June 3, 2022

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

Re: K213971
Trade/Device Name: Atrial Fibrillation History Feature
Regulation Number: 21 CFR 870.2790
Regulation Name: Photoplethysmograph analysis software for over-the-counter use
Regulatory Class: Class II
Product Code: QDB
Dated: May 2, 2022
Received: May 3, 2022

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)*
K213971

Device Name
Atrial Fibrillation History Feature

Indications for Use *(Describe)*
The Atrial Fibrillation (AFib) History Feature is an over-the-counter ("OTC") software-only mobile medical application intended for users 22 years of age and over who have a diagnosis of atrial fibrillation (AFib). The feature opportunistically analyzes pulse rate data to identify episodes of irregular heart rhythms suggestive of AFib and provides the user with a retrospective estimate of AFib burden (a measure of the amount of time spent in AFib during past Apple Watch wear).

The feature also tracks and trends estimated AFib burden over time, and includes lifestyle data visualizations to enable users to understand the impact of certain aspects of their lifestyle on their AFib. It is not intended to provide individual irregular rhythm notifications or to replace traditional methods of diagnosis, treatment, or monitoring of AFib.

The feature is intended for use with the Apple Watch and the Health app on iPhone.

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.

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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	May 28, 2022

5.2 Device Names and Classifications

Subject Device:

Name of Device	Atrial Fibrillation History Feature
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)	K212516

5.3 Device Description

The Atrial Fibrillation History Feature (AFib History Feature) is comprised of a pair of mobile medical apps - one on Apple Watch and the other on the iPhone.

The AFib History Feature is intended to analyze pulse rate data collected by the Apple Watch PPG sensor on Apple Watch Series 4, Series 5, and SE to identify episodes of irregular heart rhythms consistent with AFib and provides the user with a retrospective estimate of AFib burden (a measure of the amount of time spent in AFib during past Apple Watch wear).

The AFib History Feature uses PPG pulse rhythm data from compatible Apple Watches. Apple Watch uses green LED lights paired with light-sensitive photodiodes to detect relative changes in the amount of blood flowing through a user's wrist at any given moment. When the heart beats it sends a pressure wave down the vasculature, causing a momentary increase in blood volume when it passes by the sensor. By monitoring these changes in blood flow, the sensor detects individual pulses when they reach the periphery and thereby measure beat-to-beat intervals.

The AFib History Feature 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.

The AFib History Feature provides users visualizations of AFib burden estimate data alongside clinically relevant lifestyle data and presents estimates of AFib burden in three different ways. These visualizations empower users to observe and understand the impact of lifestyle on their AFib burden, and to better understand their condition generally.

- Weekly Estimate - an estimate of the amount of time a user was in Atrial Fibrillation over the past calendar week during watch wear, presented to the user as a percentage.
- Day of Week Estimate - an estimate of the amount of time a user was in Atrial Fibrillation on each day of the week over the previous 42 days during watch wear, presented to the user as a percentage. That is, all Mondays over the past 42 days, all Tuesdays over the past 42 days.
- Time of Day Estimate - an estimate of the amount of time a user was in Atrial Fibrillation on 4-hour segments of the day over the previous 42 days during watch wear, presented to the user as a percentage. That is, all 12 am - 4 am segments over the past 42 days, all 4 am - 8 am segments over the past 42 days.

The AFib History Feature is intended to serve as an extension of the predicate Irregular Rhythm Notification feature, but has been optimized for users with a diagnosis of Afib.

5.4 Indications for Use

The Atrial Fibrillation (AFib) History Feature is an over-the-counter ("OTC") software-only mobile medical application intended for users 22 years of age and over who have a diagnosis of atrial fibrillation (AFib). The feature opportunistically analyzes pulse rate data to identify episodes of irregular heart rhythms suggestive of AFib and provides the user with a retrospective estimate of AFib burden (a measure of the amount of time spent in AFib during past Apple Watch wear).

The feature also tracks and trends estimated AFib burden over time, and includes lifestyle data visualizations to enable users to understand the impact of certain aspects of their lifestyle on their AFib. It is not intended to provide individual irregular rhythm notifications or to replace traditional methods of diagnosis, treatment, or monitoring of AFib.

The feature is intended for use with the Apple Watch and the Health app on iPhone.

