DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
19701 Fairchild Irvine, CA 92612-2445 (949)608-2900 Fax:(949)608-4417	7/25/2022-8/12/2022* FEI NUMBER 3021769057

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Mark W. Hughes, Vice President of Manufacturing

FIRM NAME	STREET ADDRESS
iRhythm Technologies, Inc.	6550 Katella Ave
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Cypress, CA 90630-5102	Medical Device Manufacturer

This document lists observations made by the FDA representative(s) during the inspection of your facility. They are inspectional observations, and do not represent a final Agency determination regarding your compliance. If you have an objection regarding an observation, or have implemented, or plan to implement, corrective action in response to an observation, you may discuss the objection or action with the FDA representative(s) during the inspection or submit this information to FDA at the address above. If you have any questions, please contact FDA at the phone number and address above.

The observations noted in this Form FDA-483 are not an exhaustive listing of objectionable conditions. Under the law, your firm is responsible for conducting internal self-audits to identify and correct any and all violations of the quality system requirements.

DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

OBSERVATION 1

Procedures for corrective and preventive action have not been adequately established.

Specifically,

A) Your firm manufactures the Zio AT Cardiac Monitoring System, intended for near real time cardiac event monitoring for high risk patients and "timely detection of clinically actionable arrhythmia during the wear period", with immediate notification to clinicians (MD Notification); however, Complaint COMP-2021-6388, dated 10/25/2021, reports "a patient death occurred while using the Zio AT, and the prescribing account was not notified [immediately] of the event [Ventricular Tachycardia and Ventricular Fibrillation before Pauses and Asystole] which caused the patient's death". In another complaint (COMP-2022-2077, received 04/27/2022), the customer reported a "patient wearing a zio patch (irhythm) AT device and had 32 minutes of sustained ventricular tachycardia with loss of consciousness. Device designed to report daily events remotely and failed to report this life-threatening arrhythmia until 1 week later…".

Your investigation into the reported issue indicated the device had reached its upper limit of notifications that can be transmitted (maximum of (b) (4) asymptomatic transmissions). (b) (4)
(b) (4)

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE		DATE ISSUED
	Alexandria L Capuano, Investigator Janet Pulver, Investigator	X Alexandria L Capuano Investigator Signed By: Alexandria L. Capuano -S Date Signed: 08-12-2022 13:16:01	8/12/2022

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
19701 Fairchild Irvine, CA 92612-2445 (949)608-2900 Fax:(949)608-4417	7/25/2022-8/12/2022* FEI NUMBER 3021769057

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Mark W. Hughes, Vice President of Manufacturing	
FIRM NAME iRhythm Technologies, Inc.	STREET ADDRESS 6550 Katella Ave
CITY, STATE, ZIP CODE, COUNTRY Cypress, CA 90630-5102	TYPE ESTABLISHMENT INSPECTED Medical Device Manufacturer

(b) (4) . Since June 2019, your firm has received 28 complaints reporting patient episodes deemed severe enough to warrant MD Notification that were not reported to the physicians during the wear period due to this maximum threshold for asymptomatic transmissions, for example:

- COMP-2019-2312, dated 12/19/2019 (Atrial Flutter)
- COMP-2020-0443, dated 01/31/2020 (Ventricular Tachycardia)
- COMP-2021-5397, dated 09/07/2021 (Complete Heart Block)
- COMP-2021-5586, dated 09/17/2021 (Pauses)
- COMP-2021-5672, dated 09/21/2021 (Atrial Fibrillation)
- COMP-2021-6385, dated 10/25/2021 (Complete Heart Block and Asystole leading to death)
- COMP-2021-6928, dated 11/18/2021 (Ventricular Tachycardia).

However, your firm has yet to implement corrective actions to address this device limitation that your firm has been aware of since 2019 that can contribute to failure to notify clinicians of severe patient episodes, including life-threatening arrhythmias such as Ventricular Fibrillation. Furthermore, when this (b) (4) max transmission limit is reached, the device does not provide any indication to the patient that the device is not transmitting asymptomatic events; in fact, the labeling provided to patients ("Wearing your Zio" Manual) states that "The gateway wirelessly sends heart rhythm data recorded by your patch to iRhythm. iRhythm analyzes the data and provides a report to your doctor…When they are working normally, the patch and gateway do not flash or make noise."

