August 26, 2026

Heartvue.ai, Inc.
% Mary Vater
Director of Regulatory Affairs
Innolitics, LLC
1101 W. 34th St. #550
Austin, Texas 78705

Re: K260811
Trade/Device Name: Heartvue.Proton
Regulation Number: 21 CFR 892.2050
Regulation Name: Medical Image Management And Processing System
Regulatory Class: Class II
Product Code: QIH, LLZ
Dated: July 31, 2026
Received: July 31, 2026

Dear Mary Vater:

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 Management System Regulation (QMSR) (21 CFR Part 820), which includes, but is not limited to, ISO 13485 clause 7.3 (Design controls), ISO 13485 clause 8.3 (Nonconforming product), ISO 13485 clause 8.5.2 (Corrective action), and ISO 13485 clause 8.5.3 (Preventative action). Please note that regardless of whether a change requires premarket review, the QMSR requires device manufacturers to review and approve changes to device design and production (ISO 13485 clause 7.3 and ISO 13485 clause 7.5) and document changes and approvals in the Medical Device File (ISO 13485 clause 4.2.3).

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 Management System Regulation (QMSR) (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)*
K260811

Device Name
Heartvue.Proton

Indications for Use *(Describe)*
Heartvue.Proton is indicated for use in clinical settings where quantified results are needed to support the visualization and analysis of MR images of the heart and blood vessels for use on individual patients with cardiovascular disease. When the quantified results provided by Heartvue.Proton are used in a clinical setting on MR images of an individual patient, they can be used to support the clinical decision making for the diagnosis of the patient. In this case, the results are explicitly not to be regarded as the sole, irrefutable basis for clinical diagnosis, and they are only intended for use by the responsible clinicians.

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

Device: Heartvue.Proton

510(k) Number: K260811

Prepared on: August 25, 2026

1. Contact Details

Applicant

Applicant Name	Heartvue.AI Inc.
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Correspondent

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Contact	Mrs. Mary Vater
Email	fda@innolitics.com

2. Device Name and Classification

Device Trade Name	Heartvue.Proton
Common Name	Automated Radiological Image Processing Software
Classification Name	Medical image management and processing system
Regulation Number	21 CFR 892.2050

Product Code(s)	QIH, LLZ
Regulatory Class	Class II
Review Panel	Radiology

3. Predicate Device

Predicate Device Name	Medis Suite MR-CT VVA
Manufacturer	Medis Medical Imaging Systems BV
510(k) Number	K140587
Product Code	LLZ
Regulation Number	21 CFR 892.2050
Regulation Name	Radiological Image Processing System
Regulatory Class	Class II
Review Panel	Radiology

4. Device Description Summary

Heartvue.Proton is a software-only medical device that provides semi-automated radiological image processing and quantitative analysis of cardiac MRI studies. The software generates reproducible cardiac measurements that support physicians in visualizing and assessing cardiac structure and function in patients with known or suspected cardiovascular disease.

Heartvue.Proton operates as a web-based application with cloud-hosted services for data transfer, processing, and secure storage. MRI studies are received through configured PACS integrations. After upload, the software prepares the data and applies machine learning algorithms that segment cardiac anatomy and derive quantitative metrics. Post-processing workflows compute a set of standard cardiac measurements.

The software displays processed images and measurement results through a secure web interface for use by qualified healthcare professionals. Heartvue.Proton is

intended for adult patients 18 – 89 years of age who have undergone cardiac MRI imaging and does not directly interact with patients or imaging hardware.

The device comprises 25 machine learning models organized across 8 processing pipelines that together produce 48 quantitative cardiac measurements (both directly measured and derived). The machine learning models generate three output types: (1) slice-index selection within an acquisition; (2) user-editable segmentation masks that are displayed to the user and from which downstream measurements are recomputed; and (3) localization masks used to derive measurement endpoints that are not surfaced for direct editing. All automated measurements can be reviewed and edited by the interpreting clinician.

Heartvue.Proton also includes a suggestive grading feature that pre-populates measurement grades (e.g., "normal" or "abnormal") based on fixed normative reference ranges drawn from peer-reviewed medical literature; the interpreting physician may override any assigned grade. This feature is a non-device clinical decision support function and is not diagnostic.

