July 18, 2025

HeartFlow, Inc.
Kristen Dejeu
Senior Manager, Regulatory and Quality Affairs
331 E. Evelyn Avenue
Mountain View, California 94041

Re: K250902
Trade/Device Name: HeartFlow Analysis
Regulation Number: 21 CFR 870.1415
Regulation Name: Coronary Vascular Physiologic Simulation Software Device
Regulatory Class: Class II
Product Code: PJA, LLZ, QIH
Dated: June 19, 2025
Received: June 20, 2025

Dear Kristen Dejeu:

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 (the 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 available 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.

FDA's substantial equivalence determination also included the review and clearance of your Predetermined Change Control Plan (PCCP). Under section 515C(b)(1) of the Act, a new premarket notification is not required for a change to a device cleared under section 510(k) of the Act, if such change is consistent with an established PCCP granted pursuant to section 515C(b)(2) of the Act. Under 21 CFR 807.81(a)(3), a new

premarket notification is required if there is a major change or modification in the intended use of a device, or if there is a change or modification in a device that could significantly affect the safety or effectiveness of the device, e.g., a significant change or modification in design, material, chemical composition, energy source, or manufacturing process. Accordingly, if deviations from the established PCCP result in a major change or modification in the intended use of the device, or result in a change or modification in the device that could significantly affect the safety or effectiveness of the device, then a new premarket notification would be required consistent with section 515C(b)(1) of the Act and 21 CFR 807.81(a)(3). Failure to submit such a premarket submission would constitute adulteration and misbranding under sections 501(f)(1)(B) and 502(o) of the Act, respectively.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

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 Part 803) for devices or postmarketing safety reporting (21 CFR Part 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 Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label and package (21 CFR 801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR 801.18. The UDI Rule (21 CFR 830.300(a) and 830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For additional information on these requirements, please see the UDI System webpage at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 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,

for

Jessica Lamb, Ph.D.
Assistant Director
Imaging Software Team
DHT8B: Division of Radiological Imaging
Devices and Electronic Products
OHT8: Office of Radiological Health
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: 07/31/2026
See PRA Statement below.

510(k) Number *(if known)*

K250902

Device Name

Heartflow Analysis

Indications for Use *(Describe)*

The Heartflow Analysis is an AI-based medical device software for the clinical quantitative and qualitative analysis of previously acquired Computed Tomography DICOM data for adult patients (ages 22 years and older) with suspected coronary artery disease. It provides anatomic data, plaque localization and characterization, as well as the calculations of FFR_{CT}, a coronary physiological simulation, computed from simulated pressure, velocity and blood flow information obtained from a 3D computer model generated from static coronary CT images. The Heartflow Analysis is intended to support the risk assessment and functional evaluation of coronary artery disease.

The Heartflow Analysis is provided to support qualified clinicians to aid in the evaluation and risk assessment of coronary artery disease. The Heartflow Analysis is 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.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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Heartflow

1. Submitter Information

Submitter / Manufacturer Name:	Heartflow, Inc. 331 E. Evelyn Ave Mountain View, CA 94041
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Date Prepared:	March 25, 2025

2. Device Identification

Product Name	Heartflow Analysis		
Product Feature Description	**Product Code**	**Classification**	**Classification Name**
FFR_{CT}	PJA (primary)	870.1415	Coronary vascular physiologic simulation software device
RoadMap™ Analysis	LLZ (secondary)	892.2050	Medical image management and processing system
Plaque Analysis	QIH (secondary)	892.2050	Medical image management and processing system
Planner	PJA (secondary)	870.1415	Coronary vascular physiologic simulation software device

3. Predicates

This submission leverages Heartflow Analysis (K213857) as the primary predicate and Autoplaque (K122429) as an additional predicate, for validation of the plaque feature.

4. Device Description

The Heartflow Analysis is an AI-based medical device 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 in the risk stratification and evaluation of coronary artery disease.

The software displays coronary anatomy and functional information using graphics and text, including computed and derived quantities of percent stenosis, plaque volumes, blood flow, pressure and velocity, to aid the clinician in the assessment and treatment planning of coronary artery disease.

The Heartflow Analysis is performed on previously physician-acquired image data and is unrelated to acquisition equipment and clinical workstations.

5. Indications for Use

The Heartflow Analysis is an AI-based medical device software for the clinical quantitative and qualitative analysis of previously acquired Computed Tomography DICOM data for adult patients (ages 22 years and older) with suspected coronary artery disease. It provides anatomic data, plaque localization and characterization, as well as the calculations of FFR_{CT}, a coronary physiological simulation, computed from simulated pressure, velocity and blood flow information obtained from a 3D computer model generated from static coronary CT images. The Heartflow Analysis is intended to support the risk assessment and functional evaluation of coronary artery disease.

