DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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August 24, 2016

HeartFlow, Inc.
Windi Hary
Vice President, Clinical, Quality and Regulatory
1400 Seaport Boulevard
Building B
Redwood City, CA 94063

Re: K161772
Trade/Device Name: FFR_{CT} v2.0
Regulation Number: 21 CFR 870.1415
Regulation Name: Coronary Physiologic Simulation Software Device
Regulatory Class: Class II
Product Code: PJA
Dated: June 22, 2016
Received: June 28, 2016

Dear Windi Hary:

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. 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); good manufacturing practice requirements as set forth in

the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. 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 http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely,

Bram D. Zuckerman, M.D.
Director
Division of Cardiovascular Devices
Office of Device Evaluation
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: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K161772

Device Name
FFRct v2.0

Indications for Use *(Describe)*
HeartFlow FFRCT is a coronary physiologic simulation software for the clinical quantitative and qualitative analysis of previously acquired Computed Tomography DICOM data for clinically stable symptomatic patients with coronary artery disease. It provides FFRCT, a mathematically derived quantity, computed from simulated pressure, velocity and blood flow information obtained from a 3D computer model generated from static coronary CT images. FFRCT analysis is intended to support the functional evaluation of coronary artery disease.

The results of this analysis are provided to support qualified clinicians to aid in the evaluation and assessment of coronary arteries. The results of HeartFlow FFRCT are intended to be used by qualified clinicians in conjunction with the patient's clinical history, symptoms, and other diagnostic tests, as well as the clinician's professional judgment.

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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5.0 510(K) SUMMARY

This 510(k) summary of device performance information is submitted in accordance with the requirements of 21 CFR Part 807.87(h).

5.1 Submitter Information

Submitter / Manufacturer Name: HeartFlow, Inc.
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Date Prepared: June 22, 2016

5.2 Device Identification

Device Name:	FFR_{CT} v2.0
Device Trade Name:	FFR_{CT} v2.0
Common Name:	HeartFlow FFR_{CT}
Classification Name:	Coronary Physiologic Simulation Software Device
Product Code:	PJA
Product Class:	Class II (21 CFR 870.1415)

5.3 Predicate and Description of Change

HeartFlow FFR_{CT} v2.0 (K152733) is the identified predicate for this submission, there is no product change only a change to the indications for use.

Original K152733 cleared indications for use are below, and redlined to show the proposed changes under review. This change is supported by the same data that was submitted under the predicate 510(k).

HeartFlow FFR_{CT} is a ~~post processing~~coronary physiologic simulation software for the clinical quantitative and qualitative analysis of previously acquired Computed Tomography DICOM data for clinically stable symptomatic patients with coronary artery disease. It provides FFR_{CT}, a mathematically derived quantity, computed from simulated pressure, velocity and blood flow information obtained from a 3D computer model generated from static coronary CT images. FFR_{CT} analysis is intended to support the functional evaluation of coronary artery disease.

The results of this analysis are provided to support qualified clinicians to aid in the evaluation and assessment of coronary arteries. The results of HeartFlow FFR_{CT} are intended to be used by qualified clinicians in conjunction with the patient's clinical history, symptoms, and other diagnostic tests, as well as the clinician's professional judgment.

5.4 Device Description

FFR_{CT} v2.0 is coronary physiologic simulation software developed for the clinical quantitative and qualitative analysis of CT DICOM data. It is a tool for the analysis of CT DICOM-compliant cardiac images and data, to assess the anatomy and function of the coronary arteries.

The software displays the anatomy combined with functional information using graphics and text, including computed and derived quantities of blood flow, pressure and velocity, to aid the clinician in the assessment of coronary artery disease.

FFR_{CT} is independent of imaging equipment, imaging protocols and equipment vendors; the clinical validation report (*VOL_003 FFR_{CT} v2.0 Clinical Validation Report*) includes identification of vendors and equipment used in the clinical validation of the product. This data is summarized in the product labeling, and can be found in the Clinical User Instructions for Use (*Attachment VOL_003 Instructions for Use - Customers*). HeartFlow FFR_{CT} analyses are performed on previously physician-acquired image data and are unrelated to acquisition equipment and clinical workstations.

5.5 Intended Use

HeartFlow FFR_{CT} is a coronary physiologic simulation software for the clinical quantitative and qualitative analysis of previously acquired Computed Tomography DICOM data for clinically stable symptomatic patients with coronary artery disease. It provides $FFR_{CT,}$ a mathematically derived quantity, computed from simulated pressure, velocity and blood flow information obtained from a 3D computer model generated from static coronary CT images. FFR_{CT} analysis is intended to support the functional evaluation of coronary artery disease.

The results of this analysis are provided to support qualified clinicians to aid in the evaluation and assessment of coronary arteries. The results of HeartFlow FFR_{CT} are intended to be used by qualified clinicians in conjunction with the patient's clinical history, symptoms, and other diagnostic tests, as well as the clinician's professional judgment.

5.5.1 Contraindications

The FFR_{CT} v2.0 Customer Instructions for Use (*VOL_003 Instructions for Use – Customers*) clearly identify for which patient populations and CT scanner manufacturers the product has been clinically validated.

5.5.2 Warnings and Precautions

The warnings and precautions can be found in the FFR_{CT} v2.0 product labeling (*VOL_003 Instructions for Use – Customers*).

5.6 Technological Characteristics of Device

The HeartFlow FFR_{CT} device is a software medical device that allows for the quantitative and qualitative analysis of Coronary Computed Tomography Angiography (cCTA). This product has the same technological characteristics as the FFR_{CT} v2.0 product submitted and cleared per K152733.

