has a current skin infection or injury at location for study device placement.
3. Participant is a member of a vulnerable population.
4. Participant is a current or prior employee of iRhythm.
5. Participant is unable or unwilling to participate or comply with study protocol.
6. The local Investigator deems the participant has a condition that could limit their ability or willingness to participate in the study, or ability to comply with study required procedures and/or follow-up visits.
7. Participant has experienced symptomatic episodes where instance variations in cardiac performance could result in immediate danger to the participant.
8. Participant has an external cardiac defibrillator or may be exposed to high frequency surgical equipment near strong magnetic fields or devices such as MRI during the wear period.
9. Participant has a neuro-stimulator, as it may disrupt the quality of ECG data.
10. Participant does not have the competency to wear the device for the prescribed monitoring period.
11. Participant does not have the ability to consent for themselves (i.e., no LARs).

4.4 Participant Enrollment and Inclusion

Participants are considered enrolled after they have signed the Informed Consent Form and patch application has been attempted. Attempted patch application is defined as the opening of the Patch kit and initiation of the first step necessary for skin preparation.

Enrolled participants on whom patch application is attempted will be included in the analysis population. Consistent with recent FDA guidance on increasing diversity in clinical trial enrollment (Enhancing the Diversity of Clinical Trial Populations – Eligibility Criteria, Enrollment Practices, and Trial Designs: Guidance for Industry, Issued November 2020), iRhythm will attempt to implement measures to ensure that the study population reflects the characteristics of clinically relevant population. Section 4.1 above describes measures taken to ensure enrollment of a relevant population with respect to age, sex and device application (in-clinic or self-application).

In addition, diversity across races and ethnic groups will be considered in selection of study sites and through recruitment activities. The study intends to enroll a diverse group of participants representative of the US population at large.

4.5 Participant Payment

Participants who meet eligibility and are enrolled in the study may be eligible to receive a stipend. The recruitment firm will manage all activities for payments including reporting of the payments to the Internal Revenue Service, if required.

The amount of the participant stipend will be included in the Informed Consent Form and approved by the IRB.

4.6 Participant Discontinuation

Participants shall remain in the study until completion of the required follow-up period, unless the device experiences early detachment. The participant's involvement in any clinical study is voluntary and the participant has the right to withdraw at any time without penalty or loss of benefit. Conceivable reasons for discontinuation may include, but are not limited to, the following:

- Participant death
- Participant voluntary withdrawal
- Participant withdrawal by physician as clinically-indicated
- Participant lost-to follow-up as described below.

The Sponsor Study Staff must be notified of the reason(s) for participant discontinuation. Study staff are required to report this to the central IRB as defined by the IRB's requirements.

No additional follow-up will be required or data recorded from participants once withdrawn, except for the status (deceased/alive).

4.6.1 Lost-to-Follow-up:

If the participant misses the scheduled follow-up time point and the attempts at contacting the participant detailed below are unsuccessful, then the participant is considered lost to follow-up. Study personnel shall make all reasonable efforts to locate and communicate with the participant (and document these efforts in the source documents), including the following, at each contact time point:

- A minimum of 2 telephone calls or emails on different days over a 10-day period to contact the participant should be recorded in the source documentation, including date, time and initials of study personnel trying to make contact.
- If these attempts are unsuccessful, a certified letter should be sent to the participant. The letter will request the participant to contact the Investigator. Study staff will also request return of the Zio monitor to iRhythm as soon as possible.

4.7 Number of Participants Required to be Included in the Study

A total of up to 150 participants will be included in the study.

4.8 Estimated Time Needed to Enroll this Number

It is anticipated that it may take up to 16 weeks to enroll all required participants.

4.9 Expected Duration of Each Participant's Role

The expected duration of participation is approximately 30 days.

4.10 Total Expected Duration of the Study

The time to complete the Study is estimated to be approximately six months (four months to complete participant enrollment, one month follow-up and one month to complete analysis and generate the study report).

4.11 Study Participant Completion

A participant is considered to have completed the study when any of the following has occurred:

- The participant is considered lost to follow-up per the above definition
- The participant withdraws consent
- The Investigator withdraws the participant from the Study

- The participant has died
- The Study has been completed (e.g., the participant's 30-day or final follow-up time point has been reached)
- The patch has prematurely detached from the participant (in the case of early detachment the participant should notify study staff of the date and time of detachment, and a study completion visit will be scheduled)
- The Sponsor has terminated the Study.

Sponsor must be notified of the reason for participant discontinuation. Investigators must also report this to their IRB, as required. Participants will not be replaced.

5.0 BASELINE VISIT AND FOLLOW-UP ASSESSMENTS

5.1 Baseline (Visit 1)

During the Baseline visit (Visit 1) the participant will be consented, and the informed consent process will be documented prior to patch application. Additional activities include:

Baseline health and demographic information:

The following information will be gathered from each participant in order to establish representation of the population and includes minimum:

- Medical Background/History as reported by the participant, including:
  - Cardiac Disease History
    - Including indication for monitoring if enrolled at a clinical care site
  - Skin characteristics as reported by the participant
    - Skin Type (e.g., dry, oily, or normal)
    - Hyperhidrosis Status (e.g., primary, secondary, or none – see definitions in appendix)
    - Fitzpatrick Skin Type (e.g., Type I-VI) – using the Fitzpatrick Skin Type assessment questionnaire completed by the participant
    - Chest Hair Density by visual inspection (e.g., smooth/no hair, some hair, moderately hairy, or very hairy) in the target patch placement area
- Demographic Information

–	Age	–	Sex at birth
–	Race	–	Ethnicity
–	Weight	–	Height

Patch application:

The Zio monitor will be applied to the participant's left upper chest/pectoral region and may be completed by either the participant (self-application) or by a Health Care Provider (HCP) or designee (i.e., the Study Coordinator or cardiac technician). There are two phases to this study. The application process for the first 75 study participants was conducted as outlined in the Zio Monitor Instructions for Use – LB10262.A. All 75 study participants have been enrolled as of 28 February 2025. Phase two of enrollment will include an additional 75 study participants using an updated skin prep process, the formal labeling instructions are not yet finalized pending the outcome of this study, but the following steps will be utilized in phase two:

- Identify the area of skin to be prepared for application.
- Shave the area for all genders even if there is no visible hair present.
  - Proceed with shaving

- Wipe away the hair shavings
- Make sure the skin is dry before continuing

- Exfoliate the area with 20 strokes to remove dead skin.
  - 10 strokes up and down, 10 strokes left to right
  - If discomfort occurs, decrease the pressure of the strokes
- Clean the prepared skin with the alcohol wipe.
- Wait one minute for the skin to dry. Study Staff to take a photo of the prepared skin
- Proceed with applying the Zio monitor.
- Study Staff to take a photo of the skin after the Zio monitor has been applied.