The Heartflow Analysis is provided to support qualified clinicians to aid in the evaluation and risk assessment of coronary artery disease. The Heartflow Analysis is 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.

6. Technological Characteristics of Device

The Heartflow Analysis is a software medical device that allows for the quantitative and qualitative analysis of Coronary Computed Tomography Angiography (cCTA). The predicates and this product have the same technological characteristics.

The core technology remains unchanged from the primary predicate and continues to be trained using deep learning (AI and machine learning) since 2015, to incorporate learnings from the volumes of CT data and studies. All algorithms are then frozen and validated prior to product

release. There are no significant differences between the subject device and the predicate with respect to the intended use. The revised indications for use clarifies the patient population to be adult patients ages 22 years and older.

6.1 Algorithm Updates

Heartflow is writing this 510(k) submission to propose the implementation of changes to the Heartflow Analysis device. The subject device with updated plaque algorithm has been modified as part of this premarket submission. These changes include a retrained and validated plaque analysis algorithm, additional plaque visualization and quantification capabilities, and automation of internal quality controls functions.

Table 1. Predicate Device Comparison: Heartflow Analysis (K213857) vs. Heartflow Analysis (K250902)

	Heartflow Analysis	**Heartflow Analysis**
510(k)	K213857	K250902
Manufacturer	HeartFlow, Inc.	HeartFlow, Inc.
Version	3.18	4.0
Regulation Number	870.1415	870.1415
Regulation Name	Coronary Physiologic Simulation Software Device	Coronary Physiologic Simulation Software Device
Classification	Class II	Class II
Device Common Name	Heartflow Analysis	Heartflow Analysis
Product Code	• FFRCT: PJA (primary) • RoadMapTM Analysis: LLZ (secondary) • Plaque Analysis: LLZ (secondary) • Planner: PJA (secondary)	• FFRCT: PJA (primary) • RoadMapTM Analysis: LLZ (secondary) • Plaque Analysis: **QIH** (secondary) • Planner: PJA (secondary)
Functions	• Extract anatomical and plaque data from digital cardiac images for the display and visualization of the anatomy of patient's coronary arteries • Compute FFR_{CT}	• Extract anatomical and plaque data from digital cardiac images for the display and visualization of the anatomy of patient's coronary arteries • Compute FFR_{CT}
Intended Use	• Review of CT angiographic images to confirm the coronary vessels • Semi-automated tools for extraction of anatomic data (including heart structures) for coronary physiologic simulation to aid in diagnosis of coronary artery disease • Centerline detection • Provide additional data derived from coronary CT anatomy and pathology • Provide simulated hemodynamic information	• Review of CT angiographic images to confirm the coronary vessels • Semi-automated tools for extraction of anatomic data (including heart structures) for coronary physiologic simulation to aid in diagnosis of coronary artery disease • Centerline detection • Provide additional data derived from coronary CT anatomy and pathology • Provide simulated hemodynamic information
Data Source	CT	CT

Output/Accessibility	Graphic and text results of coronary anatomy and simulated data are accessed via a device with internet connectivity	Graphic and text results of coronary anatomy and simulated data are accessed via a device with internet connectivity
Physical Characteristics	Non-invasive software package DICOM compatible	Non-invasive software package DICOM compatible
Safety	Clinician review and assessment of analysis prior to use as supplemental diagnostic aid	Clinician review and assessment of analysis prior to use as supplemental diagnostic aid
Features	• Presentation of CT images for confirmation of extracted model • Automatic extraction of anatomic data from CT images for analysis • Modeled stenosis and plaque* information • Volume rendering based on centerlines • Automatic/semi-automatic lumen boundary determination • Annotate, tag, measure, and record selected views • View the coronary vessels • Modify anatomic model to remove luminal narrowing(s) • Expose interim calculations used as input of FFRCT (e.g., mass and volume) • Calculate functional parameters of the heart (e.g., Fractional Flow Reserve, %myo) • Visualize plaque* information • Graphic and text results	• Presentation of CT images for confirmation of extracted model • Automatic extraction of anatomic data from CT images for analysis **• Modeled stenosis and plaque** information** • Volume rendering based on centerlines • Automatic/semi-automatic lumen boundary determination • Annotate, tag, measure, and record selected views • View the coronary vessels • Modify anatomic model to remove luminal narrowing(s) • Expose interim calculations used as input of FFRCT (e.g., mass and volume) • Calculate functional parameters of the heart (e.g., Fractional Flow Reserve, %myo) **• Visualize plaque** information** • Graphic and text results