5.7 Summary of Studies

The software was designed, developed, tested and validated according to written procedures. These procedures specify individuals within the organization responsible for developing and approving product specifications, coding, testing, validating and maintenance.

Validation studies included stress testing, and repeatability testing to ensure the device performance.

Software and medical device design validation was completed and reviewed as part of the predicate review (K152733). The results concluded the device was acceptable for use. The previously submitted data summarized below supports the requested change to the Indications for Use proposed under this 510(k).

5.7.1 Summary of Pre-clinical Studies

A summary of pre-clinical studies was provided and reviewed in the K152733 submission. Current submission is the same product (simply a change in indications), and no additional pre-clinical data is being provided. The previous data supports the requested change to the Indications for Use proposed under this 510(k).

5.7.2 Summary of Clinical Studies

A detailed summary of clinical studies was provided and reviewed in the K152733 submission. Current submission is the same product (simply a change in indications), and no additional clinical data is being provided. The previous data supports the requested change to the Indications for Use proposed under this 510(k). An abbreviated summary follows.

HeartFlowNXT, a prospective, multicenter, non-randomized study, provided the clinical validation for the initial device de novo clearance, FFR_{CT} v1.4 (DEN130025). The current version of software product represented in this 510(k), version 2.0, was clinically validated using the sequestered HeartFlowNXT dataset to evidence equivalence and the data was reviewed in the K152733 submission. The previously reviewed clinical validation results for 2.0 are below; detailed results can be found in *Attachments VOL_003 FFR_{CT} v2.0 Clinical Validation Report*.

Primary endpoint success required both sensitivity and specificity hypotheses to be met. The per-vessel sensitivity of FFR_{CT} in the ITD population was 84.2% with a lower one-sided 95% CI of 75.8%. As this was above the protocol specified target goal of 65%, the first null hypothesis was rejected and FFR_{CT} was considered to have met the sensitivity target goal. The per-vessel specificity of FFR_{CT} in the ITD population was 84.9%. The lower one-sided 95% CI was 80.4% and was above the protocol specified target goal of 55%, therefore the second null hypothesis was rejected and FFR_{CT} was considered to have met the specificity target goal.

Table 5-1. Primary Endpoint Analysis: Per-Vessel Sensitivity and Specificity of FFR_{CT} v2.0.2 Intent To Diagnose Population

	ESTIMATE, %	LOWER ONE-SIDED 95% CONFIDENCE BOUND	TARGET RATE	MET[1]/ NOT MET
Sensitivity	84.2%	75.8%	65%	MET
Specificity	84.9%	80.4%	55%	MET
FFR is used as the reference standard FFR_{CT}: Diseased if hemodynamically-significant obstruction is ≤ 0.80 FFR: Diseased if hemodynamically-significant obstruction is ≤ 0.80 [1]MET if 95% LCL > Target Rate				

Per-subject FFR_{CT} specificity compared to site-read cCTA demonstrated superior diagnostic ability (p<0.001) in the intent to diagnose (ITD) subjects in one or more major epicardial coronary artery segments, using invasive FFR as the reference standard and defining hemodynamically-significant obstruction of a coronary artery (positive result) as an FFR ≤ 0.80 for both FFR and FFR_{CT} and as > 50% stenosis severity for site-read cCTA. Diagnostic performance of FFR_{CT} compared to site-read

cCTA on the subject level is shown in the table below.

Table 5-2. HeartFlowNXT Per-Subject Diagnostic Performance Analysis with FFR ≤ 0.80 as the Reference Standard. Intent to Diagnose Population.

	FFR_{CT} ≤ 0.80 ESTIMATE % (95% WILSON CI)	**SITE-READ CCTA > 50% ESTIMATE % (95% WILSON CI)**
Diagnostic Accuracy	80.0% (74.4%-84.6%)	51.9% (45.5%-58.2%)
Sensitivity	87.8% (78.5%-93.5%)	93.2% (85.1%-97.1%)
Specificity	76.4% (69.3%-82.3%)	32.9% (26.1%-40.5%)
PPV	63.1% (53.5%-71.8%)	39.0% (32.1%-46.3%)
NPV	93.2% (87.5%-96.4%)	91.4% (81.4%-96.3%)

The validation study demonstrated good diagnostic performance for FFR_{CT} when all vessels were included, irrespective of size, location, or territory, and across a range of cCTA image quality measures. Further details can be found in *VOL_003 FFR_{CT} 2.0 Clinical Validation Report*.

5.8 Conclusions Drawn from Studies

5.8.1 Effectiveness Conclusions

Based on multiple studies conducted with FFR_{CT} and confirmed by clinical validation, FFR_{CT} analysis is additive to cCTA review alone by the physician when compared to an invasively measured standard. The study conclusions are not affected by the change to the Indications for Use proposed under this 510(k).

5.8.2 Safety Conclusions

Safety was not a primary objective evaluated in any study conducted by HeartFlow given the non-invasive nature of the device; FFR_{CT} is just an additional data point for consideration in patient diagnosis and treatment. Data collected in HeartFlow's studies, and commercially, has not raised any new issues related to safety of FFR_{CT}. The study conclusions are not affected by the change to the Indications for Use proposed under this 510(k).

5.8.3 Benefit-Risk Conclusions

FFR_{CT} analysis provides one additional data point to clinicians diagnosing coronary artery disease and can be performed without additional imaging, added radiation, modification of Society recommended image acquisition protocols, or administration of additional medications. The risks associated with FFR_{CT} are the same as all other non-invasive tests, a false negative or positive result. Given the increased specificity offered by FFR_{CT} over cCTA alone the benefits of using FFR_{CT} far outweigh the risks. The study conclusions are not affected by the change to the Indications for Use proposed under this 510(k).