B) Your SalesForce database includes >(b) (4) "ZTickets" for Zio AT Cardiac Monitoring System (dated August 2017- August 2022) that have been applied to the patients, activated, and transmitted data; however, the data was held in your Zeus system and not reported to the clinicians due to incomplete patient registration. For example, 39 ZTickets reviewed during the

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
19701 Fairchild Irvine, CA 92612-2445 (949)608-2900 Fax:(949)608-4417	7/25/2022-8/12/2022* FEI NUMBER 3021769057

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Mark W. Hughes, Vice President of Manufacturing	
FIRM NAME iRhythm Technologies, Inc.	STREET ADDRESS 6550 Katella Ave
CITY, STATE, ZIP CODE, COUNTRY Cypress, CA 90630-5102	TYPE ESTABLISHMENT INSPECTED Medical Device Manufacturer

inspection include MD Notification Criteria forms showing the clinicians had requested immediate notification of critical and life-threatening arrhythmias (e.g., ZTickets, #(b) (4) (b) (4), and (b) (4), dated (b) (4), and (b) (4), respectively (all still open)), but the patient data was not reported to the physician during wear due to the incomplete registration, and the records do not show follow up on the patient status to determine the impact of any delayed MD Notifications.

Your firm defined the minimum information that must be entered into the system to complete the patient registration to allow transmission of the data to clinicians. However, those registration requirements include fields that are not necessary to allow matching of data to a specific patient and have resulted in delayed reports to the clinicians. For example, ZTickets (b) (4), (b) (4), and (b) (4) contain patient information but the reports to the clinicians were held pending billing or insurance information. (b) (4) ZTickets are still open (as of 08/04/2022), (b) (4) for more than (b) (4) days. And (b) (4) of the closed ZTickets were closed (b) (4) days or more from the date opened.

Your firm has yet to implement corrective actions to address this device limitation that can contribute to failure to notify clinicians of severe patient episodes, including life-threatening arrhythmias such as Ventricular Fibrillation.

C) CAPA # CAPA-2022-0013 was initiated to address an "Activation Time Mismatch" error identified on 04/01/2022 during intake of returned Zio AT Cardiac Monitoring System patch S/N (b) (4), where the activation date/time on the actual patch did not match the date/time of activation that had been transmitted during patient wear by the companion Zio AT Gateway server to your Zio ECG Utilization Service ("ZEUS") System for analysis.

The CAPA form shows that this issue has the potential for adverse effect on product quality and is a risk that is not identified in an existing risk assessment document. The CAPA shows the issue is due to failure to erase previous patient data during your process for re-using the device's

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
19701 Fairchild Irvine, CA 92612-2445 (949)608-2900 Fax:(949)608-4417	7/25/2022-8/12/2022* FEI NUMBER 3021769057

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Mark W. Hughes, Vice President of Manufacturing	
FIRM NAME iRhythm Technologies, Inc.	STREET ADDRESS 6550 Katella Ave
CITY, STATE, ZIP CODE, COUNTRY Cypress, CA 90630-5102	TYPE ESTABLISHMENT INSPECTED Medical Device Manufacturer

printed circuit boards during manufacturing. Reportedly this could result in failure of product in the field to identify patient episodes deemed severe enough to warrant the immediate notification to the clinicians because previous patient data could use up the (b) (4) max transmissions of patient episodes (reference Observation #1A). However, your firm failed to initiate a Health Hazard Evaluation of the health hazard presented to products in the field "when an unanticipated issue arises which affects product in the field", as required per your Health Hazard Evaluation procedure, Document DOP0111, Health Hazard Evaluation, Revision 03.

OBSERVATION 2

An MDR report was not submitted within 30 days of receiving or otherwise becoming aware of information that reasonably suggests that a marketed device may have caused or contributed to a death or serious injury.

Specifically, Complaint # COMP-2021-6388, received 10/25/2021, reports a patient death that occurred while using your Zio AT Cardiac Monitoring System. The Zio AT patch and Gateway "allow timely detection of clinically actionable arrhythmia during the wear period" ("Zeus System Architecture Description", Document DES0024, dated 04/04/2022); however, the complaint states that "the prescribing account was not notified of the event [Ventricular Tachycardia (VT) and Ventricular Fibrillation (VF) before Pauses and Asystole] which caused the patient's death". The MD Notification Criteria Form for this patient shows the physician requested to be notified "Immediately" of these events, but the clinician was not notified until 8 days after these "End of Life" events. Your firm failed to submit a Medical Device Report for this event where your Zio AT was a contributing factor to the patient's death.

OBSERVATION 3

A process whose results cannot be fully verified by subsequent inspection and test has not been validated according to established procedures.