5. Indications for Use

Subject Device Indications for Use

Heartvue.Proton is indicated for use in clinical settings where quantified results are needed to support the visualization and analysis of MR images of the heart and blood vessels for use on individual patients with cardiovascular disease. When the quantified results provided by Heartvue.Proton are used in a clinical setting on MR images of an individual patient, they can be used to support the clinical decision making for the diagnosis of the patient. In this case, the results are explicitly not to be regarded as the sole, irrefutable basis for clinical diagnosis, and they are only intended for use by the responsible clinicians.

Indications for Use Equivalence Discussion

The differences between Heartvue.Proton and the predicate device do not constitute a new intended use because both devices share the same fundamental purpose: providing quantitative measurements from cardiac MR images to support clinician interpretation for patients with cardiovascular disease. As with the predicate, the results are supportive, not determinative, and intended solely for use by qualified

clinicians. The added features, such as automated measurements and suggestive grading, are workflow-enhancing technological differences that do not alter the device's clinical role and are addressed through performance validation. Therefore, the indications remain aligned with the predicate, and no new intended use is created.

6. Summary of Technological Characteristics

The primary technological difference between the subject device and the predicate is that Heartvue.Proton employs automated, machine-learning–based measurement tools, while the predicate performs these measurements manually. Despite this implementation difference, both devices operate using the same underlying measurement principles and generate the same types of quantitative cardiac MR outputs. The automated measurements in the subject device have been evaluated through performance testing that demonstrates their accuracy and consistency relative to manually derived measurements. In addition, all automated results can be reviewed and edited by the user, ensuring that clinical oversight is maintained. These validated and editable automated functions do not introduce new questions of safety or effectiveness and are consistent with the predicate device's established technological approach.

Substantial Equivalence Comparison Table

The following table compares the technological characteristics of the subject and predicate devices.

Feature or Characteristic	Subject Device	Predicate	Comments on SE
Device Name	Heartvue.Proton	Medis Suite MR-CT VVA	NA
Technology / Principle of Operation	SaMD	SaMD	Same
Stand-Alone Application	Yes	Yes	Same
Intended User	Cardiac Physician	Cardiac Physician	Same

Feature or Characteristic	Subject Device	Predicate	Comments on SE
Intended Use Environment	PACS & EHR Viewer	PACS & EHR Viewer	Same
Indications for Use	Heartvue.Proton is indicated for use in clinical settings where quantified results are needed to support the visualization and analysis of MR images of the heart and blood vessels for use on individual patients with cardiovascular disease. When the quantified results provided by Heartvue.Proton are used in a clinical setting on MR images of an individual patient, they can be used to support the clinical decision making for the diagnosis of the patient. In this case, the results are explicitly not to be regarded as the sole, irrefutable basis for clinical diagnosis, and they are only intended for use by the responsible clinicians.	MR-CT VVA is indicated for use in clinical settings where more reproducible than manually derived quantified results are needed to support the visualization and analysis of MR and CT images of the heart and blood vessels for use on individual patients with cardiovascular disease. Further, MR-CT VVA allows the quantification of T2* in MR images of the heart and the liver. Finally, MR-CT VVA can be used for the quantification of cerebral spinal fluid in MR velocity-encoded flow images. When the quantified results provided by MR-CT VVA are used in a clinical setting on MR and CT images of an individual patient, they can be used to support the clinical decision making for the diagnosis of the patient. In this case, the results are explicitly not to be regarded as the sole, irrefutable basis for clinical diagnosis, and they are only intended for use by the responsible clinicians.	Similar (Subject device not indicated for CT or Liver)

Feature or Characteristic	Subject Device	Predicate	Comments on SE
Input	MRI only	MRI & CT	Similar (Subject device is MRI only)
Types of Images	MRI T1, T2, T2*	MRI T1, T2, T2*	Same
Post-Processing MR Images of Heart	Yes	Yes	Same
2D Linear Measurement	Yes	Yes	Same
3D Volume Calculation	Yes	Yes	Same
Flow Calculation	Yes	Yes	Same
Results Can Be Edited?	Yes	Yes	Same
Output Format	PDF Report	PDF Report	Same
Technological Characteristic	ML Automation of Measurements	Manual Measurements	Difference is validated in performance testing

Feature or Characteristic	Subject Device	Predicate	Comments on SE
Suggestive Grading Feature	Yes – for certain measurements	No	This is a feature for convenience which is not diagnostic. It is a Non-Device Clinical Decision Support tool. The output of the grading determination is based on established and published medical information sources.

