October 22, 2021

Apple Inc.
Luke Olson
Regulatory Affairs Associate
1 Apple Park Way
Cupertino, California 95014

Re: K212516
Trade/Device Name: Irregular Ryhthm Notification Feature (IRNF) 2.0 App
Regulation Number: 21 CFR 870.2790
Regulation Name: Photoplethysmograph analysis software for over-the-counter use
Regulatory Class: Class II
Product Code: QDB
Dated: August 9, 2021
Received: August 10, 2021

Dear Luke Olson:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's

requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Jennifer Shih Kozen
Assistant Director
Division of Cardiac Electrophysiology,
Diagnostics and Monitoring Devices
Office of Cardiovascular Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K212516

Device Name
Irregular Rhythm Notification Feature 2.0

Indications for Use *(Describe)*
The Irregular Rhythm Notification Feature is a software-only mobile medical application that is intended to be used with the Apple Watch. The feature analyzes pulse rate data to identify episodes of irregular heart rhythms suggestive of atrial fibrillation (AFib) and provides a notification to the user. The feature is intended for over-the-counter (OTC) use. It is not intended to provide a notification on every episode of irregular rhythm suggestive of AFib and the absence of a notification is not intended to indicate no disease process is present; rather the feature is intended to opportunistically surface a notification of possible AFib when sufficient data are available for analysis. These data are only captured when the user is still. Along with the user's risk factors the feature can be used to supplement the decision for AFib screening. The feature is not intended to replace traditional methods of diagnosis or treatment.

The feature has not been tested for and is not intended for use in people under 22 years of age. It is also not intended for use in individuals previously diagnosed with AFib.

Type of Use *(Select one or both, as applicable)*

☐ Prescription Use (Part 21 CFR 801 Subpart D) ☒ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

510(k) Summary

This summary of 510(k) safety and effectiveness information is submitted in accordance with the requirements of 21 CFR §807.92:

5.1 Submitter

Applicant	Apple Inc. One Apple Park Way Cupertino, CA 95014
Primary Correspondent	Luke Olson Regulatory Affairs Phone: (408) 609-2001 Email: luke_olson@apple.com
Secondary Correspondent	Dachan Kwon Regulatory Affairs Phone: (669) 268-5659 Email: dachan_kwon@apple.com
Date Prepared	August 09, 2021

5.2 Device Names and Classifications

Subject Device:

Name of Device	Irregular Rhythm Notification Feature 2.0
Classification Name	Photoplethysmograph Analysis Software For Over-The-Counter Use, 21 CFR 870.2790
Regulatory Class	Class II
Product Code	QDB
510(k) Review Pannel	Cardiovascular

Predicate Device:

Predicate Manufacturer	Apple Inc.
Predicate Trade Name	Irregular Rhythm Notification Feature
Predicate 510(k)	DEN180042

5.3 Device Description

Irregular Rhythm Notification Feature 2.0 (IRNF 2.0) is comprised of a pair of mobile medical apps - One on Apple Watch and the other on the iPhone.

IRNF 2.0 is intended to analyze pulse rate data collected by the Apple Watch PPG sensor on Apple Watch Series 3, Series 4, Series 5, and SE to identify episodes of irregular heart rhythms consistent with AFib and provide a notification to the user. It is a background screening tool and there is no way for a user to initiate analysis of pulse rate data. IRNF 2.0 iPhone App is part of the Health App, which allows users to store, manage, and share health and fitness data, and comes pre-installed on every iPhone.

IRNF 2.0 Watch App refers to the rhythm classification algorithm, confirmation cycle algorithm, and the AFib notification generation. If an irregular heart rhythm consistent with Afib is identified and confirmed through the confirmation cycle, IRNF 2.0 Watch app will notify the user and transfer the AFib notification to the iPhone App through HealthKit sync. In addition to indicating the finding of signs of AFib, the notification will encourage the user to seek medical care.

IRNF 2.0 iPhone App contains the onboarding and educational materials that a user must review prior to use. IRNF 2.0 iPhone App is designed to work in combination with IRNF 2.0 Watch App and will display a history of all prior AFib notifications. The user is also able to view a list of times of the irregular rhythms contributing to the notification.