During the Baseline visit, participants will either have a patch applied by a Study Staff member (i.e., Study Coordinator) or participants will self-apply the patch to simulate home enrollment. In the event of self-application, the study participant will open the Zio monitor kit and the Zio monitor instructions for application and will self-apply the device in the presence of a Study Staff member. The Study Staff member is allowed to provide some guidance, but every effort should be made to allow the participant to place the patch without intervention from the Study Staff.

If there is an issue with the device after initial placement (e.g., device fails to activate), the device will be removed and a 2nd device may be applied. In the case that a 2nd device is required, the shaving and exfoliation steps may be skipped, but the alcohol wipe and drying step will still be completed.

5.2 Patch Wear Period

All consented participants in whom the Zio monitor Patch application is attempted will be considered enrolled in the study. Patch application is considered to have been attempted when the Zio monitor Patch kit is opened and the first step necessary for skin preparation has been initiated. The participant will be instructed to wear the device for as long as possible, up to the 30-day visit.

Study participants will be instructed to press and hold along the edges of the patch if they notice the patch peeling or lifting at the edges during the wear period. If a patch completely detaches from the participant's chest, the patch will not be re-applied. In the case of early patch detachment, the participant should notify study staff of the date and time of detachment, and a study completion visit should be scheduled as soon as possible.

At any time after patch application, if the device is determined to no longer be functioning (for example, if a rapidly blinking orange light is observed), the device will not be replaced. The date and time the determination of function failure will be noted as close to accurate as possible. As a non-functioning device does not present a safety concern, the participant will be asked to continue wearing the non-functioning patch for as long as possible, in order to record wear duration and wear experience data.

5.3 Protocol Required Medications

There are no protocol required medications for this study, and no medications will be administered for the study. A complete list of current medications will not be requested during the Baseline visit. However, medications used to treat an adverse event will be captured.

5.4 7-Day and 14-Day (± 3 days) Participant (Phone Call or Video Visit 2 & 3)

A phone call or video call at days 7 and 14 will be conducted in order to assess the status of the participant and the patch adherence.

5.5 21-Day (+3 days) Participant Follow-up (Visit 4)

At day 21 following patch application and up to day 24, participants will be asked to return to the clinic and the following activities will be conducted:

- Skin assessment by HCP or designee, including photograph of the area of the device
- Adverse Event review
- Answering of any questions and verification of ongoing consent to study participation

5.6 30-Day (±3 days) Participant Follow-up (Visit 5)

At day 30 following patch application and up to day 33, participants will be asked to return to the clinic and the following activities will be conducted:

- Skin assessment by HCP or designee, including photograph of the area with the device on and also upon device removal
- Adverse Event review
- Zio patch removal and visual inspection, including photograph of front and back of patch
- Patch return to iRhythm Technologies, Inc. for data download and evaluation

Participants who applied the Zio to themselves at the Baseline visit will be asked to remove the patch. They may ask a Study Staff member to provide guidance in the removal process.

Study clinical assessments and activities are summarized in **Table 2.**

Table 2: Clinical Assessment Schedule

Required Assessments to be Collected	Baseline (Visit 1)	7 & 14-Day (Visit 2 & 3)	21-Day (Visit 4)	30-Day (Visit 5)
		±3 days Phone or Video Call only	+3 days	±3 days
Informed Consent[1]	X	X	-	-
Medical and Cardiac Background/History	X	-	-	-
Fitzpatrick Skin Assessment	X	-	-	-
Skin Condition Assessment[2], Including photograph(s)	X	-	X	X
Assessment of Device Adhesion Performance, Including photograph(s)	-	-	X	X
Adverse Events[3]	X[4]	X	X	X

1. *Continued Informed Consent will be verified at each post-baseline contact.*
2. *Including chest hair density, as applicable.*
3. *Adverse Events include serious adverse events, all device-related complications, device deficiencies, device malfunctions, procedures and any hospitalizations. If AEs are ongoing at the 30-day visit, the participant should be contacted until resolution, or Day 37, whichever is sooner.*
4. *AEs are only assessed following Informed Consent and participant enrollment into the study.*

The study device will be returned to iRhythm Technologies, Inc. for download and analysis of the ECG signal collected during the wear.

Upon completion of study follow-up, all devices will be retrieved from study participants and returned to the Sponsor for analysis. Devices will be processed through the algorithm and reviewed by a clinical research qualified cardiac technician. The preliminary report will be provided to a Safety Committee and reviewed by a licensed cardiologist for finalization and determination of any safety concerns. A copy of the report will also be provided to the participant for their medical records and to share with their personal physicians.

NOTE: Following data retrieval from the Zio patch, the patch will be provided to Research & Development (R & D) for further review and inspection. Any reporting from potential findings from the device inspection by R & D is separate from this study protocol and out of scope.

6.0 ADVERSE EVENTS

Adverse events will be monitored and reviewed with the Study Investigator to determine any necessary action. To comply with standards and guidelines on clinical study adverse event reporting, the following standard definitions and reporting timelines will be adhered to for this study.

6.1 Definitions

6.1.1 Adverse Event

An adverse event (AE) is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in participants, users or other persons, whether or not related to the medical device. It is anticipated that arrhythmias will be noted on the scans. These are not considered adverse events and do not require reporting unless they have caused an adverse event (i.e., rapid atrial fibrillation is noted on scan, during this time the subject had a syncopal episode that resulted in bruising. The atrial fibrillation is not the AE but the syncopal episode is an AE and must be reported).

For this study AEs will be defined as follows:

- Mild: Transient or mild discomfort; no limitation in activity; no medical intervention/therapy required.
- Moderate: Mild-to-moderate limitation in activity, some assistance may be needed; no or minimal medical intervention/therapy required.
- Severe: Marked limitation in activity, some assistance usually required; medical intervention/therapy required, hospitalizations possible.
- Life-threatening: Extreme limitation in activity, significant assistance required; significant medical intervention/therapy required hospitalization or hospice care probable.

6.1.2 Serious Adverse Event

If the AE meets any of the criteria below, it is regarded as a serious adverse event (SAE) and is required to be reported according to the FDA guidelines for SAE reporting.

a) Led to a death,
b) Led to a serious deterioration in health that either:
    1) Resulted in a life-threatening illness or injury, or
    2) Resulted in a permanent impairment of a body structure or a body function, or
    3) Required in-patient hospitalization or prolongation of existing hospitalization, or
    4) Resulted in medical or surgical intervention to prevent life threatening illness or injury or permanent impairment to a body structure or a body function.
c) Led to fetal distress, fetal death or a congenital abnormality or birth defect.

An important medical event that may not result in death, be life-threatening, or require hospitalization but may be considered serious when, based upon appropriate medical judgment, may jeopardize the participant and/or may require intervention to prevent one of the outcomes listed in this definition may also be considered an SAE.

