Rare FDA Move Shows Stance On Remote Monitoring Devices

By **Dominick DiSabatino, Julian Klein and Audrey Crowell** (June 23, 2023)

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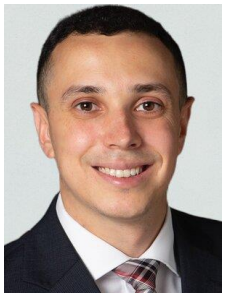

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On May 25, the U.S. Food and Drug Administration issued a warning letter to iRhythm Technologies Inc., citing a deluge of violations related to the company's heart-monitoring device — the Zio AT System.

This warning letter is one of only a handful ever issued for a remote monitoring device product.[1] In the letter, the FDA sends a clear message that it is watching companies that promote remote monitoring devices, which have become very popular in the consumer retail space, specifically those that purport to provide monitoring capabilities beyond the scope of their approved or cleared indications.

Regulatory Landscape

Devices, Generally

The FDA regulates products that fall within the broad definition of "device" under the Federal Food, Drug and Cosmetic Act.[2]

Under the FDCA, medical devices are classified into one of three categories: Class I, Class II or Class III, depending on the degree of risk associated with the intended use of the device and, in turn, the extent of manufacturer and regulatory control needed to ensure safety and effectiveness.

All device classes are subject to the FDA's general controls, which include (1) good manufacturing practice, as implemented by the Quality System Regulations, or QSR, (2) facility registration and product listing, (3) reporting of adverse medical events, as implemented by the Medical Device Reporting regulations, and (4) prohibitions on misbranding and adulteration through labeling that is "false or misleading in any particular," as well as promotion for uses that have not been cleared or approved.[3]

In addition to these general controls, Class II and III devices are subject to special controls, which are detailed in the regulations and deemed necessary by the FDA to ensure the safety and effectiveness of the device based on its intended use.

The FDA also regulates device components, which are defined as "any raw material, substance, piece, part, software, firmware, labeling, or assembly which is intended to be included as part of the finished, packaged, and labeled device."[4]

Unless an exemption applies, each medical device commercially distributed in the U.S. requires either FDA clearance of a Section 510(k) premarket notification submission or approval of a premarket application.

In this instance, iRhythm was permitted to commercially distribute the Zio AT System

pursuant to a Section 510(k) premarket notification clearance as a Class II device, subject to the FDA's general controls, as well as special controls outlined at Title 21 of the Code of Federal Regulations, Section 870.1425.

Relevant to iRhythm's situation is the important fact that, once a Section 510(k) premarket notification has been cleared by the FDA, the manufacturer is bound to the terms and content of the Section 510(k) clearance for that product — for example, a manufacturer could not redefine the intended patient population without submitting a new 510(k) notification.

Remote Monitoring Devices, Specifically

Over the past five years, the U.S. market has seen a boom in devices that purport to monitor almost any physical marker imaginable, from heart rate, to insulin level, to nightly sleep cycles.[5]

The FDA has moved quickly to keep up with the rapid growth in digital health technology by issuing various guidance documents that classify digital health products according to the FDA's perceived risk profile based on the intended use — all the while aiming to strike the elusive balance between encouraging innovation and ensuring patient safety.

The FDA has categorized digital health tools into a handful of categories that vary based on intended use and functionality, including medical device data systems, software as a medical device, software in a medical device, mobile medical apps and nondevice medical device data systems, each of which is furthered classified into Class I, II or III devices.[6]

However, due to the sheer volume of remote monitoring devices on the market, the FDA has had to determine which remote monitoring device functions pose the greatest risk to public health and, thus, warrant the FDA's enforcement attention.

Ultimately, the FDA has drawn a distinction between remote monitoring functions that are intended for active patient monitoring and remote monitoring device functions intended for supplemental monitoring.[7]

The former category, which the FDA intends to regulate, consists of remote monitoring devices "used for active patient monitoring to enable immediate awareness for potential clinical intervention."[8]

By contrast, the latter category, which the FDA does not intend to regulate, consists of "software functions that supplement professional clinical care by facilitating behavioral change or coaching patients with specific diseases or identifiable health conditions in their daily environment."[9]

Thus, the FDA is most concerned with remote monitoring device functions that invite consumers to rely on their monitoring capabilities for consistent and/or immediate use and, as indicated by the iRhythm warning letter, this is especially the case when the device is not cleared for consistent or immediate use in the first place.

Recent Enforcement Action Against iRhythm

FDA regulates the Zio AT System as a Class II device and regulates the ZEUS software system, which captures, analyzes and reports arrhythmias, is regulated as a component of the device system, subject to the same general and special controls.

In its lengthy warning letter, the FDA noted a host of violations related to the Zio AT System, but began with its primary concern — iRhythm's promotion of monitoring capabilities exceeding the scope of the device's cleared indication.

Promotional Violations

Pursuant to the Zio AT System 510(k) premarket notification, the FDA had cleared the product for capturing, analyzing and reporting symptomatic and asymptomatic cardiac events and continuous electrocardiogram information for long-term monitoring.[10]

The Section 510(k) premarket notification indicates the product for use on adult patients who may be asymptomatic or who may suffer transient cardiac symptoms, but not for use on critical care patients.

However, iRhythm's marketing materials state that the Zio AT System is intended for near real-time monitoring as a mobile cardiac telemetry monitor that can provide notifications immediately to high-risk patients.