5.4 Indications for Use

The Irregular Rhythm Notification Feature is a software-only mobile medical application that is intended to be used with the Apple Watch. The feature analyzes pulse rate data to identify episodes of irregular heart rhythms suggestive of atrial fibrillation (AFib) and provides a notification to the user. The feature is intended for over-the-counter (OTC) use. It is not intended to provide a notification on every episode of irregular rhythm suggestive of AFib and the absence of a notification is not intended to indicate no disease process is present; rather the feature is intended to opportunistically surface a notification of possible AFib when sufficient data are available for analysis. These data are only captured when the user is still. Along with the user's risk factors the feature can be used to supplement the decision for AFib screening. The feature is not intended to replace traditional methods of diagnosis or treatment.

The feature has not been tested for and is not intended for use in people under 22 years of age. It is also not intended for use in individuals previously diagnosed with AFib.

5.5 Comparison with the Predicate Device

Table 1. IRNF 2.0 Comparison with the Predicate

Item	Subject Device	Predicate Device
	IRNF 2.0 App (K212516)	IRNF App (DEN180042)
Manufacturer	Apple Inc.	Apple Inc.
Submission Reference	K212516	DEN180042
Intended Use	Photoplethysmograph analysis software for over-the-counter use. A photoplethysmograph analysis software device for over-the-counter use analyzes photoplethysmograph data and provides information for identifying irregular heart rhythms. This device is not intended to provide a diagnosis.	Photoplethysmograph analysis software for over-the-counter use. A photoplethysmograph analysis software device for over-the-counter use analyzes photoplethysmograph data and provides information for identifying irregular heart rhythms. This device is not intended to provide a diagnosis.

Item	Subject Device IRNF 2.0 App (K212516)	Predicate Device IRNF App (DEN180042)
Indications for Use	The Irregular Rhythm Notification Feature is a software-only mobile medical application that is intended to be used with the Apple Watch. The feature analyzes pulse rate data to identify episodes of irregular heart rhythms suggestive of atrial fibrillation (AFib) and provides a notification to the user. The feature is intended for over-the-counter (OTC) use. It is not intended to provide a notification on every episode of irregular rhythm suggestive of AFib and the absence of a notification is not intended to indicate no disease process is present; rather the feature is intended to opportunistically surface a notification of possible AFib when sufficient data are available for analysis. These data are only captured when the user is still. Along with the user's risk factors the feature can be used to supplement the decision for AFib screening. The feature is not intended to replace traditional methods of diagnosis or treatment. The feature has not been tested for and is not intended for use in people under 22 years of age. It is also not intended for use in individuals previously diagnosed with AFib	The Irregular Rhythm Notification Feature is a software-only mobile medical application that is intended to be used with the Apple Watch. The feature analyzes pulse rate data to identify episodes of irregular heart rhythms suggestive of atrial fibrillation (AFib) and provides a notification to the user. The feature is intended for over-the-counter (OTC) use. It is not intended to provide a notification on every episode of irregular rhythm suggestive of AFib and the absence of a notification is not intended to indicate no disease process is present; rather the feature is intended to opportunistically surface a notification of possible AFib when sufficient data are available for analysis. These data are only captured when the user is still. Along with the user's risk factors the feature can be used to supplement the decision for AFib screening. The feature is not intended to replace traditional methods of diagnosis or treatment. The feature has not been tested for and is not intended for use in people under 22 years of age. It is also not intended for use in individuals previously diagnosed with AFib
Principle of Operation	The IRN 2.0 acquires platform sensor data from Apple Watch. After acquisition, the IRN 2.0 algorithms analyze pulse rate data to identify episodes of irregular heart rhythms suggestive of atrial fibrillation (AFib) and provides notification to the user.	The IRN app acquires platform sensor data from Apple Watch. After acquisition, the IRN app algorithms analyze pulse rate data to identify episodes of irregular heart rhythms suggestive of atrial fibrillation (AFib) and provides notification to the user.