Note 1: This includes device deficiencies that might have led to a serious adverse event if a) suitable action had not been taken or b) intervention had not been made or c) if circumstances had been less fortunate. These are handled under the SAE reporting system.

Note 2: A planned hospitalization for pre-existing condition, or a procedure required by the Clinical Protocol, without a serious deterioration in health, is not considered to be a serious adverse event.

6.1.3 Device Malfunction

A device malfunction (DM) is the failure of a device to meet its performance specifications or otherwise perform as intended, when used in accordance with the IFU or protocol.

6.2 Device, Process or Procedure Relationship

Determination of whether there is a reasonable possibility that a product, process or procedure caused or contributed to an AE is to be determined by Study Staff and recorded on the appropriate CRF. Determination should be based on assessment of temporal relationships, evidence of alternative etiology, medical/biologic plausibility, and patient condition (pre-existing condition).

6.2.1 Unanticipated (Serious Adverse) Device Effect [U(S)ADE]

Unanticipated serious adverse device effect (USADE) refers to any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the protocol or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of participants. See Anticipated Device Effects (**Section 12.2**).

6.3 Adverse Event/Device Deficiency/Product Experience Reporting

6.3.1 Adverse Event Reporting

Occurrences of adverse events will be monitored for each participant during the course of the study as required by this protocol, per AE and SAE definitions as noted in the sections above.

All information must be entered in the Electronic Data Capture (EDC) system as soon as feasible. AEs need to be collected for consented participants on the appropriate AE CRF. Additional information with regards to an adverse event, including whether or not the event was anticipated, should be updated within the appropriate CRF and source records.

Serious adverse events (SAEs) that occurred in the user or persons other than the study participant should not be entered in the CRF; they should be reported to researchstudies@irhythmtech.com. Study staff will regularly monitor this email address and will investigate all events reported. These will be reported as soon as possible but no later than 3 calendar days from the day the study personnel became aware of the event. The SAE will be reported to the local IRB according to reporting requirements.

6.3.2 Unanticipated Serious Adverse Device Effect Reporting

iRhythm (the Sponsor) is required to report and document any USADE as soon as possible, but at least within 24 hours of the Investigator's knowledge of the event.

6.3.3 Device Deficiency/Device Malfunction Reporting

All device deficiencies/malfunctions should be reported on the appropriate CRF no later than 3 calendar days from the day the study personnel became aware of the event or as per the investigative location's local requirements, if the requirement is more stringent than those outlined.

An email address (researchsupport@irhythmtech.com) will be made available to allow the Investigator to report device deficiencies/malfunctions. This does not replace the CRF. All information must still be entered in the CRF as soon as feasible. Study staff will regularly monitor this email address and will investigate all events reported.

In case a device deficiency/malfunction occurred before *the patient ID has been assigned*, the device deficiency should also be reported to iRhythm via researchsupport@irhythmtech.com.

The device, if not applied or not remaining on the participant, should be returned to iRhythm Technologies, Inc.

Device deficiencies/malfunctions should be reported to the IRB per the investigative location's local requirements and IRB requirements.

6.3.4 Adverse Event Reporting to Country Regulatory Authorities by the Sponsor

Where required by local or regional requirements, the Sponsor will report the SAEs and DDs to the appropriate regulatory authority.

7.0 STATISTICAL ANALYSIS

7.1 Analysis Population

Following the Phase I completion of all participant activities an analysis will be conducted. Separately, following the Phase II completion of all participant activities an analysis will be conducted. All analyses will be performed on the population of enrolled participants in whom patch application was attempted in that Phase. Phase 1 analysis is considered separate from Phase 2 and will be conducted and reported accordingly. Sections 7.2 and beyond (detailed below) will adhere to this plan.

7.2 Sample Size Calculations and Assumptions

A prior study of 30 subjects instructed to wear the Zio monitor device up to 30 days resulted in a mean wear time of >24 days (24.9 ± 9.3 days).

Therefore, a power analysis was performed using the following assumptions:

- Performance goal: > 21 days
- Estimated wear duration with the Zio monitor patch: 24.0 days
- Estimated standard deviation of wear duration with the Zio monitor patch: 9.3 days
- Statistical test: One sample t-test
- Statistical Power: 80%
- Significance level: One-sided alpha = 0.05

Given these assumptions, enrollment of 61 participants is required to assess performance of wear duration performance.

SAS Enterprise Guide 8.3 was used for all calculations.

In order to assess the frequency of adverse events with reasonable precision, and to account for the possibility that up to 25% of enrolled participants may not provide ECG data at the 30-day visit due to device removal or loss to follow-up, enrollment of up to 75 participants is planned for each of the two (2) phases. Seventy-five participants have already been enrolled in the first phase of this study which utilized the iRhythm legacy skin preparation process. An additional 75 participants will be enrolled utilizing an updated skin prep process. A total of 150 participants will be enrolled under this protocol

7.3 Planned Interim Analyses

There is no planned interim analysis for this study. Each analysis will be considered the final analysis for that Phase of the study.

7.4 Statistical Analyses

For wear duration performance, mean wear duration, standard deviation and 95% confidence interval will be reported. For analyzable time performance, the mean percent analyzable time, standard deviation, 95% confidence interval, and percentage of patients with analyzable time >80% will be reported. Performance objectives will be met if the mean wear duration is greater than 21 days, and percent analyzable time is greater than 80% in 90% of subjects.

For other analyses, mean and standard deviation or median, interquartile range, minimum and maximum will be reported for continuous variables; counts and percentages will be reported for categorical variables.

7.4.1 Subgroup Analysis

Performance within subgroups including (but not limited to) sex, age, and application method (in-clinic HCP or designee vs. self-applied) will be assessed.

8.0 QUALITY CONTROL AND QUALITY ASSURANCE

8.1 Selection of Study Site Locations and Investigators

iRhythm Technologies, Inc. will utilize two iRhythm locations for the recruitment firm's referrals and participant enrollment. All Study Staff will be trained appropriately. Contract Study Coordinators will be utilized at these locations to decrease any biases. The primary Investigator of the study will also serve as the Principal Investigator at the iRhythm locations.

Prior to receipt of study devices all locations must be trained to the protocol, the CRFs, and other appropriate study activities. All locations MUST have IRB approval to recruit and enroll participants.

Good Clinical Practice certification is required for all study staff who will have direct contact with the study participants or their data.

8.2 Protocol Amendments

The Sponsor will provide approved Protocol amendments to the Investigator(s) prior to implementing the amendment. The Principal Investigator is responsible for notifying the IRB or equivalent committee of the Protocol amendment (administrative changes) or obtaining IRB's approval of the Protocol amendment (changes in participant care or safety), according to the instructions provided by the Sponsor with the Protocol amendment.

Acknowledgement/approval by the IRB of the Protocol amendment must be documented in writing prior to implementation of the Protocol amendment. Copies of this documentation must also be provided to iRhythm Technologies, Inc.