5.5 Comparison with the Predicate Device

Table 1. AFib History Feature Comparison with the Predicate

Item	Subject Device	Predicate Device
	AFib History Feature	IRNF 2.0 App
Manufacturer	Apple Inc.	Apple Inc.
Submission Reference	K213971	K212516
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	Predicate Device
	AFib History Feature	IRNF 2.0 App
Indications for Use	The Atrial Fibrillation (AFib) History Feature is an over-the-counter ("OTC") software-only mobile medical application intended for users 22 years of age and over who have a diagnosis of atrial fibrillation (AFib). The feature opportunistically analyzes pulse rate data to identify episodes of irregular heart rhythms suggestive of AFib and provides the user with a retrospective estimate of AFib burden (a measure of the amount of time spent in AFib during past Apple Watch wear). The feature also tracks and trends estimated AFib burden over time, and includes lifestyle data visualizations to enable users to understand the impact of certain aspects of their lifestyle on their AFib. It is not intended to provide individual irregular rhythm notifications or to replace traditional methods of diagnosis, treatment, or monitoring of AFib. The feature is intended for use with the Apple Watch and the Health app on iPhone.	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 AFib History Feature acquires platform sensor data from Apple Watch. After acquisition, the Afib History Feature algorithms analyze pulse rate data to identify episodes of irregular heart rhythms suggestive of atrial fibrillation (AFib) and aggregates those episodes to provide the user with an estimate of atrial fibrillation burden during watch wear.	The IRN 2.0 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
	AFib History Feature	IRNF 2.0 App
Clinical Performance	See below for a discussion of clinical performance testing supporting the AFib History Feature.	Apple conducted a clinical validation study to assess the performance of IRNF 2.0 app relative to that of the IRNF 1.0 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 IRNF 1.0.
Compatibility with Intended Platforms	iOS version 16.0 or later watchOS version 9.0 or later Apple Watch Series 4, 5, SE iPhone 6s and later	iOS version 15.5 or later watchOS version 8.5 or later Apple Watch Series 3, 4, 5, SE iPhone 6s and later

5.6 Performance Testing

The AFib History Feature 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.

The AFib History Feature includes a rhythm classification algorithm that leverages machine learning techniques to differentiate between AFib and non-AFib rhythms. The classifier algorithm is the same that is used in the predicate device, but has been optimized for use in the AFib History Feature's indicated use population, where there is an a priori expectation of AFib.

The 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, Test, 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.

The classifier algorithm's performance on the development studies dataset when used in both the AFib History Feature & the Irregular Rhythm Notification Feature is characterized by the receiver operating characteristic (ROC) curve & table 3 below.