*Anatomical plaque calculation and visualization is supported by comparison to the Autoplaque reference device leveraged in K213857

****Anatomical plaque calculation and visualization is supported by direct CT Reader segmentation and annotation, which is new ground truthing compared to the predicate**

Table 2. Predicate Device Feature Comparison

Feature	Heartflow Analysis (primary predicate)	Heartflow Analysis (subject)
Presentation of CT images for confirmation of extracted model	x	x
Automatic extraction of anatomic data from CT images for analysis	x	x
Modeled stenosis and plaque* information	x	x
Volume rendering based on centerlines	x	x
Automatic / Semi-automatic lumen boundary determination	x	x

Annotate, tag, measure, and record selected views	x	x
View the coronary vessels	x	x
Modify anatomic model to remove luminal narrowing(s)	x	x
Expose interim calculations used as input of FFR_{CT} (e.g., mass and volume)	x	x
Calculate functional parameters of the heart (e.g., Fractional Flow Reserve, %myo)	x	x
Visualize plaque information*	x	x
Case-level and vessel-level plaque localization	x	x
Lesion-level plaque localization		x
Graphic and text results	x	x

*Anatomical plaque calculation and visualization is supported by comparison to the Autoplaque predicate device for Heartflow Analysis predicate. Anatomical plaque calculation and visualization is supported by direct CT Reader segmentation and annotation for the subject device.

7. Summary of Performance Data

Validation of the proposed deep learning algorithm was conducted to assess plaque localization and quantification performance against clinician annotations on the following endpoints at the point-wise and region-of-interest (ROI) levels: sensitivity, precision, and mean volume error difference.

Heartflow established ground truth for the validation dataset by applying the plaque annotations as a mask over the segmentations, where both annotation and segmentation datapoints were collected from expert physicians. This approach excluded the non-overlapping sub-regions from the plaque localization and quantification primary endpoints. This method ensured objective plaque localization and quantification assessment only for regions truthed for plaque location and plaque volume to be able to compare Heartflow Analysis (subject) plaque algorithm and Heartflow Analysis (predicate) plaque algorithm in an objective manner.

Following the process above, 60,555 unique ground truth areas (583 unique lesions from 100 distinct patients) were established on CT DICOM images to calculate the co-primary endpoints for localization and quantification.

The validation dataset consisted of previously completed commercial cases that are maintained in a restricted library solely used for validation testing. The restricted library aims to prevent any cases intended for validation testing, to be accidentally used for training or development purposes. The validation dataset was also stratified by the following confounders: patient age,

patient sex, image quality, scanner type, plaque type, number of ROI per case, ROI length in millimeters, total plaque volume in millimeters cube, branch type, and vessel location.

To accurately represent the commercial population, cases from various scanner manufacturers were used to create the validation dataset. Table 3 lists the scanner manufacturers represented in the case list and the percentage of images represented by each manufacturer. Refer to Tables 4-6 for a breakdown of the validation dataset's distribution of patient gender, age, and geographic location, respectively,

Table 3: Performance Assessment Dataset Scanner Manufacturer Distribution

Manufacturer	Population Percentage	Test Set Percentage Target
Siemens	52%	52%
GE Medical Systems	27%	26%
Toshiba	6.6%	6%
Philips	6%	6%
Canon Medical Systems	5%	6%
Siemens Healthineers	3%	4%
Fujifilm, Hitachi	<1%	0%

Table 4: Performance Assessment Dataset Patient Age Distribution

Age Range	Population Percentage	Test Set Percentage
<22	<1%	0%
22-29	1%	2%
30-39	4%	4%
40-49	11%	10%
50-59	22%	22%
60-69	32%	31%
70-79	24%	25%
80-89	6%	6%
>89	<1%	0%

Table 5: Performance Assessment Dataset Patient Sex Distribution

Sex	Population Percentage	Test Set Percentage Target
Male	50%	50%
Female	50%	50%

Validation data was comprised of 67 different institutions across the United States as outlined per state distribution in Table 6.

Table 6: Performance Assessment Dataset Geographic Distribution

Geographic Location (by State)	Population Percentage	Test Set Percentage Target
Alabama	<1%	1%
Arizona	2%	1%
Arkansas	1%	1%
California	9%	12%
Colorado	3%	3%
Florida	5%	7%
Georgia	4%	1%
Illinois	6%	11%
Indiana	2%	1%
Iowa	<1%	1%
Kentucky	2%	1%
Louisiana	<1%	1%
Maine	<1%	1%
Michigan	3%	1%
Minnesota	1%	3%
Mississippi	<1%	3%
Missouri	1%	1%
New Jersey	5%	2%