8.3 Training

8.3.1 Study Training

All Investigators/study personnel, designee, etc. are required to attend the study training sessions, which may be conducted at a sponsor location initiation visit (SIV) or other appropriate training sessions. Over-the-phone, video 'webinar', or self-training to the study and/or the device may take place as needed. Training of Investigators/study personnel will include, but is not limited to, the Protocol requirements, device usage, electronic CRF completion and study personnel responsibilities.

All Investigators/study personnel that are trained must sign a training log (or an equivalent) upon completion of the training. Prior to signing the training log, Investigator/study personnel must not perform any study-related activities that are not considered standard of care at the sponsor location.

All study personnel who have been trained to the study must also be listed on the Delegation of Authority log provided by iRhythm. The log must be kept updated throughout the study. A final copy of the DOA log will be collected from each study center and location for filing in the TMF for the study.

8.3.2 Training of Sponsor's Monitors

Sponsor and/or designated study monitors will be trained to the Protocol, case report forms and device usage (as appropriate). Documentation of this training will be according to written procedures.

8.4 Monitoring

Centralized monitoring will occur through routine internal data review. This monitoring is designed to identify missing and inconsistent data, data outliers, and potential Protocol deviations that may be indicative of non-compliance at the sponsor location. On-site monitoring may occur at the discretion of the Sponsor.

Prior to initiating any procedure, the Sponsor monitor (or delegate) will ensure that the following criteria are met:

- The Investigator understands and accepts the obligation to conduct the research study according to the Protocol and applicable regulations and has signed the Investigator Agreement or the Clinical Study Agreement.
- The Investigator and his/her staff have sufficient time and facilities to conduct the study and that they have access to an adequate number of appropriate participants to conduct the study.
- Source documentation (including original medical records, if applicable) must be available to substantiate proper informed consent procedures, adherence to Protocol procedures, training records and appropriate delegation of roles, adequate reporting and follow-up of adverse events, accuracy of data collected on case report forms, and device information.
- If monitoring visits are scheduled, the Investigator/sponsor location will permit access to such records. A monitoring visit sign-in log will be maintained by study staff. The Investigator will agree to dedicate an adequate amount of time to the monitoring process. The Investigator and/or research coordinator will be available for monitoring visits. It is expected that the Investigator will provide the study monitor with a suitable working environment for review of study-related documents.

8.5 Deviations from Protocol

The Investigator will ensure that the study does not deviate from the IRB approved Protocol for any reason without prior written approval from Sponsor except in cases of medical emergencies, when the deviation is necessary to protect the rights, safety and well-being of the participant or eliminate an apparent immediate hazard to the participant. In that event, the Investigator will notify Sponsor immediately by phone or in writing. All deviations must be reported to the Sponsor. In participant-specific deviations from the Protocol, a Protocol deviation case report form will be completed. The occurrence of Protocol deviations will be monitored by the Sponsor for evaluation of Investigator compliance to the Protocol and regulatory requirements and dealt with according to written procedures. Investigators will inform their IRB or equivalent committee of all Protocol deviations in accordance with their specific IRB or equivalent committee reporting policies and procedures.

In the event of repeated non-compliance, as determined by the Sponsor, a Sponsor's monitor or company representative will attempt to secure compliance by one or more of the following (and not limited to):

- Visiting the Investigator and/or delegate
- Telephoning the Investigator and/or delegate
- Corresponding with the Investigator and/or delegate

Repeated non-compliance with the signed agreement, the Protocol or any other conditions of the study may result in further escalation in accordance with the Sponsor's written procedures including securing compliance or, at its sole discretion; Sponsor may terminate the Investigator's participation in the study.

8.6 Quality Assurance Audit

A Sponsor representative or designee may request access to all clinical study records, including source documentation, for inspection and duplication during a Quality Assurance audit.

In the event that an Investigator is contacted by a Regulatory Agency in relation to this clinical study, the Investigator will notify the Sponsor immediately. The Investigator and Research Coordinator must be available to respond to reasonable requests and audit queries made during the audit process. The Investigator must provide the Sponsor with copies of all correspondence that may affect the review of the current clinical study (e.g., Form FDA 483, Inspectional Observations, Warning Letters, Inspection Reports, etc.). Sponsor may provide any needed assistance in responding to regulatory audits.

9.0 DATA HANDLING AND RECORD KEEPING

All CRF data collection will be performed by authorized personnel to enter, review or correct data in a secure EDC System. Access will be strictly confidential.

For the clinical study duration, the Investigator will maintain complete and accurate documentation including, but not limited to, source documents, clinical study progress records, electronic case report forms, signed ICFs, device accountability records, correspondence with the IRB and clinical study monitor/Sponsor, adverse event reports, and information regarding participant discontinuation or completion of the clinical study. Protocol deviations are not anticipated, but if they occur, they will be recorded in the EDC System. All study related documents will be stored in a secured location.

The handling, storage, transfer and destruction of the data will comply with all applicable national and local laws.

The following persons will have access to identifiable data in order to review and ensure the Study is run appropriately: the Sponsor representatives (such as contract monitors or study managers) visiting the study sponsor location, the Study Staff participating and running the Study, regulatory (i.e., FDA) and health authorities. Participants consenting to participate will allow these persons to read the identifiable information.

The Sponsor (including persons working under the Sponsor) will have access to de-identified data only. The Sponsor will take reasonable measures to keep the data confidential and secure.

Data Management will include documentation of the systems and procedures used in data collection for the duration of the study.

All CRF data collection will be performed by personnel authorized to enter, review or correct data. Data will be strictly confidential.

All CRF data will be reformatted into a data structure acceptable to iRhythm. The data will be subjected to consistency and validation checks and will be subject to supplemental validation.

At the conclusion of the study, completed CRF images with the date-and-time stamped audit trail indicating the user, the data entered, and any reason for change (if applicable) will be archived for each sponsor location and a backup copy archived with iRhythm.

9.1 Source Documentation

Regulations and Good Clinical Practice (GCP) require that the Investigator maintain information in the participant's original source documents (including medical records) that corroborates data collected on the case report forms. In order to comply with these regulatory requirements/GCP, the following information should be included in the participant record as/if applicable to the study:

- Self-reported medical history of the participant before involvement in the study sufficient to verify Protocol entry criteria
- Dated and signed notes on the day of entry into the study referencing the Sponsor, Protocol number, participant ID number and a statement that informed consent was obtained
- Dated and signed notes from each participant visit (for specific results of procedures and exams)
- Adverse events reported and their resolution including supporting documents such as discharge summaries, catheterization laboratory reports, ECGs, and lab results, etc. including documentation of awareness of SAEs and of investigator device relationship assessment of SAEs at the sponsor location
- Notes regarding prescription medications taken during the study for the treatment of an Adverse Event, the documentation will also include start and stop dates
- Participant's condition upon completion of or withdrawal from the study
- Any other documents or records required to substantiate data entered into the CRF

9.2 Case Report Form Completion

Primary data collection based on source-document review will be performed clearly and accurately by study personnel trained on the Protocol and CRF completion. The Investigator will review and sign source documents upon study completion for each participant, unless a clinically significant event occurs. All adverse events and ECG data will be assessed by medically trained Study Staff. CRF data will be collected for all participants in the study. In the event the EDC System is unavailable, study personnel may complete paper CRFs and enter the data in the EDC System as soon as it is available.