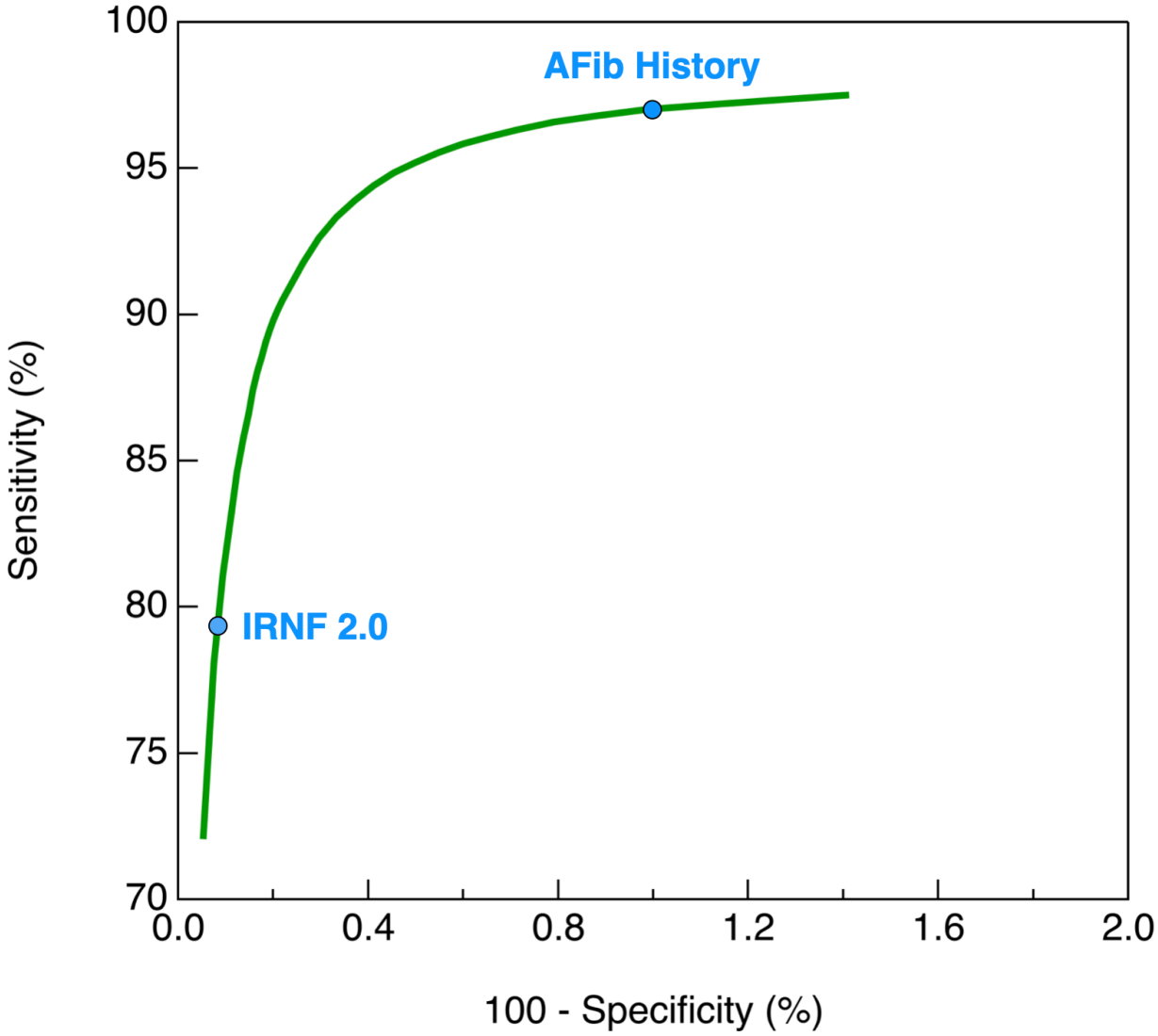

Table 3. Rhythm Classification Algorithm - Development Studies Performance

	Sensitivity	Specificity
AFib History Feature	97%	99.0%
IRNF 2.0 (predicate)	79.6%	99.9%

5.7 Clinical Performance

The performance of the AFib History Feature was extensively tested in a clinical study of 413 participants ages 22 and older with a mix of AFib diagnoses (paroxysmal & permanent). Enrolled subjects wore an Apple Watch and a reference electrocardiogram (ECG) patch concurrently for up to 13 days. Study demographic characteristics are summarized in the table below:

Table 3. IRNF 2.0 Clinical Study Subject Demographics

	N=413
Age Group (years)	
<55	59 (14.3%)
>=55 to <65	99 (24.0%)
>=65	255 (61.7%)
Sex	
Male	219 (53.0%)
Female	194 (47.0%)
Ethnicity	
Hispanic or Latino	19 (4.6%)
Non-Hispanic or Latino	394 (95.4%)
Race	
White	371 (89.8%)
Black or African American	31 (7.5%)
Other	11 (2.7%)

The objective of the study was to assess the accuracy of the weekly AFib burden estimate generated by the feature compared to a weekly AFib burden reference measurement. To do so, Apple employed a Bland-Altman Limits of Agreement (LoA) approach. A LoA approach is a way of assessing agreement accuracy between two measurement methods.

The objective of the study was to assess the accuracy of the weekly AFib burden estimate generated by the feature compared to a weekly AFib burden reference measurement. To do so, Apple employed a Bland-Altman Limits of Agreement (LoA) approach. A LoA approach is a way of assessing agreement accuracy between two measurement methods.

Of the 413 enrolled subjects, 280 contributed data to the primary endpoint analysis to determine if the level of agreement between the reference ECG AFib burden and the feature's AFib burden estimate was acceptable. Based on the results of the study, the lower and upper Bland-Altman limits (i.e., two standard deviations from the mean difference) were -11.4% and 12.8%, respectively.

The average difference between the feature's weekly burden estimate and reference weekly burden was 0.67%. 92.9% (260/280) of subjects had paired weekly AFib burden differences within ±5%; 95.7% (268/280) of subjects' weekly AFib burden estimates were within +/- 10%.

The AFib History Feature and the Irregular rhythm Notification Feature (IRNF 2.0) use the same tachogram classification algorithm that leverages machine learning techniques to differentiate between AFib and non-AFib rhythms. The classification algorithm analyzes pulse rhythm samples collected by Apple Watch and uses a convolutional neural network based architecture. For use in the AFib History Feature the algorithm's operating point was adjusted to prioritize sensitivity. Table 4 below outlines the sensitivity and specificity of the classification algorithm for the AFib History Feature and IRNF 2.0 in the clinical validation study.

Table 4. Classification Algorithm - Clinical Validation Study Performance

	Sensitivity	Specificity
AFib History Feature	92.6%	98.8%
IRNF 2.0 (predicate)	85.5%	99.6%

These results demonstrate that the AFib History Feature is effective in generating accurate AFib burden estimates.

5.8 Human Factors Testing

The AFib History Feature was found to be safe and effective as compared to the predicate for the intended users, uses, and use environments. This conclusion is supported by iterative human factors analyses and evaluations on the Feature, resulting design modifications, and the ultimate analysis of the summative/validation testing results.

5.9 Conclusion

The AFib History Feature is substantially equivalent to IRNF 2.0 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.