New York	14%	4%
North Carolina	6%	5%
Ohio	2%	4%
Pennsylvania	4%	4%
Tennessee	4%	7%
Texas	9%	11%
Washington	1%	1%
West Virginia	2%	3%
Wisconsin	2%	6%

Heartflow Analysis (subject) plaque algorithm's plaque localization sensitivity superiority compared to Heartflow Analysis (predicate) plaque algorithm at point-wise level sensitivity was 0.151 (Goal > 0, $p<0.0001$). Heartflow Analysis (subject) plaque algorithm's plaque localization performance measured with point-wise level DICE similarity coefficient was 0.8 (Goal > 0.7, $p<0.0001$), compared to Heartflow Analysis (predicate) plaque algorithm's DICE similarity coefficient of 0.8. Heartflow Analysis (predicate) and Heartflow Analysis (subject) plaque quantification mean volume error difference at region-of-interest level was 8.1mm^3 (Goal=0 mm^3, $p<0.0001$). The performance assessment results indicate that the HeartFlow Analysis (subject) algorithm demonstrated statistically significant improved sensitivity in correctly detecting plaque locations across all regions and plaque types while maintaining a similar DICE coefficient score, when compared to the HeartFlow Analysis (predicate) algorithm performance on the same validation dataset. In addition to plaque localization, HeartFlow Analysis (subject) algorithm also demonstrated statistically significant improved plaque quantification with less volume error across all regions and plaque types.

Overall, HeartFlow Analysis (subject) algorithm met all acceptance criteria and demonstrated improvement in the areas of sensitivity and volume error measurements when compared to the plaque localization and quantification algorithm that was cleared in the primary predicate, K213857.

8. Cybersecurity

Heartflow has instituted cybersecurity controls to maintain the safety and security of the Heartflow Analysis. Study transmission is accomplished using Heartflow Connect or a third-party DICOM transfer device. This enables secure and reliable transmission of CT data. Heartflow assesses real and perceived cybersecurity vulnerabilities and uses specific software testing tools to ensure that the device remains safe and effective. Software de-bugging occurs on a nearly

monthly basis to ensure that issues are resolved quickly, and issues are triaged in accordance with the level of risk associated with them.

9. 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 safety and effectiveness of the device. Software and medical device design validation has been completed. Medical device design included testing and evaluation using previously acquired diagnostic images received through Heartflow sponsored clinical trials.

Summaries of pre-clinical studies were reviewed as part of a prior predicate review (K161772, the original predicate of K182035, K190925, and K203329). The results concluded the device was acceptable for use.

Results of all current and previously referenced testing conclude the device is acceptable for use.

10. Summary of Predetermined Change Control Plan (PCCP)

The Heartflow Analysis PCCP outlines three planned modifications to improve coronary plaque detection generalizability without requiring additional FDA submissions. These include (1) optimizing training parameters to account for new training data, (2) incorporating 3D spatial context as a new input, and (3) fine-tuning post processing parameters for specific complex regions defined in the protocol. Each proposed change will be implemented according to a thorough modification protocol and must satisfy rigorous performance standards. This includes demonstrating non-inferiority to the original model within defined limits for plaque detection sensitivity and volume error; additionally, the DICE score must remain above the acceptable lower limit of 0.7. Established performance assessment and validation protocols will be used, with modifications implemented incrementally to minimize risk. Acceptance criteria must be fulfilled before any model update.

All authorized modifications made under the PCCP will be documented and included in the device's labeling as the modifications are released. User communication will follow standard software release procedures in accordance with Heartflow's quality management system. Specifically, Heartflow currently identifies version updates via the "What's New" section of the Instructions for Use which includes detailed summaries of the changes within each version.

11. Substantial Equivalence Discussion

The subject device Heartflow Analysis has a similar intended use (with a clarification on patient population age and inclusion of plaque "localization" in lieu of "identification") and identical operating principles with similar technological characteristics as the previously cleared Heartflow

Analysis. The subject device introduces modifications to the plaque analysis algorithm through retraining and validation. In addition, there are new plaque visualization and quantification capabilities. These modifications were fully validated and evaluated through Heartflow's risk assessment processes. It was concluded that the proposed modifications do not raise new questions of safety and effectiveness.

Additionally, the changes posed in the Predetermined Change Control Plan will undergo specific software testing to ensure that the performance of the device is not negatively affected by the modifications. The proposed changes to the algorithm are intended to strengthen the performance of the existing plaque algorithm through training parameter optimization and post-processing parameter refinement. These changes do not negatively impact the safety or effectiveness of the device per its intended use.

12. Conclusion

The conclusions drawn from the testing demonstrate that the device is as safe, as effective, and performs as well as the legally marketed devices identified in Section 6 above.