The FDA showed particular concern over these claims, likely because the FDA has clearly communicated that describing a patient population beyond that contemplated by the device's Section 510(k) clearance — i.e., "high-risk patients" instead of "adult patients who may be asymptomatic or who may suffer transient cardiac symptoms — requires a new Section 510(k) clearance since it could significantly affect the safety and effectiveness of the device.[11]

Furthermore, describing the product as a "near real-time monitoring" device for high-risk patients fits squarely within the FDA's enforcement focus regarding active patient monitoring devices that invite consumers to rely on their monitoring capabilities to determine the need for immediate clinical intervention and, due to the potentially fatal consequences of a system malfunction, require a higher degree of oversight to ensure consistent functionality.

Here, the high-risk patient group — who are more likely to suffer life-threatening arrhythmias and require real-time monitoring — were not approved as a patient population under the Zio AT System Section 510(k) clearance but, based on the real-time monitoring claim, would be likely to improperly rely on the product to provide an immediate alert when life-saving clinical intervention may be necessary, which is not a monitoring function that the device offers.

Unapproved Software Changes

In addition to the promotional materials, iRhythm made changes to the device without submitting a new Section 510(k). The changes included software and hardware updates, including changes to the device algorithm that were intended to improve the detection of cardiac events, all of which should have undergone testing to ensure safety and efficacy, as required for a new Section 510(k) submission.

Because these new device changes were promoted for consumer use without undergoing the requisite safety and efficacy testing, the FDA determined that the device was adulterated and misbranded under the FDCA.

Labeling Changes

The FDA also found the Zio AT system to be misbranded under FDCA because its instructions for use failed to disclose a crucial transmission limit — the device is only able to transmit a certain number of detected arrhythmias before the patient's data stops being transmitted for reporting, at which point the device stops functioning for its intended purpose.

As explained by the FDA, this information is absolutely necessary to enable patients and physicians to understand when the device can and cannot be relied on, i.e., before and after threshold number of transmissions, and, accordingly, is critical for safe and effective use of the product.

QSR Violations

The FDA found that iRhythm failed to adequately establish and maintain procedures for implementing corrective and preventive action to address known, recurring quality issues, in violation of the QSR with which all devices must comply.[12]

Failure to Report

The FDA determined that iRhythm violated its Medical Device Reporting obligations by failing to timely report information, of which iRhythm was aware, that reasonably suggested that the Zio AT System may have caused or contributed to a death or serious injury.

Industry Takeaways

The FDA's stern and extensive warning letter represents a relatively unprecedented degree of scrutiny to the industry, which should put all remote monitoring device manufacturers on notice to exercise caution with promotional claims, especially those representing that the monitoring function of a device is more active than the monitoring function for which it was cleared or approved.

In iRhythm's case, the Zio AT System was cleared to monitor long-term cardiac activity in patients who are either asymptomatic or who experience transient cardiac episodes.

Accordingly, the FDA expressed serious concern over the fact that, by claiming that the Zio AT System is capable of real-time monitoring, iRhythm invited high-risk patients to improperly use the device for the purpose of determining when immediate clinical intervention is necessary, a function that is far beyond the scope of the device's precleared intended use for long-term monitoring.

In this context, the real-time monitoring claim would require, at the least, the submission of a new Section 510(k) premarket notification, possibly including additional trial or human factor experience, to ensure the efficacy of the real-time monitoring capability.

The FDA's objection to the algorithm changes that iRhythm implemented should also signal to device manufacturers that small, seemingly minor software changes, which may be intended to improve the functionality of the device, should typically not be incorporated without a new Section 510(k) clearance.

This is because most software changes result in new or different functionalities that should not be presented to consumers without undergoing the safety and efficacy testing required as part of a Section 510(k) submission.

Over the past few years, it has appeared that the FDA's actual enforcement of its digital health device policies has failed to keep up with the growth in remote monitoring devices; however, the agency sent a message with the iRhythm warning letter.

Through this letter, the FDA communicated its intent to closely regulate pre- and post-market activities of remote monitoring devices — including, but not limited to, promotion, design, labeling, manufacturing and reporting — to ensure that manufacturers do not unilaterally expand the monitoring capabilities of their products without adhering to the safeguards that the FDA has carefully designed to ensure the safety of ultimate consumers.

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[1] Previous warning letters issued for remote monitoring device products include: Warning Letter 617539, FDA (Dec. 9, 2021) - https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/warning-letters/medtronic-inc-617539-12092021 - and Warning Letter 616354, FDA (Oct. 5, 2021) - https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/warning-letters/owlet-baby-care-inc-616354-10052021.

[2] The FDCA defines "device" as "…an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory", that is "… intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man …" or "… intended to affect the structure or any function of the body of man or other animals…." 21 USC 321(h)(1).

[3] See General Controls for Medical Devices, FDA (current as of March 22, 2018). https://www.fda.gov/medical-devices/regulatory-controls/general-controls-medical-devices.

[4] 21 CFR 820.3(c).

[5] See Remote Patient Monitoring System Market Size, Share & Trends Analysis Report, Grand View Research (2022). https://www.grandviewresearch.com/industry-analysis/remote-patient-monitoring-devices-market.

[6] See Guidance - Medical Device Data Systems, Medical Image Storage Devices, and Medical Image Communications Devices, FDA (Sept. 28, 2022) - https://www.fda.gov/media/88572/download; Guidance - Policy for Device Software Functions and Mobile Medical Applications (Sept. 28, 2022) - https://www.fda.gov/media/80958/download.

[7] See id.

[8] See 76 Fed. Reg. 8644.

[9] See Guidance - Policy for Device Software Functions and Mobile Medical Applications, supra FN 6, at p. 14.

[10] See Zio AT System 510(k) Premarket Notification, FDA (July 19, 2019). https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm?ID=K190593.

[11] See Warning Letter 643474, FDA (May 25, 2023). https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/warning-letters/irhythm-technologies-inc-643474-05252023.

[12] See 21 CFR Part 820.