Item	Subject Device	Predicate Device
	IRNF 2.0 App (K212516)	IRNF App (DEN180042)
Clinical Performance	Apple conducted a clinical validation study to assess the performance of the subject IRNF 2.0 app relative to that of the predicate device on a common sensor dataset. IRNF 2.0 person-level sensitivity (88.6%) and specificity (99.3%) were both demonstrated to be non-inferior to those of the predicate device.	In a study of 226 participants aged 22 years or older wearing Apple Watch and an electrocardiogram (ECG) patch concurrently, 57 participants received AFib notifications. Of those, 78.9% (45/57) showed concordant AFib on the ECG patch, while 98.2 % (56/57) showed AFib and other clinically relevant arrhythmias.
Compatibility with Intended Platforms	iOS version 15.5 or later watchOS version 8.5 or later Apple Watch Series 3, 4, 5, SE iPhone 6s and later	iOS 12.1.1 and later watchOS 5.1.2 and later Apple Watch Series 1 and later iPhone 5s and later

5.6 Performance Testing

IRNF 2.0 was verified and validated according to Apple's internal design control processes and in accordance with the special controls for Photoplethysmograph Analysis software for over-the-counter use (21 CFR 870.2790). The testing demonstrated that the device performed according to its specifications and that the technological and performance criteria are comparable to the predicate device.

IRNF 2.0 includes a new rhythm classification algorithm that leverages machine learning techniques to differentiate between AFib and non-AFib rhythms. The new rhythm classification algorithm uses a convolutional neural network based architecture and was trained extensively using data collected in a number of development studies. In total, the studies included over 2500 subjects and collected over 3 million pulse rate recordings on a variety of rhythms including: atrial fibrillation, normal sinus rhythm, sinus arrhythmia, and other ectopic beats (PVCs, PACs).

The studies used to train the convolutional neural network recruited demographically diverse populations with broad representation of age, sex, BMI, race, and skin tones. Table 2 below summarizes approximate development study demographic characteristics:

Table 2. Development Study Subject Demographics

Age Group (years)	
<55	39.5%
>=55 to <65	25.4%
>=65	35.1%
Sex	
Male	49.6%
Female	50.4%
BMI (kg/m2)	
<18.5	2.2%
>=18.5 to <25.0	32.7%
>=25.0 to <30.0	32.2%
>=30.0	32.9%
Race	
White	71.5%
Black or African American	18.0%
Other	10.5%

For the purpose of developing the algorithm, the data was split into four sets with matching distributions of rhythms and demographics: Training, Validation, Testing, and Sequestration sets. The model was trained on the Training set, with the Validation set used for early stopping and threshold selection. The model was then evaluated on the Testing set at regular intervals during model development. When development was complete the model was locked, and then evaluated on the Sequestration set as a last test to ensure it had not been over-fit to the development data.

5.7 Clinical Performance

The performance of the Irregular Rhythm Notification Feature (IRNF) was extensively tested in a clinical study of 573 participants ages 22 and older with a mix of diagnosed AFib and no known history of AFib. Study demographic characteristics are summarized in Table 3 below:

Table 3. IRNF 2.0 Clinical Study Subject Demographics

	N=573
Age Group (years)	
<55	123 (21.5%)
>=55 to <65	140 (24.4%)
>=65	310 (54.1%)
Sex	
Male	286 (49.9%)
Female	287 (50.1%)
Ethnicity	
Hispanic or Latino	38 (6.6%)
Non-Hispanic or Latino	535 (93.4%)
Race	
White	502 (87.6%)
Black or African American	57 (9.9%)
Other	14 (2.4%)

Enrolled subjects wore an Apple Watch and a reference electrocardiogram (ECG) patch concurrently for up to 13 days. For those subjects contributing data to the primary endpoint analysis, 32.4% (n=140/432) presented with AFib as identified on the reference ECG patch and were included in determining the device sensitivity. Of those, 124 received an IRNF irregular rhythm notification with concordant AFib on the ECG patch, and the sensitivity was 88.6%. Of the 292 subjects who did not present with AFib on the ECG patch and contributed data to the analysis of device specificity, 290 did not receive a notification. The AF detection specificity was 99.3%. The remaining subjects (n=141/573) either contributed data to only secondary endpoint analyses and/or did not complete the study. These results support the device's effectiveness in detecting AFib.

5.8 Human Factors Testing

Compared to the predicate device, there is no change to the indications for use, intended user populations, intended part of body applied to, use environment, operating principle, user interactions, use related hazards, use scenarios and critical tasks for IRNF 2.0. As such, Apple leveraged the Usability Engineering Report generated during development of the predicate device.

5.9 Conclusion

IRNF 2.0 is substantially equivalent to IRNF as they are identical with respect to intended use and there are no differences in technological or performance characteristics that raise new questions of safety and effectiveness.