9.3 Direct Access to Source Data/Documents

The Investigator/institution will permit direct access to source data/documents in order for clinical study-related monitoring, audits, IRB review and regulatory inspections to be performed.

Participants providing informed consent are agreeing to allow Sponsor and/or its designee access and copying rights to pertinent information in their source document concerning their participation in this clinical study. The Investigator will obtain, as part of the informed consent, permission for clinical study monitors or regulatory authorities to review, in confidence, any records identifying the participants in this clinical study. This information may be shared with regulatory agencies; however, Sponsor undertakes not to otherwise release the participant's personal and private information.

9.4 Record Retention

The Sponsor will archive and retain all documents pertaining to the study as per the applicable regulatory record retention requirements. The Investigator must obtain permission from Sponsor in writing before destroying or transferring control of any clinical study records.

10.0 ETHICAL CONSIDERATION

10.1 Institutional Review Board Review

Institutional Review Board approval for the Protocol, ICF and other written information provided to the patient will be obtained by the Principal Investigator at each sponsor location or community clinical study site prior to participation in this validation study. The approval letter must be received prior to the start of this validation study and a copy must be provided to the Sponsor. No changes will be made to the Protocol or ICF or other written information provided to the patient/participant without appropriate approvals, including IRB, the Sponsor, and/or the regulatory agencies.

Until the validation study is completed, the Investigator will advise the IRB of the progress of this study, per IRB requirements. Ongoing written approval will be obtained according to the IRB requirements. Additionally, any amendments to the Protocol as well as associated ICF changes will be submitted to the IRB and written approval obtained prior to implementation.

11.0 PUBLICATION POLICY

The data and results from the study are the sole property of the Sponsor. The Sponsor shall have the right to access and use all data and results generated during this wear validation study. The Sponsor may publish a manuscript regarding the study results. The recorded ECG information may be used for educational (including medical publications) or training purposes only, but only de-identified information will be used.

The preliminary and final reports from the patch for those participants who were enrolled through the community clinic study site belong to the participant as part of their medical record.

12.0 RISK ANALYSIS

12.1 Anticipated Clinical Benefits

This is a post-clearance study on the extended wear performance of the study device. Study participants will be asked to wear the device for as long as possible (up to 30 days) to validate performance of the device in up to 21 days of wear. There are no immediate potential benefits to study participants; the primary long-range potential benefit is improvement in clinical standard of care for others (altruistic benefit to study participants).

12.2 Foreseeable Adverse Events and Anticipated Adverse Device Effects

Table 3 provides a list of anticipated adverse events with wearing the study device. If a participant experiences severe reaction to the device, it is recommended that the participant remove the device.

Table 3: Foreseeable / Anticipated Adverse Device Effects

Anticipated Adverse Device Effects (ADE)	ADE Definition
Allergic reaction	Localized allergic reaction or allergic symptoms (i.e., acute urticaria) associated with serious injury.
Delayed healing	Atypical or otherwise prolonged recovery period post-wear resulting in non-permanent injury.
Discomfort	Transient physical or psychological distress.
Infection (local)	Localized evidence of tissue invasion by pathogenic microorganisms, resulting in non-permanent tissue injury.
Infection (systemic)	Evidence of pathogenic microorganism proliferation progressed to a systemic disease state associated with serious injury.
Non-functional defects	Defects that are imperceptible to participant but identified by study staff (i.e., compromised aesthetics).
Pain	Transient physical or psychological suffering or other unpleasant feelings.
Skin or soft tissue damage (permanent,	Serious injury presenting as permanent signs of tissue structural or functional damage (i.e., gross scarring, localized neuropathy).

major)	
Skin or soft tissue damage (permanent, minor)	Serious injury presenting as permanent changes in epidermis (i.e., abnormal pigmentation, blemishes).
Skin or soft tissue damage (temporary, major)	Signs of probable irritant contact dermatitis (edema, erythema, pruritus).
Skin or soft tissue damage (temporary, minor)	Minor irritation, not yet at probable irritant contact dermatitis.
Participant annoyance	Inconvenience perceptible to participant but unlikely to cause injury.
Participant inconvenience	Inconvenience imperceptible to participant but identified by study staff (i.e., burdensome packaging).

12.3 Risks Associated with Participation in Clinical Study

Participation in the study requires submission of data that may or may not be protected heath information. This information will be kept confidential, but there is a risk that some of the information could be unintentionally made non-confidential. The risk of this happening for this study is no greater than the risk of loss of confidentiality in any study.

12.4 Possible Interactions with Protocol-Required Concomitant Medications

There are no protocol-required medications being used as part of this study. Only medications used to treat adverse events will be reported.

12.5 Steps That Will be Taken to Control or Mitigate Risks

Risks associated with the use of the device during this clinical study are minimized through device design, Investigator selection and training, pre-specified patient eligibility requirements, and study monitoring to ensure adherence to the protocol.

Devices manufactured for this extended wear study will be the design cleared in K202359, with minor improvements in manufacturability and with the modifications necessary to allow for ECG recording up to 30 days. The Sponsor will have completed and documented internal Design Control requirements for all components of the study devices prior to first use in the extended wear study. All adverse events and device deficiencies will be reported to iRhythm and will be monitored internally for safety surveillance purposes.

The contraindications, warnings and precautions are listed in the IFU in the Zio monitor Clinical Reference Manual (Part Number DLB0035 or clinical study equivalent) that will be provided with all devices to be used during this study.

12.6 Risk to Benefit Rationale

Foreseeable risks are outlined in **Table 3.** There are no other types of foreseeable risk to participants by virtue of participation in this study. Apparently healthy study participants will equally be exposed to such physical risks, but will be fully informed in order to assess the wear performance of the investigational device on a human skin. The value of the information to be gained outweighs these procedural-related risks as it will support intended performance of the device.

Participants participating in this study will be receiving the latest technology of the currently cleared Zio monitor patch.

Participants participating in the study have a small risk of loss of confidentiality as part of the data collection process. This risk is mitigated to as low as possible with the use of data collection systems, methods and procedures that are used commonly in clinical research. This includes the use of only validated electronic systems, the training of study personnel and the use of pseudo anonymized data for all data entry. Based upon the established safety profile of the study device, the low risk of loss of confidentiality is adequately mitigated to justify use of the study device for participants in this study.