Specifically, your firm implemented design changes to the hardware and firmware of your Zio AT

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
19701 Fairchild Irvine, CA 92612-2445 (949)608-2900 Fax:(949)608-4417	7/25/2022-8/12/2022* FEI NUMBER 3021769057

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED	
Mark W. Hughes, Vice President of Manufacturing	
FIRM NAME iRhythm Technologies, Inc.	STREET ADDRESS 6550 Katella Ave
CITY, STATE, ZIP CODE, COUNTRY Cypress, CA 90630-5102	TYPE ESTABLISHMENT INSPECTED Medical Device Manufacturer

Cardiac Monitoring System (Project Plan: (b) (4), (b) (4), 11/23/2021) and to the Gateway tool and test fixture used in the manufacture of the Zio AT (Project Plans (b) (4) and (b) (4)). Your firm executed the Zio AT Spritz Performance Qualification (PQ) Protocol (b) (4) (dated 10/29/2021) to demonstrate that the ZIO AT manufacturing process using the updated device, tool, and fixture, performs consistently in accordance with its required specifications. However, review of the PQ Report (b) (4)) shows that the validation failed to assess the re-use of Gateway printed circuit board assemblies (PCBAs) returned from patients, to ensure that data from the previous patient was erased before using the PCBAs to manufacture new devices. No re-used boards were used in the validation; only "virgin" boards were used. Furthermore, the PQ was executed following the routine manufacturing procedure ((b) (4) Zio AT Gateway PCBA Initialize and Test); however, this procedure does not include a step to ensure that data from re-used Gateway boards is erased.

OBSERVATION 4

Procedures for receiving, reviewing, and evaluating complaints by a formally designated unit have not been adequately established.

Specifically, review of your SalesForce Customer Relationship Management system revealed records ("ZTickets") dated January 2020 - July 2022 documenting alleged deficiencies in reliability or performance of your Zio AT Cardiac Monitoring System that your firm failed to categorize as complaints. For example, the following deficiencies that can result in delayed transmission to clinicians of critical or life-threatening arrhythmias were not categorized as complaints:

- (b) (4)ZTickets reporting electrode leads status as "patch is in leads off condition" indicating no connectivity of the leads with the body (e.g., ZTickets numbers: (b) (4), and (b) (4), dated 09/08/2020, 02/01/2021, and 05/07/2021)

- (b) (4) automated z-tickets for Gateway Function errors documenting that the Gateway has gone 4 or 24 consecutive hours without communicating with the Zues Servers and unable to transmit data (e.g., ZTickets numbers: (b) (4), and (b) (4) dated 10/28/2021,

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
19701 Fairchild Irvine, CA 92612-2445 (949)608-2900 Fax:(949)608-4417	7/25/2022-8/12/2022*
	FEI NUMBER 3021769057

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

Mark W. Hughes, Vice President of Manufacturing

FIRM NAME	STREET ADDRESS
iRhythm Technologies, Inc.	6550 Katella Ave
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Cypress, CA 90630-5102	Medical Device Manufacturer

01/12/2022, and 01/18/2022, respectively)

***DATES OF INSPECTION**

7/25/2022(Mon), 7/26/2022(Tue), 7/27/2022(Wed), 7/28/2022(Thu), 7/29/2022(Fri), 8/01/2022(Mon), 8/02/2022(Tue), 8/03/2022(Wed), 8/04/2022(Thu), 8/05/2022(Fri), 8/11/2022(Thu), 8/12/2022(Fri)

X Janet Pulver
Investigator
Signed By: 2000354195
Date Signed: 08-12-2022 13:16:48

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Alexandria L Capuano, Investigator Janet Pulver, Investigator X Alexandria L Capuano Investigator Signed By: Alexandria L. Capuano -9 Date Signed: 08-12-2022 13:16:01	8/12/2022

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
19701 Fairchild Irvine, CA 92612-2445 (949)608-2900 Fax:(949)608-4417	7/25/2022-8/12/2022* FEI NUMBER 3021769057

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Mark W. Hughes, Vice President of Manufacturing

FIRM NAME	STREET ADDRESS
iRhythm Technologies, Inc.	6550 Katella Ave
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Cypress, CA 90630-5102	Medical Device Manufacturer

Annotations to Observations

Observation 1: Promised to correct

Observation 2: Promised to correct

Observation 3: Promised to correct

Observation 4: Promised to correct

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Alexandria L Capuano, Investigator Janet Pulver, Investigator X Alexandria L Capuano Investigator Signed By: Alexandria L. Capuano -S Date Signed: 08-12-2022 13:16:01	8/12/2022

The observations of objectionable conditions and practices listed on the front of this form are reported:

1. Pursuant to Section 704(b) of the Federal Food, Drug and Cosmetic Act, or
2. To assist firms inspected in complying with the Acts and regulations enforced by the Food and Drug Administration.

Section 704(b) of the Federal Food, Drug, and Cosmetic Act (21 USC 374(b)) provides:

"Upon completion of any such inspection of a factory, warehouse, consulting laboratory, or other establishment, and prior to leaving the premises, the officer or employee making the inspection shall give to the owner, operator, or agent in charge a report in writing setting forth any conditions or practices observed by him which, in his judgment, indicate that any food, drug, device, or cosmetic in such establishment (1) consists in whole or in part of any filthy, putrid, or decomposed substance, or (2) has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health. A copy of such report shall be sent promptly to the Secretary."