7. Performance Data — Nonclinical and Clinical Tests

7.1 Software Verification and Validation Testing

Software verification testing (unit, integration, and system level) and software validation testing were conducted in accordance with the FDA guidance "Content of Premarket Submissions for Device Software Functions" (2023). These activities verified that all design requirements were successfully met and validated that the device fulfills its intended use and user needs.

7.2 Nonclinical (Bench) Performance Testing

Performance testing was conducted across the device's three analysis modules — Two-Dimensional Measurement, Flow Measurement, and Volumetric Measurement — and across the eight measurement-specific evaluation pipelines (2CH End-Systolic, 4CH End-Systolic, IVC Slice, LVOT, PA Bifurcation Slice, Aortic Flow, Pulmonic Flow, and SAX Cine) to demonstrate that the automated ML-based measurements perform comparably to manually derived measurements. A comparative time-efficiency evaluation was also conducted.

- **Two-Dimensional Measurement Module:** Evaluated automated 2D linear measurements across four MR image views (Axial, LVOT, 4CH, 2CH). Primary evaluation metrics included slice localization error (mm), length error (mm), and area error (cm^2), each with pre-specified acceptability targets.
- **Flow Measurement Module:** Evaluated automated flow measurements of cardiac structures, including aortic flow and pulmonary artery flow.
- **Volumetric Measurement Module:** Evaluated automated 3D volume measurements of cardiac structures, including LVEDV, LVESV, LV mass, RVEDV, and RVESV.
- **Comparative Time-Efficiency Study:** Measured and compared the time required for automated measurements produced by Heartvue.Proton versus manual measurements.

7.3 Clinical Performance Evaluation

The clinical performance evaluation assessed standalone device performance by comparing the device's automated ML-based measurements against a reference standard. Measurement accuracy, expressed as Mean Absolute Error (MAE), was the primary endpoint; segmentation quality, expressed as the Dice similarity coefficient, is an additional acceptance criterion for segmentation-producing models, evaluated against a pre-specified threshold.

The clinical performance evaluation dataset was acquired on the following scanner models: Siemens MAGNETOM Avanto Fit, GE Signa HDxt, and Siemens MAGNETOM Vida. The dataset spanned one field strength (1.5T). Device performance has been validated for cardiac MRI images acquired at 1.5T. Acquisitions at 3.0T fall outside the validated range of the device. Subgroup performance analyses stratified by manufacturer, scanner model, and clinical site demonstrate that measurement accuracy meets the pre-specified acceptance criteria across this acquisition variability.

Acceptance Criteria and Clinical Basis

Acceptance criteria were established for each measurement type based on (1) published inter-observer variability for expert manual cardiac MRI measurements, ensuring the device performs within the range of trained human readers, and (2)

clinical decision thresholds relevant to the intended use, confirming that the maximum allowable error does not adversely affect correct clinical management.

Measurement Type	Acceptance Criterion	Basis for Acceptance Criterion
Linear dimensions	MAE ≤ 3 mm	Within published CMR inter-observer variability (2–4 mm) and conservative relative to clinical thresholds for structural remodeling.
Area	MAE ≤ 5 cm^2	Represents < 5% of typical measured areas; does not materially affect derived hemodynamic parameters such as stroke volume or valve area.
Volume	MAE ≤ 15 mL	Within expert inter-observer variability (7–12 mL); produces < 7% ejection-fraction change at typical LV volumes and preserves EF classification boundaries (35%, 50%).
Mass	MAE ≤ 20 g	Comparable to expert inter-reader disagreement (10–15 g); preserves LV hypertrophy classification margins.
Flow volume	MAE ≤ 10 mL/cycle	Within phase-contrast CMR inter-observer variability (5–10 mL/cycle); unlikely to alter regurgitation severity classification.
Frame index	MAE ≤ 2 frames	Corresponds to ~50–80 ms; resulting volume perturbation is well within the 15 mL volume criterion.
Segmentation (Dice)	Mean Dice ≥ 0.75	Lower bound of the 95% confidence interval of the lowest-performing segmentation output in the validation cohort. Applied as an independent acceptance criterion in addition to MAE, which remains the primary clinical endpoint. Modifications under the PCCP are subject to additional per-cycle and cumulative Dice conditions per FRM-ML-01.