This area intentionally left blank

APPENDIX I: ABBREVIATIONS AND ACRONYMS

AE	Adverse Event
CRF	Case Report Form
DD	Device Deficiency
DM	Device Malfunction
ECG	Electrocardiogram
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
FDA	U.S. Food and Drug Administration
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
ICF	Informed Consent Form
IFU	Instructions for Use
IRB	Institutional Review Board
SAE	Serious Adverse Event
UADE	Unanticipated Adverse Device Effect
USADE	Unanticipated Serious Adverse Device Effect

APPENDIX II: DEFINITIONS

DEATH (All Cause)

All deaths regardless of cause. Death is further divided into 2 categories:

1. CARDIOVASCULAR DEATH

   Per the Valve Academic Research Consortium (VARC) [11], as any one of the following:

   - Any death due to proximate cardiac cause (e.g., myocardial infarction (MI), cardiac tamponade, worsening heart failure)
   - Unwitnessed death and death of unknown cause
   - All procedure-related deaths, including those related to a complication of the procedure or treatment for a complication of the procedure
   - Death caused by non-coronary vascular conditions such as cerebrovascular disease, pulmonary embolism, ruptured aortic aneurysm, dissecting aneurysm, or other vascular disease.

2. NON-CARDIOVASCULAR DEATH

   Any death not covered by the VARC definitions of Cardiovascular Death, such as death caused by infection, malignancy, sepsis, pulmonary causes, accident, suicide, or trauma.

FITZPATRICK SKIN TYPE

The Fitzpatrick skin type is a 6-point scale [12].

Fitzpatrick Skin Type	Skin	Skin Reaction to Sun Exposure
I	Pale White	Always Burns, Never Tans
II	Fair	Usually Burns, Tans Minimally
III	Darker White	Sometimes Mild Burn, Tans Uniformly
IV	Light Brown	Burn Minimally, Always Tans Well
V	Brown	Very Rarely burns, Tans Very Easily
VI	Dark Brown or Black	Never Burns

HOSPITALIZATION (ALL CAUSE)

Defined as admission to inpatient unit or ward in the hospital for at least 24 hours, including emergency department stay. Excludes hospitalizations planned for pre-existing conditions, unless there is worsening of a pre-existing condition.

HYPERHYDROSIS STATE

Hyperhidrosis status will be determined by the following definition:

- Primary – Focal, visible, and excessive sweating for no apparent cause. Typically at axillae, palms, soles, inguinal areas, and face.
- Secondary – Caused by underlying medical condition. Can be either focal or general sweating.

- None – Only sweat during exercise, hot environment, physical, and/or psychological stress

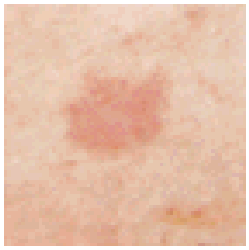
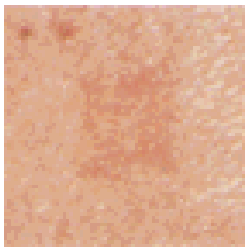
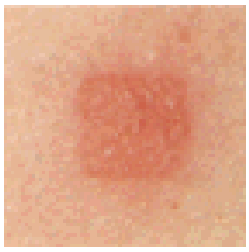
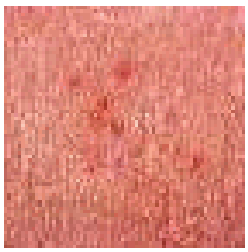
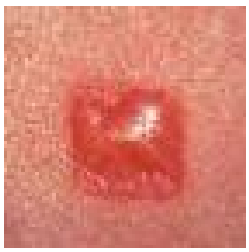
CHEST HAIR DENSITY

Chest hair density will be measured by visual inspection and classified as smooth/no hair, some hair, moderately hairy, or very hairy in the target patch placement area.

SKIN IRRITATION

Severity of skin irritation will be assessed per **Table 4** below. Interpretation of the reaction will be based on the method recommended by the International Contact Dermatitis Research Group (ICDRG) [10,13]. This scale has been modified to incorporate the U.S. Food & Drug Administration (FDA) *Guidance for Industry Skin Irritation and Sensitization Testing of Generic Transdermal Drug Products*.

Table 4: Skin Irritation Assessment

	Negative reaction (= -)		Weak positive reaction Erythema Infiltration Discrete papules (= +) FDA = 1 minimal erythema, barely perceptible
	Doubtful reaction Faint macular or homogeneous erythema, no infiltration (= ?) FDA = 0 no evidence of irritation		Strong positive reaction Erythema Infiltration Papules Discrete vesicles (= ++) FDA = 2-3 definite erythema, readily visible, papules
	Irritant reaction of different types (= IR)		Extreme positive reaction Coalescing vesicles/bullous reaction (= +++) FDA = 4-7 definite edema, erythema, papules, vesicular eruption, spreading beyond site

SKIN TYPE

Skin type will be assessed at the planned patching location of the study device.

- Normal
- Dry – Scaling (visible peeling of outer skin layer) and skin cracking; also known as xeroderma
- Oily – Excess sebum (oil) production producing shiny appearance; also known as seborrhea

VULNERABLE POPULATION (ICH E6(R3) Definition)

Individuals whose willingness to volunteer in a clinical trial may be unduly influenced by the expectation, whether justified or not, of benefits associated with participation, or of a retaliatory response from senior members of a hierarchy in case of refusal to participate. Examples are members of a group with a hierarchical structure, such as medical, pharmacy, dental, and nursing students, subordinate hospital and laboratory personnel, employees of the pharmaceutical industry, members of the armed forces, and persons kept in detention. Other vulnerable participants include those with incurable diseases, persons in nursing homes, unemployed or impoverished persons, persons in emergency situations, ethnic minority groups, homeless persons, nomads, refugees, minors, and those incapable of giving consent.

BIBLIOGRAPHY

1. Turakhia MP, Hoang DD, Zimetbaum P, Miller JD, Froelicher VF, Kumar UN, Xu X, Yang F, Heidenreich PA. Diagnostic utility of a novel leadless arrhythmia monitoring device. Am J Cardiol. 2013;112:520–524.
2. Survey data on file.
3. Knight BP, et al. Performance of a Novel Next-Generation Ambulatory ECG Long-Term Patch Monitor: A Multicenter Post- Market Evaluation. Heart Rhythm 2024;21(9 Suppl):S796.
4. Barrett PM, Komatireddy R, Haaser S, Topol S, Sheard J, Encinas J, Fought AJ, Topol EJ. Comparison of 24-hour Holter Monitoring with 14-day Novel Adhesive Patch Electrocardiographic Monitoring. The American Journal of Medicine. 2014;127:95.e11-95.e17.
5. Rosenberg MA, Samuel M, Thosani A, Zimetbaum PJ. Use of a noninvasive continuous monitoring device in the management of atrial fibrillation: a pilot study. Pacing Clin Electrophysiol. 2013;36:328–333.
6. Kaura A, Sztriha L, Chan FK, Aeron-Thomas J, Gall N, Piechowski-Jozwiak B, Teo JT. Early prolonged ambulatory cardiac monitoring in stroke (EPACS): An open-label randomised controlled trial. Eur J Med Res. 2019;24:25.
7. Gupta N, Yang J, Reynolds K, Lenane J, Garcia E, Sung SH, Harrison TN, Solomon MD, Go AS. Diagnostic Yield, Outcomes, and Resource Utilization With Different Ambulatory Electrocardiographic Monitoring Strategies. Am J Cardiol. 2022;166:38-44.
8. Reynolds MR, Passman R, Swindle J, Mohammadi I, Wright B, Boyle K, Turakhia MP, Mittal S. Comparative effectiveness and healthcare utilization for ambulatory cardiac monitoring strategies in Medicare beneficiaries. Am Heart J. 2024;269:25-34.
9. Hannun AY, Rajpurkar P, Haghpanahi M, Tison GH, Bourn C, Turakhia MP, Ng AY. Cardiologist-level arrhythmia detection and classification in ambulatory electrocardiograms using a deep neural network. Nat Med. 2019;25:65–69.
10. Fonacier L, et. al.; American Academy of Allergy, Asthma & Immunology; American College of Allergy, Asthma & Immunology; Joint Council of Allergy, Asthma & Immunology. Contact dermatitis: a practice parameter-update 2015. *J Allergy Clin Immunol Pract*. 2015 May-Jun;3(3 Suppl):S1-39.
11. Updated standardized endpoint definitions for transcatheter aortic valve implantation: The Valve Academic Research Consortium-2 consensus document. Kappetein, A. Pieter et al. The Journal of Thoracic and Cardiovascular Surgery, Volume 145, Issue 1, 6 – 23
12. Fitzpatrick TB. The validity and practicality of sun-reactive skin types I through VI. Arch Dermatol. 1988 Jun;124(6):869-71.
13. Rietschel RL, Fowler JF Jr. Fisher's Contact Dermatitis. 5th ed. Baltimore, Md: Williams & Wilkins; 2001.

REVISION HISTORY

Version #	Released Date	Description of Change
02	23 April 2025	Updated skin prep process
01	15 November 2024	Initial Release

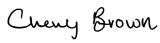
Certificate Of Completion

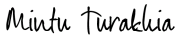
Envelope Id: EAAF9C21-1621-4B51-B6AC-44EBB134B6D3
Status: Completed
Subject: Complete with Docusign: 2025-03-03_SHASTA II Amd1 PROT V2_Clean.pdf
Source Envelope:
Document Pages: 40
Signatures: 8
Certificate Pages: 6
Initials: 0
AutoNav: Enabled
EnvelopeId Stamping: Enabled
Time Zone: (UTC-08:00) Pacific Time (US & Canada)

Envelope Originator:
Chevy Brown
650 Townsend St Ste 380
San Francisco, CA 94103-6248
chevy.brown@irhythmtech.com
IP Address: 4.53.130.26

Record Tracking

Status: Original
4/23/2025 1:54:53 PM
Holder: Chevy Brown
chevy.brown@irhythmtech.com
Location: DocuSign

Signer Events	Signature	Timestamp
Chanda Owens chanda.owens@irhythmtech.com VP Quality Security Level: Email, Account Authentication (None)	 Signature Adoption: Pre-selected Style Using IP Address: 68.5.133.129	Sent: 4/23/2025 1:59:41 PM Resent: 4/29/2025 8:16:21 AM Viewed: 4/29/2025 5:00:24 PM Signed: 4/29/2025 10:46:21 PM
Electronic Record and Signature Disclosure: Accepted: 4/28/2025 8:26:11 AM ID: a59cac65-bed4-4e8f-adf9-e4fe33d503eb		
Char Bame char.bame@irhythmtech.com Sr. Director, Clinical Research Operations Security Level: Email, Account Authentication (None)	 Signature Adoption: Uploaded Signature Image Using IP Address: 12.235.16.3	Sent: 4/23/2025 1:59:41 PM Viewed: 4/23/2025 3:16:10 PM Signed: 4/23/2025 3:16:21 PM
Electronic Record and Signature Disclosure: Accepted: 4/23/2025 3:16:10 PM ID: 7d7880cc-aca1-4f56-8657-1af6bb2593a1		
Chevy Brown chevy.brown@irhythmtech.com CR Sr. Project Manager Security Level: Email, Account Authentication (None)	 Signature Adoption: Pre-selected Style Using IP Address: 4.53.130.26	Sent: 4/23/2025 1:59:43 PM Viewed: 4/23/2025 2:00:05 PM Signed: 4/23/2025 2:00:13 PM
Electronic Record and Signature Disclosure: Not Offered via Docusign		
Christine Dunn christine.dunn@irhythmtech.com Sr. RA Mgr. International Security Level: Email, Account Authentication (None)	 Signature Adoption: Uploaded Signature Image Using IP Address: 73.239.153.221	Sent: 4/23/2025 1:59:42 PM Viewed: 4/24/2025 8:39:58 AM Signed: 4/24/2025 8:42:39 AM
Electronic Record and Signature Disclosure: Accepted: 4/24/2025 8:39:58 AM ID: e64d590e-c210-4fe0-8167-42572985fbbe		

Signer Events	Signature	Timestamp
Kevin Clarkson kevin.clarkson@irhythmtech.com Director, Zio XT Security Level: Email, Account Authentication (None)	 Signature Adoption: Pre-selected Style Using IP Address: 12.235.16.3	Sent: 4/23/2025 1:59:45 PM Viewed: 4/23/2025 2:02:47 PM Signed: 4/24/2025 3:49:56 PM
Electronic Record and Signature Disclosure: Accepted: 4/23/2025 2:02:47 PM ID: a84a549b-9910-449a-9d4b-e8acefa203da		
Mintu Turakhia mintu.turakhia@irhythmtech.com CMO Security Level: Email, Account Authentication (None)	 Signature Adoption: Pre-selected Style Using IP Address: 98.97.26.79	Sent: 4/23/2025 1:59:43 PM Resent: 4/29/2025 8:16:21 AM Resent: 4/30/2025 10:21:13 AM Viewed: 4/30/2025 10:57:55 AM Signed: 4/30/2025 10:58:43 AM
Electronic Record and Signature Disclosure: Accepted: 4/30/2025 10:57:55 AM ID: 59f36d50-897f-43c7-ba5f-d0a0e440961b		
TJ Battisti tj.battisti@irhythmtech.com Security Level: Email, Account Authentication (None)	 Signature Adoption: Pre-selected Style Using IP Address: 174.164.57.130	Sent: 4/23/2025 1:59:42 PM Viewed: 4/23/2025 2:10:24 PM Signed: 4/23/2025 2:11:18 PM
Electronic Record and Signature Disclosure: Accepted: 4/23/2025 2:10:24 PM ID: b8bb300d-aac4-4643-9b9f-b612aa94f4ec		
Vladimir Fokin vladimir.fokin@irhythmtech.com Director, Data Management and Biostatistics Security Level: Email, Account Authentication (None)	 Signature Adoption: Pre-selected Style Using IP Address: 172.58.124.244 Signed using mobile	Sent: 4/23/2025 1:59:44 PM Viewed: 4/23/2025 2:00:31 PM Signed: 4/23/2025 2:00:56 PM
Electronic Record and Signature Disclosure: Accepted: 4/23/2025 2:00:31 PM ID: c392d0f4-362e-47a5-836f-96541faa8ba5		