Results

All primary clinical measurement endpoints met their pre-specified MAE acceptance criteria across all eight pipelines, with no deviations from the evaluation plans. All segmentation outputs met the Dice acceptance criterion.

The comparative time-efficiency study showed that Heartvue.Proton reduced measurement time by a factor of 4.74× on average relative to manual measurement.

Reference Standard

The reference standard (ground truth) for the clinical performance evaluation was established by the consensus of at least three board-certified cardiologists with greater than 5 years expertise in cardiac MRI interpretation. Annotators worked exclusively from raw cardiac MR images while blinded to the device output, following published Society for Cardiovascular Magnetic Resonance (SCMR) guidelines for cardiac structure delineation. Each case was annotated independently and then reconciled through a structured consensus process requiring unanimous agreement among the assigned readers before the reference standard was finalized.

8. Predetermined Change Control Plan (PCCP)

This 510(k) includes an authorized Predetermined Change Control Plan (PCCP) that prospectively specifies certain modifications to the device's machine learning models, the methods used to develop and validate those modifications, the performance requirements that must be met before they are implemented, and the means by which users will be informed. Consistent with FDA's PCCP guidance.

8.1 Planned Modifications

The PCCP authorizes two categories of modification, both implemented in a homogeneous, global manner across all deployed instances of the device. No site-specific or per-installation model variants are contemplated.

- **MOD-1 (Retraining):** retraining of existing machine learning models on expanded or refreshed data to maintain or improve performance and generalizability.
- **MOD-2 (Rearchitecting):** changes to a model's underlying architecture, including consolidation of multiple models within a pipeline, while preserving

the device's inputs, outputs, intended use, and clinical workflow. Architectural changes are bound to a single, pre-specified class of model architectures.

8.2 Testing Methods, Validation Activities, and Performance Requirements

Before any modification is implemented, it is verified and validated against the established performance baseline and must meet pre-defined acceptance criteria that are at least equivalent to the cleared device. The validation framework includes:

- Performance validation: statistical non-inferiority testing against pre-specified acceptance criteria and margins for each measurement type.
- Segmentation quality: mean Dice evaluated for every segmentation output against a pre-specified acceptance threshold, with additional limits on change relative to the immediately preceding version and to the originally cleared baseline.
- Modification-specific requirements: acceptance criteria scaled to the type and risk of the modification, with more rigorous requirements applied to architectural changes.
- Adequate sampling: pre-specified, adequately powered sample sizes determined before data collection.
- Subgroup performance: evaluation across relevant demographic, clinical, and acquisition subgroups against pre-defined acceptable variation limits.
- Safety margins: performance required to remain within a conservative margin of the acceptance criteria.
- Data management controls: controls on the use and refresh of training, validation, and test data to limit overfitting and data leakage.
- Post-market monitoring: ongoing performance surveillance with pre-defined criteria that may trigger model review, rollback, or retraining.

8.3 Means of Informing Users

Modifications implemented under the authorized PCCP will be communicated to users through updated device labeling (including revisions to the Instructions for

Use) and accompanying release documentation that identify the modification implemented and the device version in use.

9. Conclusion

Heartvue.Proton shares similar technological characteristics, intended use, and functionality with the predicate device. There are no differences between the devices that raise new questions of safety and effectiveness.

Furthermore, non-clinical performance test data and software verification and validation demonstrate that Heartvue.Proton performs comparably to the predicate device in terms of safety and effectiveness.

Based on the device comparisons and the acceptable testing results, Heartvue.Proton is determined to be substantially equivalent to the predicate device.