In Person Signer Events	Signature	Timestamp

Editor Delivery Events	Status	Timestamp

Agent Delivery Events	Status	Timestamp

Intermediary Delivery Events	Status	Timestamp

Certified Delivery Events	Status	Timestamp

Carbon Copy Events	Status	Timestamp

Witness Events	Signature	Timestamp

Notary Events	Signature	Timestamp

Envelope Summary Events	Status	Timestamps
Envelope Sent	Hashed/Encrypted	4/23/2025 1:59:45 PM
Certified Delivered	Security Checked	4/23/2025 2:00:31 PM
Signing Complete	Security Checked	4/23/2025 2:00:56 PM
Completed	Security Checked	4/30/2025 10:58:43 AM

Payment Events	Status	Timestamps

Electronic Record and Signature Disclosure

ELECTRONIC RECORD AND SIGNATURE DISCLOSURE

From time to time, iRhythm Technologies, Inc. (we, us or Company) may be required by law to provide to you certain written notices or disclosures. Described below are the terms and conditions for providing to you such notices and disclosures electronically through the DocuSign system. Please read the information below carefully and thoroughly, and if you can access this information electronically to your satisfaction and agree to this Electronic Record and Signature Disclosure (ERSD), please confirm your agreement by selecting the check-box next to 'I agree to use electronic records and signatures' before clicking 'CONTINUE' within the DocuSign system.

Getting paper copies

At any time, you may request from us a paper copy of any record provided or made available electronically to you by us. You will have the ability to download and print documents we send to you through the DocuSign system during and immediately after the signing session and, if you elect to create a DocuSign account, you may access the documents for a limited period of time (usually 30 days) after such documents are first sent to you. After such time, if you wish for us to send you paper copies of any such documents from our office to you, you will be charged a $0.00 per-page fee. You may request delivery of such paper copies from us by following the procedure described below.

Withdrawing your consent

If you decide to receive notices and disclosures from us electronically, you may at any time change your mind and tell us that thereafter you want to receive required notices and disclosures only in paper format. How you must inform us of your decision to receive future notices and disclosure in paper format and withdraw your consent to receive notices and disclosures electronically is described below.

Consequences of changing your mind

If you elect to receive required notices and disclosures only in paper format, it will slow the speed at which we can complete certain steps in transactions with you and delivering services to you because we will need first to send the required notices or disclosures to you in paper format, and then wait until we receive back from you your acknowledgment of your receipt of such paper notices or disclosures. Further, you will no longer be able to use the DocuSign system to receive required notices and consents electronically from us or to sign electronically documents from us.

All notices and disclosures will be sent to you electronically

Unless you tell us otherwise in accordance with the procedures described herein, we will provide electronically to you through the DocuSign system all required notices, disclosures, authorizations, acknowledgements, and other documents that are required to be provided or made available to you during the course of our relationship with you. To reduce the chance of you inadvertently not receiving any notice or disclosure, we prefer to provide all of the required notices and disclosures to you by the same method and to the same address that you have given us. Thus, you can receive all the disclosures and notices electronically or in paper format through the paper mail delivery system. If you do not agree with this process, please let us know as described below. Please also see the paragraph immediately above that describes the consequences of your electing not to receive delivery of the notices and disclosures electronically from us.

How to contact iRhythm Technologies, Inc.:

You may contact us to let us know of your changes as to how we may contact you electronically, to request paper copies of certain information from us, and to withdraw your prior consent to receive notices and disclosures electronically as follows:
To contact us by email send messages to: _hr@irhythmtech.com

To advise iRhythm Technologies, Inc. of your new email address

To let us know of a change in your email address where we should send notices and disclosures electronically to you, you must send an email message to us at _hr@irhythmtech.com and in the body of such request you must state: your previous email address, your new email address. We do not require any other information from you to change your email address.

If you created a DocuSign account, you may update it with your new email address through your account preferences.

To request paper copies from iRhythm Technologies, Inc.

To request delivery from us of paper copies of the notices and disclosures previously provided by us to you electronically, you must send us an email to _hr@irhythmtech.com and in the body of such request you must state your email address, full name, mailing address, and telephone number. We will bill you for any fees at that time, if any.

To withdraw your consent with iRhythm Technologies, Inc.

To inform us that you no longer wish to receive future notices and disclosures in electronic format you may:

i. decline to sign a document from within your signing session, and on the subsequent page, select the check-box indicating you wish to withdraw your consent, or you may;

ii. send us an email to _hr@irhythmtech.com and in the body of such request you must state your email, full name, mailing address, and telephone number. We do not need any other information from you to withdraw consent.. The consequences of your withdrawing consent for online documents will be that transactions may take a longer time to process..

Required hardware and software

The minimum system requirements for using the DocuSign system may change over time. The current system requirements are found here: https://support.docusign.com/guides/signer-guide-signing-system-requirements.

Acknowledging your access and consent to receive and sign documents electronically

To confirm to us that you can access this information electronically, which will be similar to other electronic notices and disclosures that we will provide to you, please confirm that you have read this ERSD, and (i) that you are able to print on paper or electronically save this ERSD for your future reference and access; or (ii) that you are able to email this ERSD to an email address where you will be able to print on paper or save it for your future reference and access. Further, if you consent to receiving notices and disclosures exclusively in electronic format as described herein, then select the check-box next to 'I agree to use electronic records and signatures' before clicking 'CONTINUE' within the DocuSign system.

By selecting the check-box next to 'I agree to use electronic records and signatures', you confirm that:

- You can access and read this Electronic Record and Signature Disclosure; and
- You can print on paper this Electronic Record and Signature Disclosure, or save or send this Electronic Record and Disclosure to a location where you can print it, for future reference and access; and
- Until or unless you notify iRhythm Technologies, Inc. as described above, you consent to receive exclusively through electronic means all notices, disclosures, authorizations, acknowledgements, and other documents that are required to be provided or made available to you by iRhythm Technologies, Inc. during the course of your relationship with iRhythm Technologies, Inc..